

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

Standard Operating Policy/Procedure

Compliance Policy for Issuing Regulatory Actions

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Compliance Policy for Issuing Regulatory Actions

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Compliance Policy for Issuing Regulatory Actions

1. Purpose

This document describes the policy for issuing regulatory actions under the authorities of title 9, *Code of Federal Regulations* (9 CFR), parts 105.1(b), 105.2 and 105.3.

2. Background – Infraction

An infraction is considered a violation of the law falling under the administrative law legal category. An infraction is an intentional or unintentional breach from the requirements. Any violation of the Virus-Serum-Toxin Act or 9 CFR could be ruled as an infraction. Whereas any violation of the rules and regulations could be considered an infraction, the Center for Veterinary Biologics-Inspection and Compliance (CVB-IC) must use its scientific judgment and regulatory discretion to evaluate how each violation has or may affect, either directly or indirectly, the purity, safety, potency or efficacy of the veterinary biological product throughout the shelf life (expiration dating) of the product.

The January 18, 2011, Presidential Memorandum regarding Regulatory Compliance directs Agencies on how they should view regulatory compliance.

*Greater disclosure of regulatory compliance information fosters fair and consistent enforcement of important regulatory obligations. Such disclosure is a critical step in encouraging the public to hold the Government and regulated entities accountable. Sound regulatory enforcement promotes the welfare of Americans in many ways, by increasing public safety, improving working conditions, and protecting the air we breathe and the water we drink. **Consistent regulatory enforcement also levels the playing field among regulated entities, ensuring that those that fail to comply with the law do not have an unfair advantage over their law-abiding competitors.** Greater agency disclosure of compliance and enforcement data will provide Americans with information they need to make informed decisions. Such disclosure can lead the Government to hold itself more accountable, encouraging agencies to identify and address enforcement gaps.*

The Memorandum further directs Agencies to formulate the disclosure of such regulatory actions. *Agencies with broad regulatory compliance and administrative enforcement responsibilities... to the extent feasible and permitted by law, shall develop plans to make public information concerning their regulatory compliance and enforcement activities accessible, downloadable, and searchable online.*

9 CFR 105.2 describes the authority to notify the licensee of an infraction of a requirement of a product license.

- a. **Two elements must be substantiated:**
 - i. The infraction as it relates to the Product Code (product license).
 - ii. The part, and if applicable, section of 9 CFR that was violated.

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- b. Notification to the licensee/permittee
 - i. An infraction is written after all the evidence is gathered; there is no timeline on infractions. Other regulatory actions may be needed prior to the infraction to address the issue.
 - ii. Only the Compliance Section Leader or Compliance Manager or another IC Sectional Leader or Director may sign an Infraction Notice Letter according to the delegation of authority, **ICSOP0001**, *Delegation of Authority for Center for Veterinary Biologics-Inspection and Compliance*.

The CVB usually becomes aware of an infraction by:

- c. The firm notifies CVB of the violation.
- d. The CVB discovers the violation.
 - i. Through review of correspondence.
 - ii. Through inspection activities.
 - iii. Through Pharmacovigilance activities.

Background – Market Suspension

9 CFR 105.3 describes the process CVB will use to informally suspend an establishment license, product license, or permit.

9 CFR 105.3: *If at any time it appears that the preparation, sale, barter, exchange, shipment, or importation, as provided in the Virus-Serum-Toxin Act, of any biological product by any person holding a license or permit may be dangerous in the treatment of domestic animals, the Secretary may without hearing notify the licensee or permittee.....*

Also, a product may be found to be *worthless, contaminated, dangerous or harmful* if:

1. The construction of the establishment in which the biological product is prepared is defective, or the establishment is not conducted as required by the regulations in 9 CFR 101 through 118.
2. The methods of preparation of the product are faulty, or the product contains impurities or lacks potency.
3. The product is labeled or advertised as to mislead or deceive the purchaser in any particular.
4. The licensee, permittee, or the foreign manufacturer has failed:
 - a. To maintain and make available for inspection, records in connection with the development and preparation of product, or has failed to provide complete and accurate information when requested.

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- b. Has failed to provide complete and accurate information in the Outline of Production, or in reports and records.
5. The licensee or permittee has violated or failed to comply with any provision of the Virus-Serum-Toxin Act or the regulations.
6. The license or permit is otherwise used to facilitate or effect the preparation, sale, barter, exchange, shipment, or importation, contrary to the Virus-Serum-Toxin Act, of any worthless, contaminated, dangerous, or harmful biological product.
7. As described in Veterinary Services Memorandum No. 800.57, any product not made according to the filed Outline of Production may be worthless, contaminated, dangerous or harmful. A product not made according to the Outline of Production, or Special Outline, is considered worthless and harmful, and may be contaminated or dangerous until proven otherwise.

NOTE: "Harmful" is interpreted by the CVB to be harmful to the animal OR harmful to the environment OR to the general public interest or welfare.

3. Regulatory Action

- I. All violations must be assessed to determine severity and risk. All violations may affect the quality of the product and the control of the manufacturing processes and the facilities.
- II. Previous violations in relationship to the current matter must be evaluated.
 - a. Certain aspects of the previous violation contribute to the final decision regarding the current violation.
 - b. Any previous violation or regulatory action, whether the action was initiated by the firm (Voluntary Stop Distribution and Sale) or by the CVB is an indicator of a lapse of control in the manufacturing process and may have affected, directly or indirectly, the quality of the products or products manufactured.
 - c. Some of the factors that contribute to escalating the type of regulatory action:
 - i. A similar violation within the past three years.
 - ii. A similar violation within the same manufacturing area in the last three years.
 - iii. A similar violation regarding the control of the production process.

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iv. A similar violation regarding the quality assurance process.

III. There are three types of violations.

a. Minor

- i. Minor violations, when assessed accurately are likely to have minimal risk to product quality. Thus having a minimal chance of affecting the quality of the product. This type of violation may also indicate laxity or error in manufacturing control that could become more serious if not corrected.
- ii. If numerous minor violations are noted during an inspection, during an investigation, or other avenue, it is indicative of poor management, lack of manufacturing control and should be considered as having a cumulative effect and be of a higher risk.
- iii. A *Letter of Advice* may be imposed.
- iv. Examples:
 1. Minimal non critical record keeping error or errors (part 116) – *Letter of Advice*
 2. The submission of an incorrect serial number on the APHIS Form 2008 subsequently identified by the firm prior to distribution of the product (part 116) – *Letter of Advice*

b. Less Serious

- i. Less serious violations, by repetition or very nature, may affect the quality of a product, numerous products or manufacturing processes.
- ii. These violations may require further evaluation before the final regulatory action is taken by the CVB.
- iii. Holding release of serials or products through a *Hold Release* may be required.
- iv. A *Letter of Advice* or *Infraction Notice* may be imposed.
- v. Examples
 1. Expiration of Reference prior to use for serial release testing (future serials) – *Hold Release*
 2. First violation of a non-critical nature with the appropriate root cause and corrective action identified

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3. Multiple record keeping errors throughout the manufacturing (part 116) – *Infraction*
4. An APHIS Form 2008 has been submitted to the CVB for consideration for release of a serial and the firm finds that the Outline of Production/Special Outline was not adhered to. The product had not been released for marketing. The expectation is the manufacturer has reviewed the serial for quality and has committed that it is ready for release. – *Infraction*.

NOTE: It is the expectation of the CVB that the licensee/permittee has assured that the product was manufactured according to the Outline(s) and regulations prior to submission of an APHIS Form 2008.

c. Serious

- i. Violations of this degree may affect the quality of the product or numerous products. A *Hold Release* or *APHIS Mandated Stop Distribution and Sale* should be imposed until a full risk assessment can be performed by both the licensee/permittee and the CVB.

NOTE: An APHIS Mandated Stop Distribution and Sale cannot be imposed by the Biologics Specialist during inspection until approved by an IC Section Leader or IC Director at the CVB.

- ii. Regulatory actions that may take place:
 1. *Hold Release*
 2. *APHIS Mandated Stop Distribution and Sale*
 3. *Infraction Notice* (post evidence gathering)
- iii. Examples:
 1. Failure to perform ingredients of animal origin testing (part 113.53) – *Hold Release* or *Mandated Stop Distribution and Sale*
 2. Use of a media, that has not undergone growth promotion testing, for serial release testing and the subsequent submission for consideration for release or marketing release of the serial (part 113.25) – *Mandated Stop Distribution and Sale*
 3. The Biologics Specialist finds (usually during an inspection) that the Outline of Production was not adhered to during the preparation of a serial and the serial was released for marketing by the CVB (Part 102.5). – *Mandated Stop Distribution and Sale*

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4. Not adhering to the Product License or Permit Restriction –
Infraction
 5. The licensee/permittee finds that the Outline of Production was not adhered to during the preparation of a serial **and** the serial was released for marketing by the CVB.
 - a. If the firm provides reasonable investigative assurance that there was an unlikely affect to product quality from marketing release to expiration – *Infraction Notice*
 - b. If the firm does not provide reasonable investigative assurance that there was an unlikely affect to product quality or does not take the action of a *Voluntary Stop Distribution and Sale* action – *Mandated Stop Distribution and Sale*
- IV.** All violations should require an action by the licensee or permittee. Depending on the severity of the violation, a root cause analysis and corrective/preventive action should be performed by the licensee/permittee. The actions taken by the licensee/permittee to adequately address the violation may require review and comment by the Biologics Specialist.
- Note: The assessment of the product passing Section V testing as the only scientific evidence the product quality has not been affected is insufficient investigative assurance.**
- V.** Failure of a licensee or permittee to appropriately address the violation with evidence that the licensee or permittee is preparing and distributing product contrary to the Virus-Serum-Toxin Act would require the procedures addressed in 9 CFR 105.1 (a) be executed.

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