

# AMERIDOSE

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8/24/08*

50 Fountain Street, Framingham, MA 01702

August 22, 2008

Mr. John Marzilli  
Acting District Director  
Department of Health and Human Services  
Food and Drug Administration  
One Montvale Avenue  
Stoneham, MA 02180

Re: Response to Form FDA 483 issued 08/06/08 resulting from  
cGMP Inspection performed 07/21/08 – 08/06/08

Dear Mr. Marzilli:

From July 21, 2008 through August 6, 2008, representatives from the U.S. Food and Drug Administration (“FDA”) conducted an extensive cGMP inspection of all quality systems at our FDA registered facility, Ameridose, LLC, located at 50 Fountain Street, Framingham, Massachusetts, 01702.

At the conclusion of the inspection, one Form FDA 483 was issued. Our response may be found as Attachment A.

I wish to assure you that the management of Ameridose, LLC is committed to enhancing public health, welfare and safety by maintaining a high degree of quality assurance and quality control throughout our organization. In addition to complying with cGMPs, we meet or exceed all other requirements of our industry, including USP <797> as well as a myriad of State Pharmacy Board and DEA regulations. We believe that all of our actions to date, as well as our response to the Form FDA 483, are consistent with this commitment.

Should you require clarification of the contents of this response, please do not hesitate to contact me directly at 508-656-2633 or by email at [gconigliaro@ameridose.com](mailto:gconigliaro@ameridose.com).

Sincerely,

AMERIDOSE, LLC

*Gregory A. Conigliaro*  
Gregory A. Conigliaro  
Vice President and General Manager

cc: Mr. Richard H. Penta, Drug Pre-Approval Manager, Investigator

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**Attachment A**

**FDA OBSERVATION 1:**

*Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.*

**AMERIDOSE, LLC RESPONSE 1:**

Ameridose, LLC currently has strict controls in place to ensure the identity and strength of each final preparation, including but not limited to validated processes, calibrated equipment, certified commercially available ingredients, and an eleven point check process.

Ameridose, LLC shall enhance our current processes as follows:

- Identify appropriate laboratory testing methods for identification and determination of strength of active ingredients.
- Revise current SOPs and/or establish new procedures and/or create additional documents as needed to include identity and strength testing of each active ingredient of final preparations prior to release.
- Update Formulary Worksheets (Master and Batch Production Records).
- Train personnel on all associated SOPs and tasks.
- Revise SOP 9.060 "Sterility Product Process" and/or establish new procedures to reflect current practice for final preparation release related to sterility testing.

These actions shall be initiated immediately. Due to the number and variety of products, and the multiple analytical techniques that may be required, (b) (4)

(b) (4) However, target completion date of the revision of SOP 9.060 shall be (b) (4)

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OBSERVATION 2:

*Written procedures are lacking which describe in sufficient detail the identification, sampling, testing, approval and rejection of components.*

AMERIDOSE, LLC RESPONSE 2:

Ameridose, LLC utilizes only commercially available, FDA-approved APIs whose identity is certified by each FDA-approved vendor as evidenced on each certificate of analysis. Ameridose, LLC ensures the identification of all received APIs by either laboratory testing, or, in the case of FDA-registered finished and labeled preparations, by visual inspection. In all cases, accompanying certificates of analysis are obtained and reviewed by trained personnel.

Ameridose, LLC shall enhance our current processes as follows:

- Identify qualitative testing methods for identification testing utilizing USP methods or other suitable and validated technologies or techniques.
- Revise current SOP and/or establish new procedures to include an inspection and identity test for all APIs and appropriate procedures for approval and rejection of these components.
- Train personnel on all associated SOP's and tasks.

Target completion date shall be (b) (4)

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OBSERVATION 3:

*The master production and control records are deficient in that they do not include a statement of theoretical yield and minimum, maximum, and yield percentages.*

AMERIDOSE, LLC RESPONSE 3:

Ameridose, LLC was, and is, performing theoretical yield calculations and has determined minimum/maximum allowed yield percentages, as demonstrated during the Inspection. However, the calculations were documented on a separate log and not directly on the Master Formulary Worksheet (Master Production Record).

Ameridose, LLC will immediately begin revising each Master Formulary Worksheet (Master Production Record) to include the appropriate theoretical yield calculation and state the acceptable minimum, maximum and yield percentage values.

Target completion date shall be (b) (4)

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OBSERVATION 4:

*Batch production and control records do not include results of the inspection of the packaging and labeling area before and after use for each batch of drug product produced.*

AMERIDOSE, LLC RESPONSE 4:

Ameridose, LLC was, and is, performing line clearance. However, line clearance was not being documented on each Formulary Worksheet (Batch Production Record.)

Ameridose, LLC will immediately begin revising each Formulary Worksheet (Batch Production Record) to include documentation of line clearance inspection of the packaging and labeling area before and after use and shall revise existing procedures and/or establish new procedures to reflect documentation requirements.

Target completion date shall be (b) (4)

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OBSERVATION 5:

*The batch production and control records are deficient in that they do not include a statement of the actual yield and percentage of theoretical yield.*

AMERIDOSE, LLC RESPONSE 5:

Ameridose, LLC was, and is, performing actual yield calculations and has determined minimum/maximum allowed yield percentages, as demonstrated during the Inspection. However, the calculations were documented on a separate log and not directly on the Formulary Worksheet.

Ameridose, LLC will immediately begin revising each Formulary Worksheet (Batch Production Record) to include a statement of the actual yield and the percentage of theoretical yield calculation at the completion of the process. Each Formulary Worksheet will be reviewed and revised to include the appropriate actual yield and percentage yield calculations.

Target completion date shall be (b) (4)

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OBSERVATION 6:

*Written production and process control procedures are not followed in the execution of production and process control functions.*

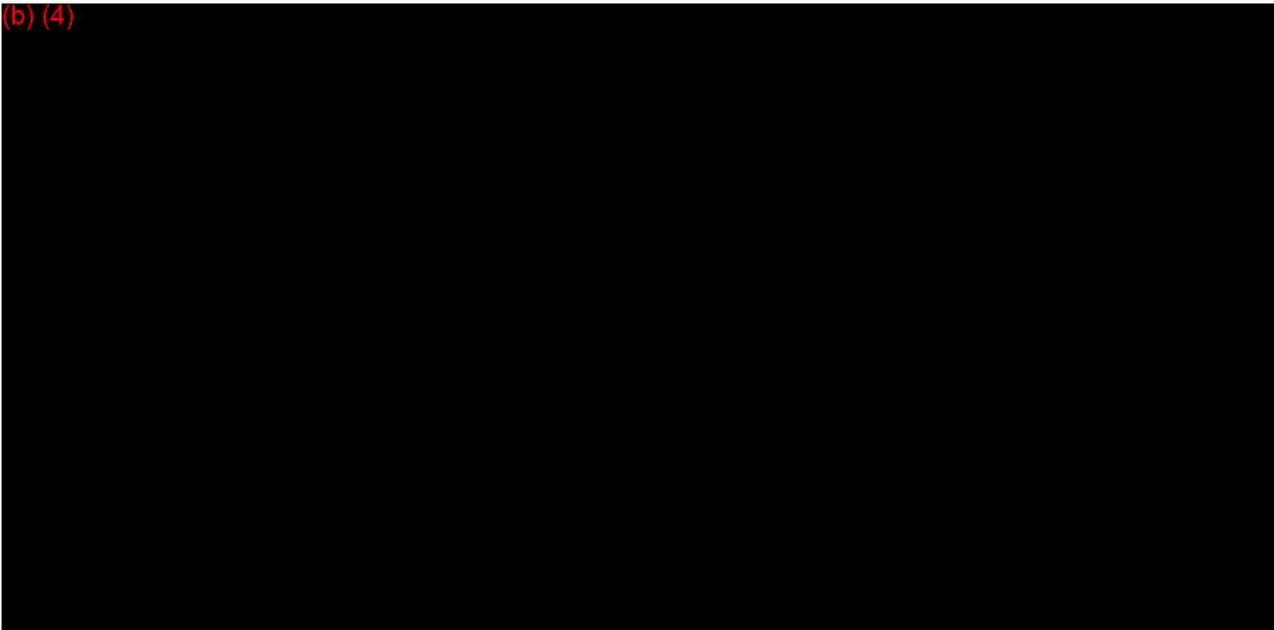
AMERIDOSE, LLC RESPONSE 6:

a) SOP 9.100 Version 2.0, Sterile Qualification (Media Fills), stated that the response to positive results requires re-training but did not specifically state the process for documenting and investigating positive result failures. However, SOP 1.060 Version 1.0 "Out of Specification Procedure" describes "how to perform and document the investigation of an Out Of Specification (OOS) result or Environmental Monitoring Action Level Excursion."

SOP 9.100 V 2.0 did not specifically cross-reference SOP 1.060 but the scope and purpose of SOP 1.060 V 1.0 is to document and investigate all out of specification and environmental monitoring results. Therefore, any positive media failures would be considered an out of specification result and would be investigated as such.

In order to clarify this relationship, SOP 9.100 Version 2.0 has been revised to Version 3.0 (effective 8/7/08) to include the following text in section 4.0 and 10.12. This addition will clarify the relationship between positive media fill results and the Out of Specification process. Appropriate staff members were trained on this version.

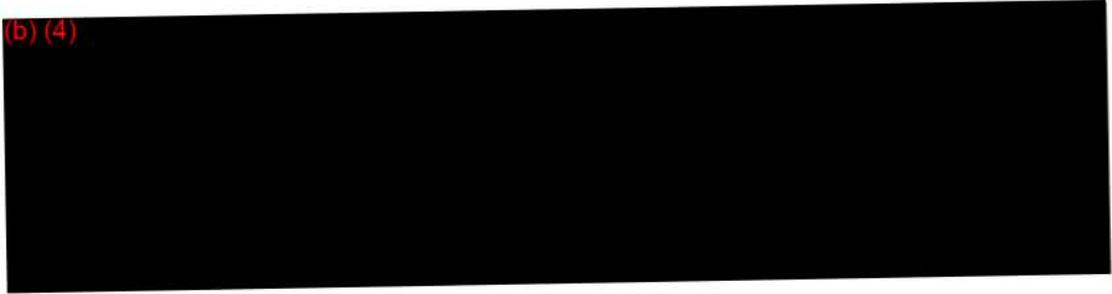
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AMERIDOSE, LLC RESPONSE 6, CON'T:

(b) (4)



b) SOP 6.021 Version 1 "QA Sample Process and Library" was cited as deficient in that step 9.4.3 stated "QA Technician shall obtain product lot samples for in house Lab testing." However, Ameridose, LLC does not perform in-house testing of samples; all samples are tested externally via an independent laboratory. This SOP contained a section for in-house testing as an alternative to step 9.4.2 which defines the process for testing via an external laboratory. Both sections were not intended to be performed but rather intended as an "either/or" contingency. In order to clarify the process, SOP 6.021 Version 1.0 will be revised to remove section 9.4.3 for in-house testing of samples.

Target completion date shall be September 30, 2008.

----- End of Ameridose, LLC Response -----