

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ETON PHARMACEUTICALS, INC.,

Petitioner

v.

EXELA PHARMA SCIENCES, LLC,

Patent Owner

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**U.S. PATENT NO. 10,478,453**

DECLARATION OF HARRY “WARREN” JOHNSON

1. My name is Harry “Warren” Johnson. I am over 21 years of age. I submit this declaration on behalf of Eton Pharmaceuticals, Inc. (hereinafter “Eton”) in connection with the above-captioned matter. I am not being compensated for my time, although, as noted below, I have an indirect, potential financial interest in this matter.

2. In connection with this Declaration, I reviewed select business records of Allergy Laboratories, Inc. (hereinafter “Allergy Labs”) and AL Pharma, Inc. (hereinafter “AL Pharma”). These records were created and maintained in the ordinary course of Allergy’s and AL Pharma’s business.

3. I also held discussions with several individuals who provided information that I also relied upon in preparing this Declaration.

4. Based on my personal knowledge and the results of my investigation, I am informed and understand that the facts stated in this Declaration are true.

### **Background**

5. From January 2001 to approximately January 2017, I served as Vice President and was a 49% owner of Allergy Labs. My wife owned the remaining shares. In or around January 2017, Allergy Labs sold some of its assets and business activities, including the Allergy Laboratories name, to ALK. Allergy Labs (which changed its name to AL Pharma, Inc. (“AL Pharma”) following the sale) retained the real estate, including its Oklahoma City plant, and the cysteine products, which,

as discussed below, Allergy Labs previously manufactured for Sandoz Inc. (“Sandoz”). ALK currently leases AL Pharma’s Oklahoma City plant. My wife and I own all outstanding shares of AL Pharma. I have served as Vice President of AL Pharma since January 2017.

6. AL Pharma has a profit sharing arrangement with Eton in connection with Eton’s proposed L-Cysteine Hydrochloride Injection drug product that is the subject of Eton’s Abbreviated New Drug Application (ANDA). I understand that Eton’s ANDA has prompted a suit for alleged patent infringement by Exela Pharma Sciences, LLC (“Exela”). I am advised that Exela contends the manufacture, use and/or sale of Eton’s proposed ANDA product would infringe one or more claims of U.S. Patent Nos. 10,478,453 and 10,583,155.

### **The Sandoz L-Cysteine Product**

7. In addition to serving as Vice President, my job responsibilities at Allergy Labs during the time frame of January 2001 through January 2017 included manufacturing, sales, accounting, inventory and purchasing. My wife, a chemist and pharmacist, was primarily responsible for quality assurance and quality control.

8. Prior to approximately 2008, Allergy Labs contract-manufactured an L-Cysteine Hydrochloride Injection, USP drug product for Parenta Pharmaceuticals (“Parenta”). Allergy Labs manufactured the Parenta L-Cysteine Product at Allergy’s manufacturing plant in Oklahoma City, Oklahoma. In or about 2008, I

understand that Parenta products were acquired by Sandoz. From that time until 2016, Allergy Labs contract-manufactured the L-Cysteine Hydrochloride Injection Product (50 mg/mL product and available in both single dose vials and pharmacy bulk package) for Sandoz (the “Sandoz L-Cysteine Product”).

9. Allergy Labs contract-manufactured the Sandoz L-Cysteine Product pursuant to Sandoz’s specifications and sold the finished product to Sandoz pursuant to purchase orders.

10. Pursuant to its agreement with Sandoz, various regulatory obligations, and as part of its ordinary business practices, Allergy Labs made and kept records associated with its manufacture of the Sandoz L-Cysteine Product. These records included, but were not limited to, batch records for each lot of Sandoz L-Cysteine Product that Allergy Labs manufactured for Sandoz.

11. A true and correct copy of an exemplary batch record is attached as **Exhibit A**. This batch record is for lot #2072115 of the Sandoz L-Cysteine Product, which was manufactured on July 21, 2015. Batch records were made at or near the time of the events recorded therein by technicians who had training and knowledge and were responsible for making a record of the manufacturing process. It was Allergy Labs’ regular practice to create batch records like that attached as Exhibit A, and such batch records were created and kept in the ordinary course of Allergy Labs’ business. As was Allergy’s practice at the time, the date on which the product

was manufactured is reflected by the lot number assigned to the product. Consistent with that practice, the numbers in the lot # that I have shown in bold represent the manufacture date (**#2072115**) of 07/21/15 and the “2” stands for manufacturing line 2 at the Oklahoma City plant.

12. The batch record for lot #2072115 includes, among other things, the following forms: a “Lot Release Approval for Customer” (*see* pp.13-16), a “Cysteine Batch Manufacturing Record” (*see* pp.19-25), a “50 mL Cysteine HCl Injection Vial Manufacturing Record” (*see* pp.26-35), a “Filled Vial Labeling Record” (*see* pp.46-50), a “Printed Container (Carton) Packaging Record” (*see* pp.51-52), a “Package Insert Record” (*see* p.56) (which includes a true and correct copy of the package insert for the Sandoz L-Cysteine Product (*see* pp.53-55)), a “Sandoz Shipping Label Record – 50 mL Cysteine” (*see* pp.57-58), a “Particulate Matter Test” (*see* p.63), and a “Certificate of Analysis” from a third-party contract laboratory KABS (*see* p.68). The Certificate of Analysis (COA) from KABS contains, among other things, the aluminum and heavy metals content of the final product. As noted on the KABS COA, the aluminum level was measured by another third-party laboratory, Metrics Inc., of Greenville, North Carolina. The KABS COA for lot #2072115 reports 17 ppb of aluminum for the sample tested by Metrics.

13. Attached as **Exhibit B** is a collection of true and correct copies of KABS COAs corresponding to lots #2012114, 2012214, 2072115, 2072215,

2081915, 2082015, 2082115, 2093015, 2100115, and 2100215. In connection with its manufacture of the Sandoz L-Cysteine Product, it was Allergy Labs' practice to have KABS analyze samples for every commercial batch of Sandoz L-Cysteine Product prior to the commercial release. As part of that practice, Allergy Labs would receive and maintain KABS COAs of the type included in Exhibit B. The KABS COAs were maintained in the ordinary course of Allergy Labs' business.

14. Pursuant to Allergy Labs' ordinary business practices, the data from the KABS COAs was included along with other data in a COA bearing the Allergy Labs letterhead. Attached as **Exhibit C** are true and correct copies of the Allergy Labs COAs that correspond to the KABS COAs of Exhibit B, namely Allergy Labs COAs for lots #2012114, 2012214, 2072115, 2072215, 2081915, 2082015, 2082115, 2093015, 2100115, and 2100215. It was Allergy Labs' practice, consistent with what I understand to be required for pharmaceuticals manufactured and distributed commercially, to generate a COA on Allergy Labs letterhead for each commercial batch of Sandoz L-Cysteine Product to assure that these products met agreed upon drug release specifications for potency and impurities. It was Allergy Labs' regular practice to create Allergy Labs COAs like those attached as Exhibit C, and such COAs were created and kept in the ordinary course of Allergy Lab's business.

15. Consistent with the aluminum levels reported in the COAs attached as Exhibits B and C, respectively, the aluminum levels initially measured in the Sandoz

L-Cysteine Products (*i.e.*, within several weeks of manufacture) were typically below about 100 ppb. Based upon stability studies of the Sandoz L-Cysteine Product, we at Allergy Labs understood that aluminum levels would increase to several hundred ppb after storage for approximately 1-24 months but remained substantially below the NMT 5,000 ppb of aluminum noted on the label of the Sandoz L-Cysteine Product. As we believed at the time, the likely source of the aluminum detected in the Sandoz L-Cysteine Product samples was aluminum leached from the glass vials in which the Sandoz L-Cysteine Product was packaged.

16. With respect to the manufacture of the Sandoz L-Cysteine Product, Allergy Labs followed materially the same manufacturing process from 2010 until 2016, which is materially the same as the process previously followed by Allergy Labs for the Parenta L-Cysteine Product since 2003. The process set forth in the “Cysteine Batch Manufacturing Record” for lot #2072115 (*see* Exhibit A) is representative of the process by which the Sandoz L-Cysteine Product was manufactured, and included the following steps, among others:

- a. Stirring water for injection, USP (WFI) in a vessel at temperature not more than (NMT) about 60 C (*see* p.22 at steps 4-6 (“Allow WFI to cool between the temperature of 20C-32C” and “Insert the mixer into the WFI . . . . Turn on the mixer and set the mixer speed at 250 +/- 10 rpms”));

- b. Allowing the vessel to cool to a temperature of NMT 30 C (*see* p.22 at steps 4-6);
- c. Contacting the WFI with L-Cysteine Hydrochloride, Monohydrate, USP (L-Cysteine) for not longer than (NLT) 15 minutes (*see* p.23 at step 9 (“With mixing, add . . . Cysteine HCl Monohydrate (item 02) and mix for 5-10 minutes”));
- d. Adjusting the pH with concentrated Hydrochloric Acid, NF and/or 5.0N Sodium Hydroxide, NF (*see* pp.23-24 at steps 11-12 (Remove sample, measure and record pH, “specification of 1.20-1.30”); the Allergy Labs process had hydrochloric acid and sodium hydroxide readily available for adjusting pH should it be needed (*see* p.20));
- e. Mixing for a minimum of about 10 minutes (*see* p.25 at step 14 (“Mix for 15 +/- 5 minutes”));
- f. Capping the vessel and allowing to stand (*see* p.25 at step 19 (“Close the lid on the tank”));
- g. Filling said mixture into container of use (*see* pp.24-25 at Vial Manufacturing Record, steps 13-16 (“Proceed with filing and stoppering of the vials”));
- h. Reducing the head space oxygen in said containers of use (*see* p.25 at Vial Manufacturing Record, step 17 (“Nitrogen purging Aero



50”)); and

- i. Sealing said containers of use (*see* p.25 at Vial Manufacturing Record, steps 18-19 (“Perform vial capping on all filled and stoppered vials”).

17. Allergy Labs was also responsible for labeling, packaging, and shipping the finished Sandoz L-Cysteine 50 mg/mL Product. Allergy labeled the filled vials and placed a package insert in each carton. (*see* pp.34-35 at Vial Manufacturing Record, steps 28, 31-38). True and correct copies of the label and package insert are included in the batch record of Exhibit A.

18. Allergy Labs followed the above-referenced manufacturing process for the Sandoz L-Cysteine Product in the ordinary course of Allergy Labs’ business and the process was generally known by Allergy Labs personnel. Allergy Labs also did not take any overt efforts to conceal the manufacturing process for the Sandoz L-Cysteine Product.

#### **AL Pharma NDA**

19. In or about January 2018, AL Pharma filed a New Drug Application No. 209649 (the “AL Pharma NDA”) with the United States Food & Drug Administration (FDA) for 5% L-Cysteine Hydrochloride Injection, USP, via the 505(b)(2) regulatory pathway, a product which was intended for the same indications as a previously FDA-approved product, 7.25% Cysteine HCl Injection, USP (NDA

019523; Hospira).

20. The Proposed Finished Product Release Specifications (“Specifications”) for the 5% L-Cysteine HCl Injection, USP, recited, among other things, an Aluminum Content of not more than (NMT) 5,000 ppb and NMT 2.0% Cystine.

21. With respect to the aluminum content of AL Pharma’s proposed specifications, by e-mail dated March 9, 2018 (a true and correct copy of which is attached as **Exhibit D**) the FDA advised AL Pharma that:

The drug product L-Cy[s]teine Hydrochloride Injection is a small volume parenteral drug product used in TPN. Based on our previous experience with small volume parenteral drug products intended for addition to the TPN, we have determined that the aluminum dose delivered by your drug product, 5% L-Cysteine Hydrochloride Injection, USP, should be limited to  $\leq 0.6$  mcg/kg/day. To comply with this limit, the aluminum content in the final drug product should be controlled to  $\leq 350$  mcg/L. This calculation is based on the clinical dose of 15 mg cysteine free base per gram of amino acid per day. Therefore, the proposed acceptance limit for the aluminum content in the finished drug product specification (3.2.P.5.1) must be revised to  $\leq 350$  mcg/L. The drug product registration batches manufactured at OKC Allergy Supplies, Oklahoma City, OK have not been shown to meet the required acceptance limit for aluminum content.

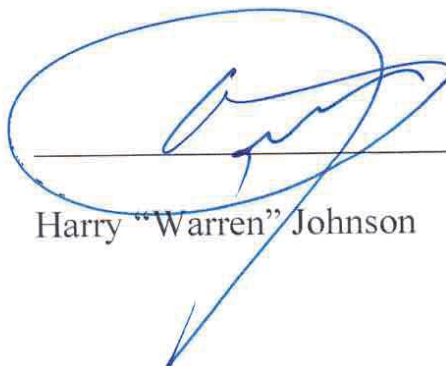
22. In response, AL Pharma amended the aluminum specification to  $\leq 350$  mcg/L ( $\leq 350$  ppb) and submitted additional information demonstrating compliance

with the FDA's proposed acceptance limit for aluminum content.

23. I hereby declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct, and that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true. I understand that willful false statements are punishable by fine or imprisonment or both. *See* 18 U.S.C. § 1001.

Date: 05-15-2020

Respectfully submitted,




Harry "Warren" Johnson

# **Exhibit A**

QA 07-15-15


08-07-15

|   |   |   |
|---|---|---|
|  | Form Title: <b>Lot Release Approval for Customer 714503</b> | Doc Number: <b>QA-032-01.02</b>         |
| Lot #: <b>2072115</b>   | Product: <b>Cysteine 50mL</b>                               | Page 1 of 4                             |
|   |   | Form Issue Date: <b>APR 30 2015</b>     |
|   |   | Form Effective Date: <b>MAY 06 2015</b> |

| Document/Process  | Document | Form #     |
|---|----------|------------|
| <input checked="" type="checkbox"/> Routine Intervention Log completed and approved by QA   |          | QA-006-02  |
| <input checked="" type="checkbox"/> QA-006-02 "Corrective Intervention Log - Line 1 & 2 Aseptic Products" completed and approved by QA                                      |          | QA-006-02  |
| <input checked="" type="checkbox"/> Batch Manufacturing Record completed and approved by the Prod. Supervisor   |          | BMR-010    |
| <input checked="" type="checkbox"/> Vial Manufacturing Record completed and approved by the Prod. Supervisor  |          | VMR-014    |
| <input checked="" type="checkbox"/> MFG-048-01 "Filling/Stopping and Capping Line Clearance Record"   |          |            |
| <input checked="" type="checkbox"/> FAE-017-01 "Volume Verification Record-Line 1"  |          |            |
| <input checked="" type="checkbox"/> FAE-033-01 "Volume Verification Record-Line 2"  |          |            |
| <input checked="" type="checkbox"/> MFG-036-01 "Filled Vial Inspection Record"  |          |            |
| <input checked="" type="checkbox"/> QC-090-01 "AQL Vial Inspection" completed and approved by QC  |          |            |
| <input checked="" type="checkbox"/> MFG-040-01 "Quarantine of Unlabeled Vials for Future Labeling Operations Form"  |          |            |
| <input checked="" type="checkbox"/> PAL-002-01 "Filled Vial Labeling Record"  |          |            |
| <input checked="" type="checkbox"/> PAL-002-07 "Printed Container (Carton) Packaging Record"  |          |            |
| <input checked="" type="checkbox"/> PAL-002-08 "Package Insert Record"  |          |            |
| <input checked="" type="checkbox"/> Sandoz Shipping Label Record  |          | PAL-002-12 |
| <input checked="" type="checkbox"/> MFG-057-24 "Calculation of Percent Yields for Bulk Solution and Final Containers of Sterile Drug Products"                              |          |            |
| <input checked="" type="checkbox"/> FAE-016-01 "Daily Autoclave Log - Equipment ID # 0002" (Line 1) Completed and Approved by QA (On file with Document Control)            |          |            |
| <input checked="" type="checkbox"/> FAE-026-01 "Daily Autoclave Log - Equipment ID # 0237 and # 0238" (Line 2) Completed and Approved by QA (On file with Document Control) |          |            |
| <input checked="" type="checkbox"/> Dry heat depyrogenating oven chart reviewed by manufacturing (Line 1) Completed and Approved by QA (On file with Document Control)      |          |            |
| <input checked="" type="checkbox"/> Tunnel report reviewed by manufacturing (Line 2) Completed and Approved by QA (On file with Document Control)                           |          |            |

Comments (Reference any Deviations, OOS, or CAPA Investigations in the Investigations section [page 3]):

None/2-108-12-15

Manufacturing Checklist Completed By/Date:  08-12-15

QA Reviewed and Approved By/Date: Heidi Wilson 08-12-15



Form Title: Lot Release Approval for Customer 714503

Doc Number: QA-032-01.02

Lot #:

Product: Cysteine 50mL

Page 2 of 4

2072115

| Document Present?<br>(Circle One)  | Document<br>(Reference any Deviations, OOS or CAPA Investigations in the investigations section [page 3])   | Results<br>(Circle One)                  | Reviewed By/Date |
|--|---|--|------------------|
| <input checked="" type="checkbox"/> Yes  | QC-066-01 "Method: Fill Volume"   | <input checked="" type="checkbox"/> Pass | MA 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | QC-073-01 "Particle Matter in Injectables"  | <input checked="" type="checkbox"/> Pass | MA 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | QC-076-01 "Gelman Acro 50, 0.2µ Filter Integrity Testing"   | <input checked="" type="checkbox"/> Pass | MA 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | QC-002-02 "Extract, Diluent, Sterile Drug Product Bioburden Sample Form"  | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | QC-011-02 "Endotoxin Test Record for Product Release"   | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | QC-118-01 "Sterility Test Form"   | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| <input checked="" type="checkbox"/> Yes  | Contract Testing Certificate of Analysis  | <input checked="" type="checkbox"/> Pass | MA 08-12-15      |
| Water for Injection (Reference any Deviations, OOS or CAPA Investigations in the investigations section [page 3])      |   |  |                  |
| Data not present in batch record   | QC-030-01 "WFI, Process Water and Steam Testing Sites for Buildings 1 and 2" WFI data reviewed for the manufacture date (date WFI into mixing tank) | <input checked="" type="checkbox"/> Pass | MA 08-12-15      |
| Environmental Monitoring (Reference any Deviations, OOS or CAPA Investigations in the investigations section [page 3]) |   |  |                  |
| Data in BioTrends  | Ensure the class 100 cleanroom EM data has been reviewed for the date of production of the lot  | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| Data in BioTrends  | Ensure the personnel monitoring data from the date of production of the lot has been reviewed   | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| Data in Lighthouse   | Ensure the non-viable particulate data from the date of production of the lot has been reviewed   | <input checked="" type="checkbox"/> Pass | JW 08-12-15      |
| Comments: None   |   |  |                  |
| QA Reviewed and Approved By/Date: <i>EW</i> 08-14-15   |   |  |                  |



Form Title: Lot Release Approval for Customer 714503

Doc Number: QA-032-01.02

Lot #:

2072115

Product: Cysteine 50mL

Page 3 of 4

| Investigation Type                                     |     | Are there any investigations associated with the manufacture of testing of this lot? (Circle one) |  | Retored By/Date |
|--|-----|---|--|-----------------|
| Deviation Reports                                      | Yes | No  | If yes, DR# (s)  | JW 08-12-15     |
| CAPAs  | Yes | No  | If yes, CAPA# (s)  | JW 08-12-15     |
| ENs  | Yes | No  | If yes, EN# (s)  | JW 08-12-15     |
| OOS  | Yes | No  | If yes, OOS# (s)   | JW 08-12-15     |
| Investigations complete and copy in batch record?      |     | Yes   | No   | JW 08-12-15     |
|  |     |   | (if investigation not complete and in batch record please provide comment) |                 |
| Comments: None   |     |   |  |                 |
| QA Reviewed and Approved By/Date: <i>Erin</i> 08-14-15 |     |   |  |                 |



Form Title: Lot Release Approval for Customer 714503

Doc Number: QA-032-01.02

Lot #:

Product: Cysteine 50mL

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|  |   |
|--|---|
| By/Date: Heidi Wilson 08-12-15   |   |
| By/Date: [Signature] 8/12/15   |   |
| Do the investigations support the release of this product?<br>(Circle One) | Yes No <input checked="" type="radio"/> N/A<br>(If No, provide comment) |
| Is the product acceptable for release?<br>(Circle One)                     | <input checked="" type="radio"/> Yes No<br>(If No, provide comment)     |
| Quality Assurance Management By/Date: [Signature] 08.14.15                 |   |
| Comments: pme  |   |

|  |       |  |
|--|-------|--|
| Quantity transferred to inventory:   | 13200 | Transferred to inventory By/Date: [Signature] 08-17-15 |
| Material Safety Data Sheet (MSDS) (one per pallet) revision # N/A TH 08-17-15                                |       |  |
| MFG-037-01 "Retention Sample Form for Sandoz Inc. (ID# 714503) Drug Products"<br>(last form in batch record) |       |  |
| Allergy Laboratories, Inc. Certificate of Analysis   |       |  |




7/28 07-15-15 07-07-15

|  |                                    |                                 |
|--|------------------------------------|---------------------------------|
| <b>Form Title: Routine Intervention Log – Line 2 Aseptic Products</b>  |                                    | Doc Number: <b>QA-006-03.01</b> |
| Lot #: <b>2072115</b>  | Product Name: <b>Cysteine 50mL</b> | Page 1 of 1                     |
| <p>Weight checks are documented on form FAE-033-01. Corrective interventions are recorded on form QA-006-02. Routine interventions do not exceed one minute. If one minute is exceeded, the intervention must be documented on the corrective intervention log. Although setup activities are routine interventions, setup time will be documented on QA-006-02.</p> |                                    |                                 |
| <p>*This form shall be copied onto autoclavable paper.</p>   |                                    |                                 |
| <p>Form Issue Date (stamp):<br/><b>MAY 05 2015</b></p>   |                                    |                                 |
| <p>Form Effective Date (stamp):<br/><b>MAY 06 2015</b></p>   |                                    |                                 |


| Area  | Glass/Inert (Glass) / 3 Doors                            | Fill Machine (FM) / 2 Doors                              | Stopper/Booster (SB) / 6 Doors                           |
|---|--|--|--|
| <b>Before Break</b><br>Time: 6:47AM - 9:57AM<br>Date: 07-21-15<br>By: JS  | 1<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0 | 1<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0 | 0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0 |
| <b>After Break</b><br>Time: 10:47AM - 12:40PM<br>Date: 07-21-15<br>By: JS | 1<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0      | 1<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0      | 0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0 |

|              |               |
|--------------|---------------|
| 0 7/21/15 JS | Jeff 08.12.15 |
|--------------|---------------|

7/11 07-15-15 071115

|   |                                       |  |
|---|---------------------------------------|--|
|  |                                       | <b>Form Title: Corrective Intervention Log – Line 1 &amp; 2 Aseptic Products</b><br><b>Doc Number: QA-006-02.02</b><br>Page 1 of 1 |
| <b>Lot #:</b><br>2072115  | <b>Product Name:</b><br>Cysteine 50mL | *This form shall be copied onto autoclavable paper.  |
| <b>Setup Start Time:</b><br>6:12AM  | <b>Setup End Time:</b><br>6:43AM      | <b>Form Issue Date (stamp):</b><br>MAY 05 2015   |
|   |                                       | <b>Form Effective Date (stamp):</b><br>MAY 06 2015   |

Although setup is a routine activity, setup times are recorded on this form to show the full length of the intervention period during setup activities. Weight checks are documented on form FAE-017-01 or FAE-033-01. Routine interventions are recorded on form QA-006-01 or QA-006-03. Notify production management of any corrective interventions that may result in a deviation.

| Corrective Interventions   |  | Setup Time | Intervention |
|--|--|------------|--------------|
| <small>Any interventions listed on QA-006-01 or QA-006-03, regardless of the number of the batch, is open to personal audit. Also include other interventions that also apply that are not listed.</small> |  |            |              |
| <p>2072115<br/>7/11</p>    |  |            |              |
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|  |  |            |              |

08.12.15  
 Keegi 08.22.15  
 08.12.15

07-17-15

Form Title: Cysteine Batch Manufacturing Record (750L) -Line 2

Doc Number: **BMR-010.00**

Page 1 of 6

Form Effective Date: ~~DEC 11 2013~~ **DEC 19 2013**

Formulation # **F1000** Product **Cysteine HCl Injection 50mg/mL** Company **Sandoz Inc.** Lot # **2072115**

Written by: *[Signature]* / 11-22-13

Approved by: *[Signature]* / 11-25-13

Approved by: *[Signature]* / 12-05-13

Approved by: *[Signature]* / 12-19-13

Batch Size: 750L/762.0kg

Date Issued: *NA* 07-15-15

Production Started: *2* 107-20-15

Production Completed: 07-20-15

Qty lost: 0

Yield (%): 100

Initial: *[Signature]*

See attached pg. 1 for customer approval. TH 12-19-13

| Lot Number  | Ingredients              | Qty. Required | Qty. Used       | Exp. Date | Quantity | Date     | Dispensed          | Checked            |
|-------------|--------------------------|---------------|-----------------|-----------|----------|----------|--------------------|--------------------|
| 1. EX-10000 | Water for Injection USP  | 0.90mL        | 686.0kg         | N/A       | 686.0kg  | 07-20-15 | <i>[Signature]</i> | <i>[Signature]</i> |
| 2. AP-10000 | Cysteine HCl Monohydrate | 50mg          | 37.5kg          | 05-11-16  | 0.056kg  | 07-20-15 | <i>[Signature]</i> | <i>[Signature]</i> |
| 3. EX-10040 | Hydrochloric Acid NF     | Q.S.          | To adjust pH    | 05-11-16  | 37.444kg | 07-20-15 | <i>[Signature]</i> | <i>[Signature]</i> |
| 4. EX-10030 | Sodium Hydroxide-NF      | Q.S.          | To adjust pH    | N/A       |          |          |                    |                    |
| 5. EX-10000 | Water for Injection USP  | Q.S.          | Q.S. to 762.0kg | N/A       | 38.5kg   | 07-20-15 | <i>[Signature]</i> | <i>[Signature]</i> |

|  |                                |                        |       |
|--|--------------------------------|------------------------|-------|
| Form Title: Cysteine Batch Manufacturing Record (750L) -Line 2 |                                | Doc Number: BMR-010.00 |       |
| Formulation #  | Product                        | Company                | Lot # |
| F1000  | Cysteine HCl Injection 50mg/mL | Sandoz Inc.            |       |
|  |                                | Page 1 of 6            |       |
|  |                                | Form Effective Date:   |       |

|                                 |                               |
|---------------------------------|-------------------------------|
| Written by/date:                | <i>[Signature]</i> / 11-22-13 |
| Approved by Production by/date: | <i>[Signature]</i> / 11-25-13 |
| Approved by QA by/date:         | <i>[Signature]</i> / 12-05-13 |
| Approved by Customer by/date:   | McFadden Rachael              |

|                                |              |                     |                       |
|--------------------------------|--------------|---------------------|-----------------------|
| Batch Size: 750L/762.0kg       | Date Issued: | Production Started: | Production Completed: |
| Qty manufactured: 750L/762.0kg | Qty lost:    | Yield (%):          | Initial:              |

COPY

Specific approval by McFadden Rachael  
 11/25/13 11:25 AM  
 12/05/13 12:05 PM  
 12/05/13 12:11 PM  
 12/05/13 12:11 PM

| Item # | Part Number | Ingredients              | Qty/mL | Qty required    | Lot | Expiration date | Qty dispensed | Date dispensed | Dispensed by | Checked by |
|--------|-------------|--------------------------|--------|-----------------|-----|-----------------|---------------|----------------|--------------|------------|
| 1.     | EX-10000    | Water for Injection USP  | 0.90mL | 686.0kg         | N/A | N/A             |               |                |              |            |
| 2.     | AP-10000    | Cysteine HCl Monohydrate | 50mg   | 37.5kg          |     |                 |               |                |              |            |
| 3.     | EX-10040    | Hydrochloric Acid NF     | Q.S.   | To adjust pH    |     |                 |               |                |              |            |
| 4.     | EX-10030    | Sodium Hydroxide NF      | Q.S.   | To adjust pH    |     |                 |               |                |              |            |
| 5.     | EX-10000    | Water for Injection USP  | Q.S.   | Q.S. to 762.0kg | N/A | N/A             |               |                |              |            |

|  |                                |             |                        |             |
|--|--------------------------------|-------------|------------------------|-------------|
| Form Title: Cysteine Batch Manufacturing Record (750L) -Line 2 |                                |             | Doc Number: BMR-010.00 |             |
| Formulation #  | Product                        | Company     | Lot #                  | Page 2 of 6 |
| F1000  | Cysteine HCl Injection 50mg/mL | Sandoz Inc. | 2072115                |             |

| PRE-VENTILATING   |      |   |                    |          |
|---|------|---|--------------------|----------|
| Equipment   | ID#  | Equipment with full certification (Y/N) | Signature          | Date     |
| Stainless Steel Tank (ID# 0331 or 0333)                   | 0331 | N/A                                     | <i>[Signature]</i> | 07-20-15 |
| Mixer   | 0188 | yes                                     | <i>[Signature]</i> | 07-20-15 |
| Mixing shaft with blade                                   | 0266 | N/A                                     | <i>[Signature]</i> | 07-20-15 |
| pH Meter  | 0205 | Yes                                     | MA                 | 07-20-15 |
| Floor scale (Range: 0.00-1,500.0kg)<br>(ID# 0245 or 0244) | 0245 | yes                                     | <i>[Signature]</i> | 07-20-15 |
| Weigh Scale (Range: 0.000-15.000kg)                       | 0263 | yes                                     | <i>[Signature]</i> | 07-20-15 |
| Temperature Measuring Device                              | 0267 | yes                                     | <i>[Signature]</i> | 07-20-15 |

|  |                                |                        |         |
|--|--------------------------------|------------------------|---------|
| Form Title: Cysteine Batch Manufacturing Record (750L) -Line 2 |                                | Doc Number: BMR-010.00 |         |
| Formulation #  | Product                        | Company                | Lot #   |
| F1000  | Cysteine HCl Injection 50mg/mL | Sandoz Inc.            | 2072115 |
|  |                                | Page 3 of 6            |         |

| Step # | Manufacturing Process  | By       | Date            | Checked by | Date            |
|--------|--|----------|-----------------|------------|-----------------|
| 1.     | Ensure all raw materials are available for compounding and are within expiration date. Record the raw materials lot number and expiration date on page 1 of this form.   |          |                 |            |                 |
| 2.     | Ensure that the mixing/compounding room # 2130 and equipment in the room is clean and all cleaning forms have been signed. Verify that cleaning has been performed by referencing MFG-031-03 "Building 2 Vial Production Cleaning Checklist."  |          |                 |            |                 |
| 3.     | Verify that the floor scale is within calibration and record verification on page 1 of this form. Zero floor scale and roll the tank onto the scale. Record the tank and floor scale ID#s on page 2.<br>Record the tank weight <u>387.3</u> kg. Label the tank as QUARANTINE. Proceed to tare the scale. | <u>R</u> | <u>07-20-15</u> | <u>ELM</u> | <u>07-20-15</u> |
| 4.     | Add 686.0 kg of USP WFI (item #1) to the tank. Record results on Page 1 of the batch record.<br>WFI source (✓one): <input checked="" type="radio"/> 2130HE <input type="radio"/> 2131<br>When using WFI source 2130HE refer to the instruction in FAE-004 for operation of the heat exchanger.           | <u>R</u> | <u>07-20-15</u> | <u>R</u>   | <u>07-20-15</u> |
| 5.     | Allow WFI to cool between the temperatures of 20°C-32°C.<br>Temperature of WFI: <u>29.0</u> °C<br>Verify that the temperature measuring device ID# <u>0267</u> is within calibration.  | <u>R</u> | <u>07-20-15</u> | <u>R</u>   | <u>07-20-15</u> |
| 6.     | Insert the mixer into the WFI. Set-up the mixer so the shaft is in the center of the tank opening. The location of the mixing blade should be set at the middle depth of the solution in the tank. Turn on the mixer and set the mixer speed at 250 ± 10 rpms.<br>Record mixing speed: <u>260</u> rpm.   | <u>R</u> | <u>07-20-15</u> | <u>R</u>   | <u>07-20-15</u> |
| 7.     | Check the raw materials for the correct name, item code and quantity. Record results on Page 1 of this form.   | <u>R</u> | <u>07-20-15</u> | <u>R</u>   | <u>07-20-15</u> |

|   |                                |                               |         |
|---|--------------------------------|-------------------------------|---------|
| Form Title: <b>Cysteine Batch Manufacturing Record (750L) -Line 2</b> |                                | Doc Number: <b>BMR-010.00</b> |         |
| Formulation #   | Product                        | Company                       | Lot #   |
| F1000   | Cysteine HCl Injection 50mg/mL | Sandoz Inc.                   | 2072115 |
|   |                                | Page 4 of 6                   |         |

|   |  |   |
|---|--|---|
| <p><b>STEP 8: MANUFACTURING PROCESS</b></p> <p>To weigh the required amount of Cysteine. Place an empty sampling container on scale ID# 0263. Verify that the scale is displaying in "kg". Tare the scale and remove the sampling container. Add the required amount of Cysteine to the sampling container. If more than one sampling container is required, then repeat this step. Record the sampling container weights below. (* indicates Critical Process Parameter)</p> <p>37.500kg* of Cysteine is required:</p> <p>Lot #: <u>6947-4</u> Exp. date: <u>05-11-16</u> (Record lot number and expiration date on Page 1 of this form)</p> <p><u>6947-5</u> <u>05-11-16</u></p> <p>Sampling container 1: <u>0.056</u> kg <u>6947-4</u></p> <p>Sampling container 2: <u>13.436</u> kg <u>6947-5</u></p> <p>Sampling container 3: <u>12.906</u> kg <u>6947-5</u></p> <p>Sampling container 4: <u>11.102</u> kg <u>6947-5</u></p> <p>Sampling container 5: _____ kg</p> <p>Sampling container 6: _____ kg</p> <p><u>07-20-15</u> <u>37.500</u> kg (Record on page 1 of this form)</p> |  | <p><u>26</u></p> <p><u>07-20-15</u></p> |
| <p>8. With mixing, add 37.500kg of Cysteine HCl Monohydrate (item 02) and mix for 5-10 minutes.</p> <p>Start time: <u>3:42pm</u> End time: <u>3:48pm</u> Total mixing time: <u>6 min.</u></p> <p>If raw material is dissolved, proceed to Step 10.</p> <p>If raw material is not dissolved within 5-10 minutes notify supervisor.</p>   |  | <p><u>26</u></p> <p><u>07-20-15</u></p> |
| <p>9. Using a clean container remove approximately 3L from the bottom valve of the tank and place into the top of the tank.</p>   |  | <p><u>26</u></p> <p><u>07-20-15</u></p> |
| <p>10. Remove a 10mL sample and submit to QA/QC for pH testing.</p>   |  | <p><u>26</u></p> <p><u>07-20-15</u></p> |

|   |                                |             |                               |  |
|---|--------------------------------|-------------|-------------------------------|--|
| Form Title: <b>Cysteine Batch Manufacturing Record (750L) -Line 2</b> |                                |             | Doc Number: <b>BMR-010.00</b> |  |
| Formulation #   | Product                        | Company     | Lot #                         |  |
| F1000   | Cysteine HCl Injection 50mg/mL | Sandoz Inc. | 2072115                       |  |

|  |  |        |                |                |
|--|--|--------|----------------|----------------|
| <p>12. Measure pH with pH meter ID# 0205. Verify that the pH meter is in calibration.</p> <p>Record pH <u>1.28</u>, specification of 1.20-1.30.</p> <p>If pH is within range, go to step 14. If pH is not within range, go to step 13.</p>   |  | QA/QC: | MA<br>07-20-15 | 52<br>57.20.15 |
| <p>13. If pH is not within range, remove a 100ml sample for QC testing to determine acid/base quantity required for pH correction. The required quantity of Hydrochloric Acid (item 03) or Sodium Hydroxide (item 04) must be dissolved in WFI (item 01).<br/>Add slowly and mix 15 min before retest.</p> <p>pH Before _____</p> <p>pH After _____</p> <p>Time start _____</p> <p>Time finish _____</p> <p>Total mixing time _____</p> <p>Quantity of Hydrochloric Acid (item 03) required _____</p> <p>Quantity of Sodium Hydroxide (item 04) required _____</p> <p>Quantity of Hydrochloric Acid (item 03) added _____</p> <p>Quantity of Sodium Hydroxide (item 04) added _____</p> <p>Include the test results and calculation in batch production records.</p> |  | QA/QC: |                |                |



Form Title: **Cysteine Batch Manufacturing Record (750L) - Line 2** Doc Number: **BMR-010-00**

|               |                                |             |         |
|---------------|--------------------------------|-------------|---------|
| Formulation # | Product                        | Company     | Lot #   |
| F1000         | Cysteine HCl Injection 50mg/mL | Sandoz Inc. | 2072115 |

Page 6 of 6

| Step | MANUFACTURING PROCESSES  | BY/DATE                         | CHECKED BY/DATE                |
|------|--|---------------------------------|--------------------------------|
| 14.  | <p>Q.S. WFI (item 05) to a final weight of 762kg*. (* indicates Critical Process Parameter)</p> <p>Total weight = <u>762.0</u> kg</p> <p>Mix for 15 ± 5 minutes.</p> <p>Start time: <u>4:05pm</u> End time: <u>4:15pm</u> Total mixing time: <u>10min.</u></p>   | <u>[Signature]</u><br>07-20-15  | <u>[Signature]</u><br>07-20-15 |
| 15.  | Remove a 10mL sample into a cleaned container and submit to QA/QC for pH testing.  | <u>[Signature]</u><br>07-20-15  | <u>[Signature]</u><br>07-20-15 |
| 16.  | <p>Measure pH with pH meter ID# 0205. Verify that the pH meter is in calibration.</p> <p>pH specification (1.20-1.30) pH actual results <u>1.25</u> * (if pH does not meet specification, notify supervisor)</p> <p>(* indicates Critical Process Parameter)</p> | QA/QC:<br><u>MA</u><br>07-20-15 | <u>[Signature]</u><br>07-20-15 |
| 17.  | Remove the mixer from the tank. Clean the mixing shaft with blade according to MFG-045 "Post-Manufacturing Equipment Cleaning Procedure - Line 2".   | <u>[Signature]</u><br>07-20-15  | <u>[Signature]</u><br>07-20-15 |
| 18.  | <p>QA/QC RELEASE:</p> <p>Prior to filling operation, identify the tank as being released and include product name, lot number, volume, initials and date.</p> <p>Close the lid on the tank.</p>  | QA/QC:<br><u>MA</u><br>07-20-15 | <u>[Signature]</u><br>07-20-15 |
| 19.  | Process completion time: <u>4:24pm</u> (Filling must commence within 24 hours*)  | <u>[Signature]</u><br>07-20-15  | <u>[Signature]</u><br>07-20-15 |

Production Supervisor/date: [Signature] 07-20-15

Quality Assurance/date: [Signature] 08-12-15

MFG

Document Review and Approval

01/17/15

**50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2**

Doc Number: **VMR-014.00**

Page 1 of 9

Form Effective Date: **FEB 10 2014**

Form Issue Date: **JAN 30 2014**

**2072115**      Cysteine HCl Injection 50mg/mL      CYS-002      50mL in 50mL

07/17      07-21-15      7/17/15

7/17/15      01-28-14

1/28/14

01-28-14

See attached page 1 for customer approval. MCOI-29-14

| Item # | Part Number                | Description                         | Lot #                              | Quantity Required | Qty received | Inspected By | Qty Used  | Qty returned                                      | Classified by |
|--------|----------------------------|-------------------------------------|------------------------------------|-------------------|--------------|--------------|---|---|---------------|
| 1.     | CYS-002                    | Cysteine HCl 50mg/mL                | 2072115                            | 51.5mL            | 762.0kg      | ADH 07-20-15 | 750.544kg   | Quantity discarded: 11.456kg - 41456 - 5-07-21-15 |               |
| 2.     | G-16                       | 50mL 20mm Clear Glass Vial          | G-16-012115                        | 1                 | 13940        | ADH 07-21-15 | 13940   | 0   | AD            |
| 3.     | ST-07                      | 20mm Rubber Stopper                 | ST-07-041114                       | 1                 | 15000        | ADH 07-17-15 | 15000   | 0   | AD            |
| 4.     | S-023                      | 20mm Aluminum Flip-off White Seal   | S-023-062211                       | 1                 |              |              | N/A   |   |               |
| 5.     | KVGLS04HH3                 | Opticap 4" 0.22µ Sterilizing Filter | CL1MA14478                         | N/A               |              |              | N/A   |   |               |
| 6.     | L-018-XX (current version) | Vial Label                          | L-018-01-062215                    | 1                 |              |              | See PAL-002-01 for vial labeling operations.      |   |               |
| 7.     | L-023-XX (current version) | Vial Tray                           | L-023-01-121913<br>L-023-01-070215 | 5 vials per tray  |              |              | See PAL-002-07 for vial carton operations.        |   |               |
| 8.     | L-028-XX (current version) | Package Insert                      | L-028-00-061915                    | 1 per tray        |              |              | See PAL-002-08 for package insert operations.     |   |               |
| 9.     | PC-40070                   | Shipping Box AL3050                 | N/A                                | 5 trays per box   |              |              | N/A   |   |               |
| 10.    | L-032-XX (current version) | Shipping Box Label                  | N/A                                | 1 per box         |              |              | See PAL-002-12 for shipping box label operations. |   |               |

Doc Number: VMR-014.00

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

|                           |                                |         |              |                      |
|---------------------------|--------------------------------|---------|--------------|----------------------|
| Sandoz Inc.               | Cysteine HCl Injection 50mg/mL | CYS-002 | 50mL in 50mL | Page 1 of 9          |
| Originator/date:          | <i>Thad V. Whaley</i> 01.28.14 |         |              | Form Effective Date: |
| Department Approval/date: | <i>Justin</i> 1/28/14          |         |              | Form Issue Date:     |
| QA Approval/date:         | <i>CP - 2nd</i> 01.28.14       |         |              |                      |
| Customer Approval/date:   | Mcfadden Rachael               |         |              |                      |

COPY

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| Item | Material                                       | Quantity         | Quantity discarded:                           |
|------|--|------------------|---|
| 1.   | CYS-002 Cysteine HCl 50mg/mL                   | 51.5mL           |   |
| 2.   | G-16 50mL 20mm Clear Glass Vial                | 1                | 13940 ADH 13940 <i>0 2/15/15</i>              |
| 3.   | ST-07 20mm Rubber Stopper                      | 1                |   |
| 4.   | S-023 20mm Aluminum Flip-off White Seal        | 1                | N/A   |
| 5.   | KVGLS04HH3 Opticap 4" 0.22µ Sterilizing Filter | N/A              | N/A   |
| 6.   | L-018-XX (current version) Vial Label          | 1                | See PAL-002-01 for vial labeling operations.  |
| 7.   | L-023-XX (current version) Vial Tray           | 5 vials per tray | See PAL-002-07 for vial carton operations.    |
| 8.   | L-028-XX (current version) Package Insert      | 1 per tray       | See PAL-002-08 for package insert operations. |
| 9.   | PC-40070 Shipping Box AL3050                   | 5 trays per box  | N/A   |
| 10.  | L-032-XX (current version) Shipping Box Label  | 1 per box        | N/A   |

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

|             |                                |         |         |                               |
|-------------|--------------------------------|---------|---------|-------------------------------|
| Company     | Product                        | Plant   | Lot #   | Manufacture Date (MM/DD/YYYY) |
| Sandoz Inc. | Cysteine HCl Injection 50mg/mL | CYS-002 | 2072115 | 07/17                         |

| Equipment  | ID (Asterisked)  | Calibrator/Probe | Checked By | Date     |
|--|--|------------------|------------|----------|
| Vial washer  | 0239   | N/A              | SB         | 07.20.15 |
| Steam sterilizing autoclave(s)                       | 0237 & 0238  | 12.15            | SB         | 07.20.15 |
| Depyrogenating tunnel                                | 0242   | 12.15            | SB         | 07.20.15 |
| Vial filling and stoppering machine                  | 0336   | N/A              | SB         | 07.20.15 |
| Vial capping machine                                 | 0250   | N/A              | SB         | 07.20.15 |
| Weight scale (Range: 0.000-310.000g) (Steps 12 & 13) | 0262   | 8.15             | SB         | 07.20.15 |
| Weight scale (Range: 0.000-35.000kg) (Step 20)       | 0263   | 8.15             | SB         | 07.20.15 |
| Floor scale (Range: 0.0-2,250.0kg) (Step 20)         | 0245   | 8.15             | SB         | 07.20.15 |
| Floor scale (Range: 0.0-2,250.0kg) (Step 20)         | 0244   | 8.15             | SB         | 07.20.15 |
| Vial labeling machine                                | <input checked="" type="checkbox"/> 0257<br><input type="checkbox"/> 0295<br><input type="checkbox"/> 0153 | N/A              | SB         | 07.20.15 |
| Carton printing machine                              | <input type="checkbox"/> 0120<br><input type="checkbox"/> 0289<br><input checked="" type="checkbox"/> 0391 | N/A              | SB         | 07.20.15 |
| Shrink wrap machine                                  | <input checked="" type="checkbox"/> 0261<br><input type="checkbox"/> 0215                                  | N/A              | SB         | 07.20.15 |

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

Doc Number: VMR-014.00

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07/17

2072115

CYS-002

Cysteine HCl Injection 50mg/mL

Sandoz Inc.

| Line | Description   | Equipment   | Quantity                                | Lot                            | Date                             | Signature                   |                               |                             |                                  |                              |                 |                 |
|------|---|---|---|--------------------------------|----------------------------------|-----------------------------|-------------------------------|-----------------------------|----------------------------------|------------------------------|-----------------|-----------------|
| 1.   | Ensure that the vial prep room (2129) and equipment in the room are clean and all cleaning checklist forms have been completed and signed. (MFG-031-03 "Building 2 Vial Production Cleaning Checklist" and MFG-005-03 "Manufacturing Daily Checklist for Line 2 Support Rooms# 2125-2131")  |   |   |                                | ELM<br>07-17-15                  | ELM<br>07-17-15             |                               |                             |                                  |                              |                 |                 |
| 2.   | a. Obtain depyrogenated rubber stoppers for the lot.<br>b. Record the stopper lot number and the number of stoppers received on page 1, Item 3.<br>c. Sterilize the stoppers* according to the instructions in FAE-026 "Operation of the Getinge Steam Sterilizers, ID#s 0237 and 0238."<br>d. Include a copy of FAE-026-01 "Daily Autoclave Log/Equipment ID# 0237 and # 0238" and cycle printouts for the autoclave cycle #s with the batch record.<br>e. At cycle completion, transfer the sterilized stoppers to the aseptic support room # 2119. | Rubber closure (Item 3) autoclave cycle #(s)*:<br>0238-1715-1 |   |                                | ELM<br>07-17-15                  | ELM<br>07-17-15             |                               |                             |                                  |                              |                 |                 |
| 3.   | Prepare equipment required for the production run according to MFG-044 "Equipment Preparation for SEV and Sterile Filled Vials, Building 2."  |   |   |                                | ELM<br>07-17-15                  | ELM<br>07-17-15             |                               |                             |                                  |                              |                 |                 |
| 4.   | Sterilize the equipment* and record cycle numbers for the following equipment required for this run. Include a copy of FAE-026-01 "Daily Autoclave Log/ Equipment ID# 0237 and # 0238" and cycle printouts for the autoclave cycle #s with the batch record.  | Filling surge tank: ELM 07-17-15<br>0238-071715-2             | Filling machine manifold: 0238-071715-2 | Filling needles: 0238-071715-2 | Nitrogen manifold: 0238-071715-2 | Stopper bowl: 0238-071715-2 | Stopper hopper: 0238-071715-2 | Stopper tray: 0238-071715-2 | Stopper inhibitor: 0238-071715-2 | Stopper wheel: 0238-071715-2 | ELM<br>07-17-15 | ELM<br>07-17-15 |
| 5.   | Place all prepared equipment and components in the Aseptic Support Room ID# 2119.   |   |   |                                | ADH<br>07-17-15                  | ADH<br>07-17-15             |                               |                             |                                  |                              |                 |                 |

\*Critical Process Parameter

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

| Company   | Product   | Part/Code                    | Lot     | Expiration | By/Date      | Checked by/Date |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
|---|---|------------------------------|---------|------------|--------------|-----------------|---------|-------------|------------------------------|------------|-------------|----------|---------------|------------------|------------------|---------------------------|---------|--|---------------------------|---|--|---------------------------|---|--|---------------------------|---------|--|---------------------------|--------|--|---------------------------|---------|--|---------------------------|-----------|--|---------------------------|-------|--|---------------------------|-----------|--|---------------------------|---|--|
| Sandoz Inc.   | Cysteine HCl Injection 50mg/mL  | CYS-002                      | 2072115 | 07/17      | AMH/07-21-15 | ELM/07-21-15    |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| <p>6. Ensure that the vial prep room # 2129 and equipment in the room is clean and all cleaning checklist forms have been completed and signed. Verify that cleaning has been performed by referencing MFG-031-03 "Building 2 Vial Production Cleaning Checklist" and MFG-005-03 "Manufacturing Daily Checklist for Line 2 Support Rooms# 2125-2131."</p> <p>Wash the 50mL 20mm vials (Item 2) according to the instructions in FAE-025 "Operation of the PennTech Rotary Vial Washer, ID # 0239." Depyrogenate the vials* according to the instructions in FAE-024 "Operation of the Sterilne Depyrogenating Tunnel, Model ST6, ID# 0242."</p>   |   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| <p>7. Vial Washing &amp; Depyrogenation</p> <table border="1"> <thead> <tr> <th>Item</th> <th>Lot</th> <th>Released</th> </tr> </thead> <tbody> <tr> <td>Cart</td> <td>G-16-011215</td> <td>03-19-15</td> </tr> <tr> <td>Tunnel run #</td> <td>N/A AMH/07-21-15</td> <td>N/A AMH/07-21-15</td> </tr> <tr> <td># of vials per drink wrap</td> <td>2072115</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>Verified? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(A) 205</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(B) 68</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(C) 705</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(D) 13940</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(E) 0</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>(F) 13940</td> <td></td> </tr> <tr> <td># of vials per drink wrap</td> <td>0</td> <td></td> </tr> </tbody> </table> |   |                              |         |            |              |                 | Item    | Lot         | Released                     | Cart       | G-16-011215 | 03-19-15 | Tunnel run #  | N/A AMH/07-21-15 | N/A AMH/07-21-15 | # of vials per drink wrap | 2072115 |  | # of vials per drink wrap | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |  | # of vials per drink wrap | Verified? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |  | # of vials per drink wrap | (A) 205 |  | # of vials per drink wrap | (B) 68 |  | # of vials per drink wrap | (C) 705 |  | # of vials per drink wrap | (D) 13940 |  | # of vials per drink wrap | (E) 0 |  | # of vials per drink wrap | (F) 13940 |  | # of vials per drink wrap | 0 |  |
| Item  | Lot   | Released                     |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| Cart  | G-16-011215   | 03-19-15                     |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| Tunnel run #  | N/A AMH/07-21-15  | N/A AMH/07-21-15             |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | 2072115   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No           |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | Verified? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (A) 205   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (B) 68  |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (C) 705   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (D) 13940   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (E) 0   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | (F) 13940   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| # of vials per drink wrap   | 0   |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| <p>8. Prior to filling operations, the release of the bulk product must be verified.</p> <table border="1"> <thead> <tr> <th>Product</th> <th>Lot number:</th> <th>Weight of bulk product (kg):</th> </tr> </thead> <tbody> <tr> <td>L-Cysteine</td> <td>2072115</td> <td>762.0 kg</td> </tr> <tr> <td>Release date:</td> <td>07-20-15</td> <td></td> </tr> </tbody> </table>   |   |                              |         |            |              |                 | Product | Lot number: | Weight of bulk product (kg): | L-Cysteine | 2072115     | 762.0 kg | Release date: | 07-20-15         |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| Product   | Lot number:   | Weight of bulk product (kg): |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| L-Cysteine  | 2072115   | 762.0 kg                     |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |
| Release date:   | 07-20-15  |                              |         |            |              |                 |         |             |                              |            |             |          |               |                  |                  |                           |         |  |                           |   |  |                           |   |  |                           |         |  |                           |        |  |                           |         |  |                           |           |  |                           |       |  |                           |           |  |                           |   |  |

\*Critical Process Parameter

Doc Number: VMR-014.00

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\*This page shall be copied onto autoclavable paper.

|   |                               |
|---|-------------------------------|
| <b>50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2</b> |                               |
| Company: <b>Sandoz Inc.</b>   | Product Code: <b>CYS-002</b>  |
| Material: <b>Cysteine HCl Injection 50mg/mL</b>                       | Lot #: <b>2072115</b>         |
| Manufacturing Date: <b>07/17</b>                                      | Expiration Date: <b>07/17</b> |

**Vial filling**

| Step       | Manufacturing Process  | By Date         | Checked By Date |        |        |        |        |        |        |                |                 |
|------------|--|-----------------|-----------------|--------|--------|--------|--------|--------|--------|----------------|-----------------|
| 9.         | <p>Ensure that the vial filling room and equipment in the room are clean and all cleaning checklist forms have been completed and signed. (MFG-031-03 "Building 2 Vial Production Cleaning Checklist" and MFG-005-07 "Manufacturing Daily Checklist for Line 2 Filling Suite Rooms# 2114-2124")</p>  | JS<br>07-21-15  | EUH<br>07-21-15 |        |        |        |        |        |        |                |                 |
| 10.        | <p>Set-up filling and stoppering machine according to FAE-033 "Operation of the Bosch Fill Machine, ID # 0336."</p>  | JS<br>07-21-15  |                 |        |        |        |        |        |        |                |                 |
| 11.        | <p>Record sterilizing filter pressure*<br/> <u>25</u> psi (must be ≤ 30 psi)*<br/>                     Initial Filtration Time: <u>6:45AM</u><br/>                     Final Filtration Time: <u>12:38PM</u><br/>                     Total Filtration Time: <u>5</u> hrs <u>53</u> min (not to exceed 6 hrs 0 min)*</p>   | JS<br>07-21-15  |                 |        |        |        |        |        |        |                |                 |
| 12.        | <p>Set fill volume according to FAE-033 "Operation of the Bosch Fill Machine, ID # 0336." Use scale ID# 0262 to set the fill volume.<br/>                     Calculation of fill weight: Formula: Density (g) x fill volume (mL) = fill weight (g)<br/>                     L-Cysteine HCl 50mg/mL density=1.015g</p> <table border="1"> <thead> <tr> <th>Volume(mL)</th> <th>Weight (g)</th> </tr> </thead> <tbody> <tr> <td>50.0mL</td> <td>50.75g</td> </tr> <tr> <td>51.5mL</td> <td>52.27g</td> </tr> <tr> <td>53.0mL</td> <td>53.80g</td> </tr> </tbody> </table>   | Volume(mL)      | Weight (g)      | 50.0mL | 50.75g | 51.5mL | 52.27g | 53.0mL | 53.80g | JS<br>07-21-15 | EUH<br>07-21-15 |
| Volume(mL) | Weight (g)   |                 |                 |        |        |        |        |        |        |                |                 |
| 50.0mL     | 50.75g   |                 |                 |        |        |        |        |        |        |                |                 |
| 51.5mL     | 52.27g   |                 |                 |        |        |        |        |        |        |                |                 |
| 53.0mL     | 53.80g   |                 |                 |        |        |        |        |        |        |                |                 |
| 13.        | <p>Proceed with filling and stoppering of the vials. After the initial fill volume check, verify the fill volume once approximately every 10 minutes as the filling process continues. Do not exceed 15 minutes. Rotate through all eight filling needles, 4 filling needles at a time. Record the fill volumes on FAE-033-01 "Volume Verification Record-Line 2." Refer to FAE-033-01 for fill start and end time.</p> <p>Filling start time: <u>6:47AM</u><br/>                     Is start time within 24 hours of completion of the batch manufacturing process?* <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No<br/>                     Fill end time: <u>12:41PM</u><br/>                     Total fill time: <u>5 HRS 54 MIN.</u></p> | JS<br>07-21-15  |                 |        |        |        |        |        |        |                |                 |
| 14.        | <p>Transfer all filled and stoppered vials to the vial capping machine.</p>  | JS<br>07-21-15  | EUH<br>07-21-15 |        |        |        |        |        |        |                |                 |
| 15.        | <p>Approximate # of empty vials discarded during filling and stoppering: <u>40</u><br/>                     Approximate # of filter vials discarded during filling and stoppering: <u>20</u></p>   |                 |                 |        |        |        |        |        |        |                |                 |
| 16.        | <p>Prior to completion of sterile filtration, pull a 3mL non-sterile sample of Cysteine HCl and place into a sterile empty vial. Label the vial with 'Bioburden', the vial contents and lot#. Submit the sample to QC and log onto QC-038-01 "Sample Log and Quality Control Analytical Results Tracking."</p>   | EUH<br>07-21-15 | EUH<br>07-22-15 |        |        |        |        |        |        |                |                 |

\*Critical Process Parameter

Doc Number: VMR-014.00

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

Page 6 of 9  
\*This page shall be copied onto autoclavable paper.

|             |                                |         |         |                         |
|-------------|--------------------------------|---------|---------|-------------------------|
| Company     | Product                        | Part #  | Lot #   | Expiration Date (month) |
| Sandoz Inc. | Cysteine HCl Injection 50mg/mL | CYS-002 | 2072115 | 07/17                   |

Vial filling

| Step  | Manufacturing Process   | By Date  | Checked by      |
|---|---|--|-----------------|
| 17.   | Nitrogen purging Acro 50 0.2µ filter (PN 4250) lot #:   | 07-21-15   | EUY<br>07-21-15 |
|   | Acro 50 0.2µ vent filter #1 (PN 4250) lot #:  |  |                 |
|   | Acro 50 0.2µ vent filter #2 (PN 4250) lot #:  |  |                 |
|   | Millipore Opticap 4" 0.22µ sterilizing filter (catalog #: KVGLS04HBB) lot #:  |  |                 |
|   | Sterilizing filter post-fill bubble point (alt 50 psi)*:  |  |                 |
|   | Vent filter #1 post-fill bubble point (alt 13 psi w/methanol):<br>Submit vent filter to QC and log onto QC-038-01 "Sample Log and Quality Control Analytical Results Tracking." |  |                 |
| Vent filter #2 post-fill bubble point (alt 13 psi w/methanol):<br>Submit vent filter to QC and log onto QC-038-01 "Sample Log and Quality Control Analytical Results Tracking." | 59 psi  | See QC-076-01 "Gelman Acro 50 0.2µ Filter Integrity Testing" for documentation |                 |
|   |   | See QC-076-01 "Gelman Acro 50 0.2µ Filter Integrity Testing" for documentation |                 |

\*Critical Process Parameter



|   |                                |                         |                                    |  |
|---|--------------------------------|-------------------------|------------------------------------|--|
| <b>50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2</b> |                                |                         |                                    | Doc Number: <b>VMR-014.00</b>                                      |
| <b>Company</b>  | <b>Product</b>                 | <b>Lot #</b>            | <b>Expiration Date (24 months)</b> | Page 7 of 9<br>*This page shall be copied onto autoclavable paper. |
| Sandoz Inc.   | Cysteine HCl Injection 50mg/mL | 2072115                 | 07/17                              |  |
|   |                                | <b>Proprietary Code</b> |                                    |  |
|   |                                | CYS-002                 |                                    |  |

**Vial capping**

| Step | Manufacturing Process   | By Date        | Checked by Date |
|------|---|----------------|-----------------|
| 18.  | Set-up capping machine according to the instructions in FAE-029 "Operation of the Westcapper Model RW600 - Line 2, ID# 0250."                                 | JS<br>07-21-15 | EWY<br>07-21-15 |
| 19.  | Perform vial capping on all filled and stoppered vials according to the instructions in FAE-029 "Operation of the Westcapper Model RW600 - Line 2, ID# 0250." | JS<br>7-21-15  |                 |
| 20.  | Approximate # of vials that disintegrated during capping<br>3   |                |                 |
| 21.  | Using a conveyor belt, transfer vials to the inspection area.   |                |                 |

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

07/17

2072115

CYS-002

Cysteine HCl Injection 50mg/mL

Sandoz Inc.

| Step | Manufacturing Process  | Inspected By | Checked By                                    |
|------|--|--------------|---|
| 22.  | Weigh any unused solution on the bench top scale or floor scale. Document the amount unused on page 1. Discard all unused solution after weighing.   | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 23.  | Upon completion of the filling operations, the filling equipment must be cleaned according to the instructions in MFG-045 "Post-Manufacturing Equipment Cleaning Procedure - Line 2."  | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 24.  | After use of mixing tank has completed, the mixing tank must be cleaned according to the instructions in MFG-045 "Post-Manufacturing Equipment Cleaning Procedure - Line 2."<br>A stopper reconciliation will be performed by manufacturing personnel.   | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 25.  | Approximate # of stoppers at beginning of production (Item 3, page 1 Qty received)   | EUJ 07-21-15 | EUJ 07-21-15                                  |
|      | Approximate # of stoppers returned to equipment prep room (room # 2129)  | 0            |   |
|      | Approximate # of stoppers used during production [ (A) - (B) ] = (C)   | 1500         |   |
| 26.  | All vials shall be inspected according to the instructions in MFG-036 "Manual Inspection of Filled Vials." Document the inspection process on MFG-036-01 "Filled Vial Inspection Record."  | EUJ 07-21-15 | See MFG-036-01 for vial inspection signatures |
| 27.  | Once vials have been inspected place vials in trays and transfer vials to the labeling area.   | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 28.  | Begin labeling vials according to the instructions in the SOP that corresponds with the equipment ID# on page 2. Record all labeling data on PAL-002-01 "Filled Vial Labeling Record." QA/QC must approve PAL-002-01 prior to labeling vials.  | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 29.  | Pull labeled sample vials from the production line for testing. Place samples into appropriate cartons (Item 7). Samples are pulled from the beginning, middle and end of lot.<br><br>Sterility = 20 vials (7 from beginning, 6 from middle, 7 from end)<br>Particulate Matter = 4 vials (2 from beginning, 1 from middle, 2 from end)<br>Bacterial Endotoxin = 2 vials (1 from beginning, 1 from end)<br>Fill Volume = 1 vial (1 from beginning)<br>Contract Testing = 7 vials (2 from beginning, 3 from middle, 2 from end)<br>Aluminum = 1 vial (1 from middle)<br>Total = 35 vials<br>Other requirements (# of vials):<br>NA TH 08-17-15 | EUJ 07-21-15 | EUJ 07-21-15                                  |
| 30.  | Submit 20 sample vials for sterility testing to the QC Technician responsible for Sterility Testing. Submit the remaining sample vials to QC and complete QC-038-01 "Sample Log and Quality Control Analytical Results Tracking."  | EUJ 07-21-15 | EUJ 07-21-15                                  |

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2

07/17

2072115

CYS-002

Cysteine HCl Injection 50mg/mL

| Step | Manufacturing Process   | By Date           | Checked/Date   |
|------|---|-------------------|----------------|
| 31.  | Place labeled vials into the appropriate trays (Item 7).  | L.M<br>07-21-15   | EU<br>07-21-15 |
| 32.  | Place a package insert (Item 8) within each tray.   | D.L.G<br>07-21-16 |                |
| 33.  | Set-up carton printing machine according to the instructions in the SOP that corresponds with the equipment ID# on page 2. Record carton printing data on PAL-002-07 "Printed Container Packaging Record." QA/QC must approve PAL-002-07 prior to printing trays. Print lot # and exp. date on all trays. | U<br>07-21-15     | EU<br>07-21-15 |
| 34.  | Once trays have been labeled, shrink wrap the trays according to the instructions in FAE-023 "Operation of Lantech Shrink Wrappers, ID#'s 0215 and 0261."   | EU<br>07-21-15    | S<br>07-21-15  |
| 35.  | Randomly pull the required amount of retention sample vials requested on MFG-037-01 "Retention Sample Form for Sandoz Inc. Drug Products" for the corresponding products. Document the data on MFG-037-01.  | EU<br>07-21-15    | S<br>07-21-15  |
| 36.  | Place 5 shrink-wrapped trays in applicable shipping box (Item 9).   | EU<br>08-10-15    | S<br>08-10-15  |
| 37.  | Prepare the shipping box labels. Place a label on PAL-002-12 "Sandoz Shipping Label Record - 50mL Cysteine" and submit to QA for approval.  | EU<br>07-21-15    | S<br>07-21-15  |
| 38.  | Apply the approved shipping box labels (Item 10) to each shipping box.  | EU<br>08-10-15    | S<br>08-10-15  |
| 39.  | Load finished product onto carts or pallets and transfer to quarantine area.  | EU<br>08-10-15    |                |
| 40.  | Document lot reconciliation on MFG-057-24 "Calculation of Percent Yields For Bulk Solution and Final Containers of Sterile Drug Products."  | EU<br>07-22-15    | S<br>07-22-15  |

Manufacturing Supervisor Review

Review by/date:  08-11-15

7/17/15 07-15-15 07-17-15

|   |  |                                  |
|---|--|----------------------------------|
| <b>Form Title: Filling/Stoppering and Capping Line Clearance Record</b> |  | Doc Number: MFG-048-01.01        |
| Lot #: 2072115  |  | Page 1 of 1                      |
| Product: Cysteine 50mL  | * This form shall be copied onto autoclavable paper. |                                  |
| Form Issue Date: JAN 30 2014  |  | Form Effective Date: MAR 26 2014 |

**Filling/Stoppering Area:**

Pre Line Clearance Performed by/date/time: JS 07-21-15 6:01AM. Verified by/date/time: Q 7-21-15 6:50AM

Post Line Clearance Performed by/date/time: JS 07-21-15 12:41pm. Verified by/date/time: Q 7-21-15 12:50pm

**Capping Area:**

Pre Line Clearance Performed by/date/time: JS 07-21-15 6:03AM. Verified by/date/time: Q 7-21-15 6:50AM

Post Line Clearance Performed by/date/time: Q 7-21-15 12:50pm. Verified by/date/time: JS 07-21-15 12:52pm.

Comments: JS 7-21-15

Performed by/date: JS 7-21-15

NA 07-15-15 07-17-15

Form Title: Volume Verification Record-Line 2

|   |                               |                          |                                  |
|---|-------------------------------|--------------------------|----------------------------------|
| Doc Number: <b>FAE-033-01.02</b>                    |                               | Page 1 of 3              |                                  |
| *This form shall be copied onto autoclavable paper. |                               |                          |                                  |
| Form Issue Date: <b>JAN 30 2014</b>                 |                               |                          |                                  |
| Form Effective Date: <b>MAR 20 2014</b>             |                               |                          |                                  |
| Lot #: <b>2072115</b>                               | Type of Soln: <b>Cysteine</b> | Fill volume: <b>50mL</b> | Vial Size: <b>50mL 20mm</b>      |
| Weight Range: <b>50.75g - 53.80g</b>                | Target Weight: <b>52.27 g</b> | Scale ID#: <b>0262</b>   | Calibration due: <b>08-06-15</b> |

| Needle   | Weight | Time | Time    |
|----------|--------|------|---------|
| Needle 1 | 51.84  | ✓    | 0:47AM  |
| Needle 2 | 52.29  | ✓    | 12:41pm |
| Needle 3 | 53.06  | ✓    |         |
| Needle 4 | 52.77  | ✓    |         |

Sample the volume of 4 of the filling needles at least every 10 minutes (not to exceed 15 minutes) during filling operations. Rotate through all 8 filling needles, 4 needles at a time. When 50mL and 100mL vials are being filled weight checks will only be performed on needles 5-8 due to the filling format.

| Needle | Weight | Time | Time   |
|--------|--------|------|--------|
| 1      | 51.84  | ✓    | 8:10AM |
| 2      | 51.95  | ✓    |        |
| 3      | 52.69  | ✓    |        |
| 4      | 52.23  | ✓    |        |
| 5      | 51.84  | ✓    | 8:20AM |
| 6      | 52.10  | ✓    |        |
| 7      | 52.63  | ✓    |        |
| 8      | 52.30  | ✓    |        |
| 1      | 51.80  | ✓    | 8:30AM |
| 2      | 51.86  | ✓    |        |
| 3      | 52.59  | ✓    |        |
| 4      | 52.06  | ✓    |        |
| 5      | 52.73  | ✓    | 8:40AM |
| 6      | 52.90  | ✓    |        |
| 7      | 53.34  | ✓    |        |
| 8      | 52.72  | ✓    |        |



Form Title: Volume Verification Record-Line 2

Corresponding SOP(s) #: FAE-033

Lot #: 2072115

Weight Range: 50.75g - 53.80g

Target Weight: 52.27 g

Doc Number: FAE-033-01.02

Page 2 of 3

\*This form shall be copied onto autoclavable paper.

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 8:50AM | 51.99 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.10 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.47 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.06 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:50AM | 51.87 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.01 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.25 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 51.82 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:40AM | 51.74 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.88 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.96 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.82 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:00AM | 52.88 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.96 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 53.19 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.71 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 10:48AM | 51.80 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.94 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.13 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.79 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:50AM | 52.43 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.42 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.54 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.38 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:10AM | 52.08 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.14 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.41 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 51.98 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:00AM | 52.87 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.89 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 53.11 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.84 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 12:00PM | 51.94 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.17 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.27 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.08 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:20AM | 52.08 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.07 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.46 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 51.76 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:10AM | 52.64 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.80 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.68 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.42 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 17:10PM | 51.82 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.02 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.16 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.85 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:30AM | 52.81 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.87 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 53.20 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.89 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:20AM | 52.76 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.84 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 53.09 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.72 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 12:20PM | 51.70 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.85 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.13 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.80 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|        |       |                          |                                     |   |
|--------|-------|--------------------------|-------------------------------------|---|
| 9:40AM | 52.68 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.66 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.82 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.46 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|        | 52.46 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 11:30AM | 52.32 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 51.98 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.69 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.37 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

|         |       |                          |                                     |   |
|---------|-------|--------------------------|-------------------------------------|---|
| 12:30PM | 52.10 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.08 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.16 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |
|         | 52.24 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | S |

507-21-5 \* STOPPERS FOR BREAK



Form Title: **Volume Verification Record-Line 2**  
 Corresponding SOP(s) #: **FAE-033**  
 Lot #: **2072115**

Doc Number: **FAE-033-01.02**  
 Page 3 of 3

Net Weight: **53.80g**

Target Weight: **2.27 g**

\*This form shall be copied onto autoclavable paper.

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 5 | 6 | 7 | 8 |
|---|---|---|---|
|   |   |   |   |
|   |   |   |   |
|   |   |   |   |

| 9 | 10 | 11 | 12 |
|---|----|----|----|
|   |    |    |    |
|   |    |    |    |
|   |    |    |    |

*Handwritten:* 2072115-1  
 2072115-2  
 2072115-3

Reviewed by/date:  
*Signature* 08.12.15  
*Signature* 08.12.15

JFK 07-15-15 07-17-15

Form Title: Filled Vial Inspection Record

Doc Number: MFG-036-01.04

Page 1 of 4



Lot #: 2072115  
Solution type: Cysteine

Fill volume: 50mL  
Vial size: 50mL 20mm

Form Issue Date: FEB 26 2015

Form Effective Date: MAR 18 2015

| Performed by (name/time) | Verified by (date/time) |
|--------------------------|-------------------------|
| EUM 07-21-15 6:12am      | AR 07-21-15 6:21am      |

Light intensity verification. This step must be performed BEFORE vial inspection operations begin.

| Inspection Station/Area | Inspection Station Location | Specification: $\geq 2000$ EDX<br>Reading at white background | Acceptance                              |   | Calibrated Light Meter | ID# | Calibration Due: | Light intensity verification performed by | Date       | Time                        |
|-------------------------|-----------------------------|---|---|---|------------------------|-----|------------------|---|------------|-----------------------------|
|                         |                             |   | <input checked="" type="radio"/> Line 1 | <input checked="" type="radio"/> Line 2     |                        |     |                  |   |            |                             |
| Area 1                  | 6200                        | 3600  | <input checked="" type="radio"/> Yes    | <input type="radio"/> No, notify Supervisor |                        | EUM | 07-21-15         |   | 03-25-2016 | SUM 07-21-15<br>6:20 6:24am |
| Area 2                  | 5200                        | 4200  | <input checked="" type="radio"/> Yes    | <input type="radio"/> No, notify Supervisor |                        | EUM | 07-21-15         |   |            | 6:24am                      |
| Area 3                  | 8400                        | 3600  | <input checked="" type="radio"/> Yes    | <input type="radio"/> No, notify Supervisor |                        | EUM | 07-21-15         |   |            | 6:24am                      |
| Area 4                  | 9200                        | 4400  | <input checked="" type="radio"/> Yes    | <input type="radio"/> No, notify Supervisor |                        | EUM | 07-21-15         |   |            | 6:25am                      |

According to MFG-056 "Manual Inspection of Filled Vials" each inspector MUST take a 15 minute break for every 2 hours ± 30 min. of inspection.

| Inspected by (name/time) | Times of inspection (time-time) | Inspected by (name/time) | Times of inspection (time-time) | Inspected by (name/time) | Times of inspection (time-time) |
|--------------------------|---------------------------------|--------------------------|---------------------------------|--------------------------|---------------------------------|
| EUM 07-21-15             | 6:20am - 9:20am                 | AR 07-21-15              | 6:50am - 9:20am                 | AR 07-21-15              | 6:50am - 9:20am                 |
| AR 07-21-15              | 9:36am - 9:51am                 | AR 07-21-15              | 9:37am - 10:00am                | AR 07-21-15              | 9:37am - 10:00am                |
| AR 07-21-15              | 10:49am - 12:00pm               | AR 07-21-15              | 10:50am - 12:31pm               | AR 07-21-15              | 10:53am - 12:15pm               |
| AR 07-21-15              | 12:25pm - 12:45pm               | AR 07-21-15              | 12:25pm - 12:45pm               | AR 07-21-15              | 12:25pm - 12:45pm               |



Form Title: Filled Vial Inspection Record

Doc Number: MFG-036-01.04

Page 2 of 4



Lot #:

2072115

Inspection Results:

| Category    | Defect   | Description (not limited to the following)  | # Rejected | Total # rejected from each category | Recorder by/Date | Verifier by/Date |   |
|-------------|--|---|------------|-------------------------------------|------------------|------------------|---|
| Critical    | Glass defect   | Broken, cracked, internal contamination, spike, bird swing  | 5          | (A) 16                              | ELM<br>07-21-15  | AR<br>07-21-15   |   |
|             | Seal integrity   | Leaking vial, missing stopper   | 2          |                                     |                  |                  |   |
|             | Particles  | Glass   |            |                                     |                  |                  | 4 |
|             |  | Rubber  |            |                                     |                  |                  | 6 |
|             |  | Metal   |            |                                     |                  |                  | 0 |
|             |  | Fibers  |            |                                     |                  |                  | 3 |
|             |  | Other   |            |                                     |                  |                  | 2 |
| Fill volume | Overfill (excluding diluents $\geq 30\text{mL}$ ) or underfill | 0   |            |                                     |                  |                  |   |
| Major       | Glass defect   | Bent, chipped, crizzle, flared, leaner, rocker, bulge, bump check ( $>2.36\text{mm}$ )  | 15         | (B) 41                              | ELM<br>07-21-15  |                  |   |
|             | Seal Integrity   | Partial crimp, missing cap  | 26         |                                     |                  |                  |   |
|             | No Fill  | No product in vial  | 0          |                                     |                  |                  |   |
|             | Cosmetic   | Dented caps, blemishes, scratches ( $>0.2\text{mm}$ wide, full body length, or exceeds 360 degrees, spotting, brush marks, seams, external contamination, bump check, bubbles, stones | 60         |                                     |                  |                  |   |
| Minor       | Fill volume  | Overfill (diluents $\geq 30\text{mL}$ )   | 0          | (C) 60                              |                  |                  |   |

Note - Refer to PDA tubular/molded glass lexicon for defect description if necessary

| Other Defect (Description) | # Rejected (Add to A/B or C above) | Recorder by/Date | Verifier by/Date | MFG Assigned Category (Critical-Major-Minor) | QA Review Final Date | Accepted (Inspector No) |
|----------------------------|------------------------------------|------------------|------------------|--|----------------------|-------------------------|
|                            |                                    | ALL              | ELM 07-21-15     |  |                      |                         |
|                            |                                    |                  |                  |  |                      |                         |
|                            |                                    |                  |                  |  |                      |                         |



Form Title: Filled Vial Inspection Record

Doc Number: MFG-036-01.04

Page 3 of 4

Lot #:

2072115


**Calculations:**

|   | Total # of vials inspected | Recorded by/Date |
|---|----------------------------|------------------|
| Total # of rejects A+B+C=D  | (D) 117                    | ELM<br>07-22-15  |
| # of labeled vials discarded (E) from P.A.L.-002-01                       | (E) 5                      |                  |
| # of labeled and packaged vials (F) from P.A.L.-002-01                    | (F) 13301                  |                  |
| # of un-labeled vials discarded during labeling (G) from P.A.L.-002-01    | (G) 0                      |                  |
| # of inspected unlabeled vials submitted for GC testing (when applicable) | (H) 315                    |                  |
| D+E+F+G+H=J, the total # of vials inspected                               | (J) 13738                  |                  |


|  | Defect Rate                | Meets Specification?  | Performed by/Date | Verified by/Date |
|--|----------------------------|---|-------------------|------------------|
| <b>Critical Defects:</b>                                 |                            |   |                   |                  |
| # rejected (A) 16 / # inspected (J) 13738 x 100 = 0.12 % | Alert > 1.2% Action > 1.7% | <input checked="" type="checkbox"/> Yes (≤ 1.2%) Acceptable<br><input type="checkbox"/> Alert (> 1.2 and ≤ 1.7%)* Acceptable<br><input type="checkbox"/> Action (> 1.7%)** Not Acceptable | ELM<br>07-22-15   | AKR<br>07-22-15  |
| <b>Major Defects:</b>                                    |                            |   |                   |                  |
| # rejected (B) 41 / # inspected (J) 13738 x 100 = 0.30 % | Alert > 2.4% Action > 3.4% | <input checked="" type="checkbox"/> Yes (≤ 2.4%) Acceptable<br><input type="checkbox"/> Alert (> 2.4 and ≤ 3.4%)* Acceptable<br><input type="checkbox"/> Action (> 3.4%)** Not Acceptable |                   |                  |
| <b>Minor Defects:</b>                                    |                            |   |                   |                  |
| # rejected (C) 60 / # inspected (J) 13738 x 100 = 0.44 % | Alert > 3.6% Action > 5.1% | <input checked="" type="checkbox"/> Yes (≤ 3.6%) Acceptable<br><input type="checkbox"/> Alert (> 3.6 and ≤ 5.1%)* Acceptable<br><input type="checkbox"/> Action (> 5.1%)** Not Acceptable |                   |                  |

\* Check and document trending in comment section. CAPA required if alert level is exceeded for 3 consecutive days or 3 consecutive lots of same product.  
 \*\* 100% re-inspection and CAPA required.  
 \*\*\* Check and document trending in comment section. Minor defects do not impact product quality or process capability.

| Post-Inspection Time Clearance | Performed by/date/time | Verified by/date/time |
|--------------------------------|------------------------|-----------------------|
| ELM 07-22-15 3:00 PM           | AL 07-21-15 3:00 P.m   |                       |

|   |  |                                  |
|---|--|----------------------------------|
|  | <b>Form Title: Filled Vial Inspection Record</b> | <b>Doc Number: MFG-036-01.04</b> |
|   | <b>Lot #: 2072115</b>                            | Page 4 of 4                      |

|                 |           |
|-----------------|-----------|
| <b>Comments</b> | ✓ 5.11.15 |
|-----------------|-----------|

|  |   |
|--|---|
| <b>Manufacturing Supervisor Review</b> | Review by/date:  08.11.15 |
|--|---|

7/8 07-15-15 07/15/15

Form Title: **AQL Vial Inspection**  
 Product: **Cysteine** Lot #: **2072115**  
 Vial Size: **50mL 20mm** Fill Volume: **50mL**  
 Doc Number: **QC-090-01.01** Page 1 of 2  
 Form Issue Date: **JAN 15 2015**  
 Form Effective Date: **JUL 02 2015**

Vial ID: **13940** Vial Lot: **315**

Inspection Station: **0412** ID#: **0294** Cal Due: **03-25-2016**  
 Performed By: **6400** Date: **07-22-15** Time: **11:55 am**  
 Performed By: **4000** Date: **07-22-15** Time: **11:55 am**

Check one:  Normal Inspection  Tightened Re-Inspection

| Lot/Batch Size | Sample Size | Count | Acceptance/Rejection Ratio | Pass/Fail |
|----------------|-------------|-------|----------------------------|-----------|
| 9-15           | 2           | 0/1   | 0/1                        | 0/1       |
| 16-25          | 3           | 0/1   | 0/1                        | 0/1       |
| 26-50          | 8           | 0/1   | 0/1                        | 1/2       |
| 51-90          | 13          | 0/1   | 0/1                        | 1/2       |
| 91-150         | 20          | 0/1   | 0/1                        | 2/3       |
| 151-280        | 32          | 0/1   | 0/1                        | 3/4       |
| 281-500        | 50          | 0/1   | 1/2                        | 5/6       |
| 501-1,200      | 80          | 1/2   | 2/3                        | 7/8       |
| 1,201-3,200    | 125         | 2/3   | 3/4                        | 10/11     |
| 3,201-10,000   | 200         | 3/4   | 5/6                        | 14/15     |
| 10,001-35,000  | 315         | 5/6   | 7/8                        | 21/22     |
| 35,001-150,000 | 500         | 7/8   | 10/11                      | 21/22     |
| Rejected       | 0           | 0     | 0                          | 0         |

| Lot/Batch Size | Sample Size | Count | Acceptance/Rejection Ratio | Pass/Fail |
|----------------|-------------|-------|----------------------------|-----------|
| 9-15           | 2           | 0/1   | 0/1                        | 0/1       |
| 16-25          | 3           | 0/1   | 0/1                        | 0/1       |
| 26-50          | 8           | 0/1   | 0/1                        | 1/2       |
| 51-90          | 13          | 0/1   | 0/1                        | 1/2       |
| 91-150         | 20          | 0/1   | 0/1                        | 1/2       |
| 151-280        | 32          | 0/1   | 1/2                        | 2/3       |
| 281-500        | 50          | 1/2   | 1/2                        | 3/4       |
| 501-1,200      | 80          | 1/2   | 1/2                        | 5/6       |
| 1,201-3,200    | 125         | 1/2   | 2/3                        | 8/9       |
| 3,201-10,000   | 200         | 2/3   | 3/4                        | 12/13     |
| 10,001-35,000  | 315         | 3/4   | 5/6                        | 18/19     |
| 35,001-150,000 | 500         | 5/6   | 8/9                        | 18/19     |
| Rejected       | N/A         | N/A   | N/A                        | N/A       |

\*Describe all defects in comments section. Refer to SOP QC-090 and/or PDA TR43 Lexicon which contains defect descriptions and pictures.



Form Title: AQL Vial Inspection

Doc Number: QC-090-01.01

2072115

Page 2 of 2

|                                    |  |
|------------------------------------|--|
| Comment<br>Describe defect(s) here | N/A<br><br>NJ 07-22-15   |
| Results                            | Check one: <input checked="" type="checkbox"/> PASS or <input type="checkbox"/> FAIL If fail, notify the Manufacturing Supervisor. |
| Inspection Performed By            | Initials/Date<br>NJ 07-22-15   |
| VOC Reviewed                       | Initials/Date<br>MA 07-23-15   |

Form Title: Filled Vial Labeling Record

Doc Number: PAL-002-01.03  
Page 1 of 5  
Form Effective Date  
APR 25 2014

Form Issue Date  
APR 15 2014

Lot #  
2072115

|   |   |
|---|---|
| Label Information                         | Label Information (Check this box if you are using a pre-printed label) |
| Lot #<br>2072115                          | QA recorded by/date<br>JNA 07-15-15                                     |
| Fill volume<br>50 mL                      | Manufacturing Supervisor verified by/date<br>ECM 07-21-15               |
| Expiration date<br>07/17                  | Performed by/date/time<br>JNA 07-21-15<br>7:33 AM                       |
| Type of diluent/drug solution<br>Cysteine | Checked by/date/time<br>JNA 07-21-15<br>7:33am                          |
| Company<br>Sandoz                         |   |

ID# 0153 (Building 1)     ID# 0295 (Building 1)     ID# 0257 (Building 2)

QA recorded by/date (using PAL-004)  
 JNA 07-15-15

Verified by/date (using PAL-004)  
 ECM 07-21-15

L-018-01  
 13,940  
 16,000  
 L-018-01-062615  
 A 07-21-15

Place label sample here (roll #1) (affix all additional roll label samples to pages 4 and 5 of this form)

**L-Cysteine Hydrochloride Injection, USP**  
 50 mg/mL  
 For IV Use Only After Dilution  
 Do Not Dispense As A Unit

SANDOZ  
 NDC 66758-005-01  
 PHARMACY BULK PACKAGE  
 NOT FOR DIRECT INFUSION

Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP; Water for Injection, USP, q.s., Air  
 Directions for Use: See package insert.  
 Warning: For IV use only. Must be diluted before use. Contents should be dispensed promptly after initial closure puncture. Discard unused contents after 4 hours.  
 Store at controlled room temperature 15-30°C (59-86°F). Do not freeze.  
 Contains no more than 5,000 mcg/L of aluminum.  
 Manufactured for: Sandoz Inc., Princeton, NJ 08540  
 Rev. 06-2012  
 Date Time Entered:

Correct label part # (refer to Label Request and Invoice above)  
 Lot #  
 Fill volume  
 Exp. date  
 Type of diluent/drug solution  
 Company  
 Overprint  
 Diluent labels (3 lines)    Drug 2mL - 5mL labels (2 lines)  
 Drug 10mL - 50mL labels (1 line)

QA label approval by/date  
JHW 07-21-15



Form Title: Filled Vial Labeling Record

Doc Number: PAL-002-01.03

Page 2 of 5

Lot #: 2072115

| Via label challenge performed by/date/time  |   | Via label challenge checked by/date/time  |  |
|---|---|---|--|
| <input checked="" type="checkbox"/> 07-21-15 8:03 AM<br><input type="checkbox"/> 07-21-15 8:03 AM   | <input checked="" type="checkbox"/> 07-21-15 1.M<br><input type="checkbox"/> 07-21-15 8:03 AM   |   |  |
| <input checked="" type="checkbox"/> Cap Color<br><input checked="" type="checkbox"/> Seal<br><input checked="" type="checkbox"/> Label<br><input checked="" type="checkbox"/> Green<br><input checked="" type="checkbox"/> L.S.<br><input checked="" type="checkbox"/> Color<br><input checked="" type="checkbox"/> Orange<br><input checked="" type="checkbox"/> Purple<br><input checked="" type="checkbox"/> Pink<br><input checked="" type="checkbox"/> Blue<br><input checked="" type="checkbox"/> White | <div style="text-align: center;">N/A</div>  |   |  |
| <input checked="" type="checkbox"/> Label Recognition<br><input checked="" type="checkbox"/> Label Readability<br><input checked="" type="checkbox"/> Label Alignment<br><input checked="" type="checkbox"/> Label Position<br><input checked="" type="checkbox"/> Label Orientation<br><input checked="" type="checkbox"/> Label Color<br><input checked="" type="checkbox"/> Label Contrast<br><input checked="" type="checkbox"/> Label Durability<br><input checked="" type="checkbox"/> Label Adhesion   | <div style="text-align: center;">N/A</div>  |   |  |
| <input checked="" type="checkbox"/> 3,940<br><input type="checkbox"/> 13,205 N/A + 60 + 36<br><input checked="" type="checkbox"/> N/A<br><input checked="" type="checkbox"/> 07-21-15   | <div style="text-align: center;">N/A</div>  |   |  |
| <input checked="" type="checkbox"/> L.M 07-21-15 8:15 AM<br><input checked="" type="checkbox"/> DD16 07-21-15 12:26 PM<br><input checked="" type="checkbox"/> A.L 07-21-15 1:21 PM  | <input checked="" type="checkbox"/> 10<br><input checked="" type="checkbox"/> 10<br><input checked="" type="checkbox"/> 10<br><input checked="" type="checkbox"/> N/A | <input checked="" type="checkbox"/> yes <input type="checkbox"/> no<br><input checked="" type="checkbox"/> yes <input type="checkbox"/> no<br><input checked="" type="checkbox"/> yes <input type="checkbox"/> no<br><input type="checkbox"/> yes <input type="checkbox"/> no<br><input type="checkbox"/> yes <input type="checkbox"/> no<br><input type="checkbox"/> yes <input type="checkbox"/> no | <input checked="" type="checkbox"/> 07-21-15 |



Form Title: Filled Vial Labeling Record

Doc Number: PAL-002-01.03  
Page 3 of 5

Lot #: 2072115

|     |        |  |
|-----|--------|--|
| (A) | 5      | For similar labeling form  |
| (B) | 80     | For vials (only) based on  |
| (C) | 5      | of labels with discrepancy   |
| (D) | 13,301 | of labeled and checked vials   |
| (E) | 13,391 | Total number of vials  |
| (F) | 8      | of non-labeled vials discrepancy   |
| (G) | 2,590  | of labeled vials discrepancy   |
| (H) | 15,981 | Total number of vials  |
| (I) | 99.8 % | Must be within 98-102%   |
|     |        | Reconciliation <input checked="" type="checkbox"/> Pass <input type="checkbox"/> Fail<br>If fail, request a CAPA for investigation |

RA  
07-22-15

EW  
07-22-15

Vial label challenge performed by/date/time  
 EW 07-21-15 1:34 PM A.L 07-21-15 1:34 PM

Vial label challenge checked by/date/time  
 EW 07-21-15 1:35 PM GR 07-21-15 1:35 PM  
 EW 07-22-15 7:40 AM

Vials labeled by/date  
 EW 07-21-15

Comments  
 N/A  
 EW 07-21-15

① DOCUMENTS ON 08.19.15. 8 08.19.15





Form Title: Filled Vial Labeling Record

Doc Number: PAL-002-01.03

Page 4 of 5

Lot #: 2072115

Additional Label Samples

|   |   |
|---|---|
| <p>Roll # 2</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b><br/>Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE<br/>NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution<br/>Do Not Dispense As A Unit</p> <p>50 mL</p> <p>▲ SANDOZ</p> <p>Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP; Water for Injection, USP, q.s.; Air replaced with Nitrogen, pH 1.0-2.5</p> <p>Directions for Use: See package insert.</p> <p>Warnings: For IV use only. Must be diluted before use. Contents should be dispensed promptly after initial closure puncture. Discard unused contents after 4 hours.</p> <p>Store at controlled room temperature 15°-30°C (59°-86°F). Do not freeze.</p> <p>Contains no more than 5,000 mcg/L of aluminum.</p> <p>Manufactured for: Sandoz Inc., Princeton, NJ 08540</p> <p>Rev. 06-2012</p> <p>Date/Time Entered:</p> <p>L 2072115 E 07/17</p> <p>(01)00366758005019</p> | <p>Roll # 6</p> <p>Approval by/date</p> <p>Roll # 6</p> |
| <p>Roll # 3</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b><br/>Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE<br/>NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution<br/>Do Not Dispense As A Unit</p> <p>50 mL</p> <p>▲ SANDOZ</p> <p>Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP; Water for Injection, USP, q.s.; Air replaced with Nitrogen, pH 1.0-2.5</p> <p>Directions for Use: See package insert.</p> <p>Warnings: For IV use only. Must be diluted before use. Contents should be dispensed promptly after initial closure puncture. Discard unused contents after 4 hours.</p> <p>Store at controlled room temperature 15°-30°C (59°-86°F). Do not freeze.</p> <p>Contains no more than 5,000 mcg/L of aluminum.</p> <p>Manufactured for: Sandoz Inc., Princeton, NJ 08540</p> <p>Rev. 06-2012</p> <p>Date/Time Entered:</p> <p>L 2072116 E 07/17</p> <p>(01)00366758005019</p> | <p>Roll # 7</p> <p>Approval by/date</p> <p>Roll # 7</p> |
| <p>Roll # 4</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b><br/>Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE<br/>NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution<br/>Do Not Dispense As A Unit</p> <p>50 mL</p> <p>▲ SANDOZ</p> <p>Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP; Water for Injection, USP, q.s.; Air replaced with Nitrogen, pH 1.0-2.5</p> <p>Directions for Use: See package insert.</p> <p>Warnings: For IV use only. Must be diluted before use. Contents should be dispensed promptly after initial closure puncture. Discard unused contents after 4 hours.</p> <p>Store at controlled room temperature 15°-30°C (59°-86°F). Do not freeze.</p> <p>Contains no more than 5,000 mcg/L of aluminum.</p> <p>Manufactured for: Sandoz Inc., Princeton, NJ 08540</p> <p>Rev. 06-2012</p> <p>Date/Time Entered:</p> <p>L 2072115 E 07/17</p> <p>(01)00366758005019</p> | <p>Roll # 8</p> <p>Approval by/date</p> <p>Roll # 8</p> |
| <p>Roll # 5</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b><br/>Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE<br/>NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution<br/>Do Not Dispense As A Unit</p> <p>50 mL</p> <p>▲ SANDOZ</p> <p>Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP; Water for Injection, USP, q.s.; Air replaced with Nitrogen, pH 1.0-2.5</p> <p>Directions for Use: See package insert.</p> <p>Warnings: For IV use only. Must be diluted before use. Contents should be dispensed promptly after initial closure puncture. Discard unused contents after 4 hours.</p> <p>Store at controlled room temperature 15°-30°C (59°-86°F). Do not freeze.</p> <p>Contains no more than 5,000 mcg/L of aluminum.</p> <p>Manufactured for: Sandoz Inc., Princeton, NJ 08540</p> <p>Rev. 06-2012</p> <p>Date/Time Entered:</p> <p>L 2072116 E 07/17</p> <p>(01)00366758005019</p> | <p>Roll # 9</p> <p>Approval by/date</p> <p>Roll # 9</p> |

Handwritten notes: R/A, 07-21-15, 07-21-15



Form Title: Filled Vial Labeling Record

Doc Number: PAL-002-01.03

Page 5 of 5

Lot #:

2072115

Additional label samples

|                               |                               |
|-------------------------------|-------------------------------|
| Roll # 10<br>Approval by/date | Roll # 14<br>Approval by/date |
| Roll # 11<br>Approval by/date | Roll # 15<br>Approval by/date |
| Roll # 12<br>Approval by/date | Roll # 16<br>Approval by/date |
| Roll # 13<br>Approval by/date | Roll # 17<br>Approval by/date |

*Handwritten notes:*  
- In the cell for Roll # 11: M/A  
- In the cell for Roll # 12: A  
- In the cell for Roll # 12: 07-21-15  
- A large diagonal line is drawn across the table from the top-left to the bottom-right.

Manufacturing Supervisor  
Reviewed by Date

08-11-15

7/15/15 07-17-15

**Form Title: Printed Container (Carton) Packaging Record**

Doc Number: PAL-002-07.03 Page 1 of 2

Lot # **2072115** Product **Cysteine 50mL**

Vial size **50mL 20mm** Printed container name/part # (see Vial Manufacturing Record page 1) **Cysteine / L-023-01**

Form Issue Date **APR 15 2014**

Form Effective Date **APR 25 2014**

|   |                                   |                         |   |
|---|-----------------------------------|-------------------------|---|
| Printed Container Request and Check-Out | # of printed containers requested | Requested by/date       | Attach a sample of the printed container to the back of this form |
|   | 2788                              | U07-17-15               |   |
|   | 3055                              | U07-17-15               |   |
|   | Printed container part #          | Printed container lot # |   |
|   | L-023-01                          | L-023-01-121913 (1105)  |   |
|   |                                   | L-023-01-070215 (1950)  |   |

|                   |   |   |           |
|-------------------|---|---|-----------|
| Print Contents    | Lot or L <b>2072115</b>                 | Sample container printed by                   | By/date   |
|                   | Exp or E <b>07 / 17</b> (format: mm/yy) | QA approval (insert printed sample contained) | U07-17-15 |
| Carton Codes Used | AL ID # <b>0391</b>                     |   | U07-17-15 |

Pre-Packaging Line Clearance

Performed by/date/time **ELM07-21-15 7:22am**

Checked by/date/time **AK 07-21-15 7:22am**

|                                  |   |              |                |                |   |
|----------------------------------|---|--------------|----------------|----------------|---|
| Printed Container Reconciliation | (A) <b>2655</b>   | (B) <b>1</b> | (C) <b>119</b> | (D) <b>279</b> | Printed containers returned to inventory by date <b>U07-21-15</b> |
|                                  | # used & returned (A+B+C+D) = Total # accounted for <b>3054</b>                       |              |                |                |   |
|                                  | # cartons issued (100) = <b>99.97</b>   |              |                |                |   |
|                                  | Reconciliation performed by/date <b>ELM07-22-15</b>                                   |              |                |                |   |
|                                  | Reconciliation <input checked="" type="checkbox"/> Pass <input type="checkbox"/> Fail |              |                |                |   |
|                                  | Calculations checked by/date <b>ELM 08/11/15</b>                                      |              |                |                |   |



Form Title: Printed Container (Carton) Packaging Record

Doc Number: PAL-002-07.03

Page 2 of 2

Lot #

2072115


| Inspection                 | Inspected by/date/time | # of packages checked | Packaging corresponds with approved sample                          | Packaging contains correct # of units                               |
|----------------------------|------------------------|-----------------------|---|---|
| 1 <sup>st</sup> inspection | EM 07-21-15 3:00 PM    | 10                    | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| 2 <sup>nd</sup> inspection | LM 07-21-15 5:00 PM    | 10                    | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| 3 <sup>rd</sup> inspection | AR 07-22-15 7:00 AM    | 10                    | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| Additional inspection      | N/A                    |                       | <input type="checkbox"/> Yes <input type="checkbox"/> No            | <input type="checkbox"/> Yes <input type="checkbox"/> No            |
| Additional inspection      | EM 07-22-15            |                       | <input type="checkbox"/> Yes <input type="checkbox"/> No            | <input type="checkbox"/> Yes <input type="checkbox"/> No            |
| Additional inspection      |                        |                       | <input type="checkbox"/> Yes <input type="checkbox"/> No            | <input type="checkbox"/> Yes <input type="checkbox"/> No            |

| Post Packaging Line Clearance | Performed by/date/time | Checked by/date/time |
|-------------------------------|------------------------|----------------------|
|                               | EM 07-21-15 5:12 PM    | LM 07-21-15 5:12 PM  |

Comments

N/A EM 07-22-15

Manufacturing Supervisor review by/date

 08-11-15

# L-Cysteine Hydrochloride Injection, USP 0.5 g/10 mL (50 mg/mL)

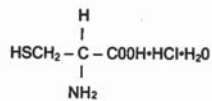
PHARMACY BULK PACKAGE  
NOT FOR DIRECT INFUSION

## DESCRIPTION

L-Cysteine Hydrochloride Injection, USP, 50 mg/mL, is a sterile, nonpyrogenic solution. Each mL contains: 50 mg of L-Cysteine Hydrochloride Monohydrate USP; Water for Injection, USP q.s.; Air replaced with Nitrogen. pH 1.0-2.5

L-Cysteine is a sulfur-containing amino acid. In premixed solutions of crystalline amino acids, cysteine is relatively unstable over time, eventually converting to insoluble cystine. To avoid such precipitation, L-Cysteine Hydrochloride Injection USP is intended to be used as an additive with Crystalline Amino Acid Injections immediately prior to administration to the patient.

The structural formula of Cysteine Hydrochloride Monohydrate USP is:



## Molecular Weight

175.63

## Molecular Formula

$\text{C}_3\text{H}_7\text{NO}_2\text{S} \cdot \text{HCl} \cdot \text{H}_2\text{O}$

## CLINICAL PHARMACOLOGY

L-Cysteine is synthesized from methionine via the trans-sulfuration pathway in the adult, but newborn infants lack the enzyme necessary to effect this conversion. Therefore, L-Cysteine is generally considered to be an essential amino acid in infants.

## INDICATIONS AND USAGE

L-Cysteine Hydrochloride Injection, USP is intended for use only after dilution as an additive to Crystalline Amino Acid Injections to meet the intravenous amino acid nutritional requirements of infants receiving total parenteral nutrition.

## CONTRAINDICATIONS

This preparation should not be used in patients with hepatic coma or metabolic disorders involving impaired nitrogen utilization.

## WARNINGS

Peripheral intravenous infusion of amino acids may induce a rise in blood urea nitrogen (BUN) especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued if BUN levels exceed normal postprandial limits and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

Solutions containing sodium ion should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

Solutions which contain potassium ion should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion such as severe hepatic insufficiency.

Hyperammonemia is of special significance in infants, as it can result in mental retardation. Therefore it is essential that blood ammonia levels be measured frequently in infants.

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined but may involve genetic defects and immature or subclinically impaired liver function.

**Frequent Clinical Evaluation and Laboratory Determinations are Necessary for Proper Monitoring During Administration.** Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolality and hemogram. White blood count and blood cultures are to be determined if indicated. Urinary osmolality and glucose should be determined frequently.

Safe use during pregnancy has not been established, therefore, infusion of amino acids should be undertaken during pregnancy only when this is deemed essential to the patients' welfare, as judged by the physician.

**WARNING:** This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

## PRECAUTIONS

Special care must be taken when administering hypertonic glucose to provide calories in diabetic or prediabetic patients.

Because of its antianabolic activity, concurrent administration of tetracycline may reduce the nitrogen sparing effects of infused amino acids.

Do not withdraw venous blood for blood chemistries through the peripheral infusion site, as interference with estimations of nitrogen containing substances may occur.

Intravenous feeding regimens which include amino acids should be used with caution in patients with a history of renal disease, pulmonary disease, or with cardiac insufficiency so as to avoid excessive fluid accumulation.

The effect of infusion of amino acids, without dextrose, upon carbohydrate metabolism of children is not known at this time.

Nitrogen intake should be carefully monitored in patients with impaired renal function. For long-term total nutrition, or if a patient has inadequate fat stores, it is essential to provide adequate exogenous calories concurrently with the amino acids. Concentrated dextrose solutions are an effective source of such calories. Such strongly hypertonic nutrient solutions should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.

## ADVERSE REACTIONS

Local reactions consisting of a warm sensation, erythema, phlebitis and thrombosis at the infusion site have occurred with peripheral intravenous infusion of amino acids, particularly if the other substances, such as antibiotics, are also administered through the same site. In such cases the infusion site should be changed promptly to another vein. Use of large peripheral veins, inline filters, and slowing the rate of infusion may reduce the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medications may need to be injected at another venous site.

Generalized flushing, fever and nausea also have been reported during peripheral infusions of amino acid solutions.

**Drug Abuse and Dependence:** None known.

## DOSAGE AND ADMINISTRATION

L-Cysteine Hydrochloride Injection USP is intended for use only after dilution in Crystalline Amino Acid Injection. Each 0.5 gram of L-Cysteine Hydrochloride Monohydrate should be combined aseptically with 12.5 grams of Crystalline Amino Acid Injection, such as that present in 250 mL of 5% Crystalline Amino Acid Injection. The admixture is then diluted with 250 mL of dextrose 50% or such lesser volume as indicated. Equal volumes of 5% Crystalline Amino Acid Injection and dextrose 50% produce a final solution which contains Crystalline Amino Acid Injection 2.5% in dextrose 25%, which is suitable for administration by central venous infusion. Administration of the final admixture should begin within one hour of mixing. Otherwise, the admixture should be refrigerated immediately and used within 24 hours of the time of mixing. For the recommended rate of administration, see the Crystalline Amino Acid Injection package insert.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

## DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE:

The pharmacy bulk package is for use in a Pharmacy Admixture Service only.

Use of this product is restricted to a suitable work area, such as a laminar flow hood. Prior to entering the vial, remove the flip-off seal and cleanse the rubber closure with a suitable antiseptic agent.

The container closure may be penetrated only one time, utilizing a suitable sterile transfer device or dispensing set which allows measured distribution of the contents. The date and time the vial was initially opened should be recorded in the space provided on the label. Transfer individual doses(s) to appropriate intravenous infusion solutions. Use of a syringe with needle is not recommended. Multiple entries increase the potential of microbial and particulate contamination.

The withdrawal of container contents should be accomplished without delay using aseptic technique. However, should this not be possible, a maximum time of 4 hours from initial closure entry is permitted to complete fluid transfer operations.

## RECOMMENDED STORAGE CONDITIONS AFTER OPENING:

Keep under laminar flow hood at room temperature. Any unused portion of the vial must be discarded within 4 hours after initial entry.

## HOW SUPPLIED

L-Cysteine Hydrochloride Injection, USP (50 mg/mL) is supplied as follows:

### PHARMACY BULK PACKAGE

| NDC Number   | Volume    |
|--------------|-----------|
| 66758-005-01 | 50 mL     |
| 66758-005-02 | 5 x 50 mL |

### Also available as: SINGLE DOSE VIAL

| NDC Number   | Volume     |
|--------------|------------|
| 66758-004-01 | 10 mL      |
| 66758-004-02 | 10 x 10 mL |

Store at controlled room temperature 15°-30°C (59°-86°F) Do not freeze.

For Sandoz Inc. Customer Service, call 1-800-525-8747

Rx only

Manufactured for:

 **SANDOZ**  
Princeton, NJ 08540

Revised: November 2009  
L-028-00

Each mL contains: 50 mg L-Cysteine Hydrochloride Monohydrate, USP;  
Water for Injection, USP, q.s.; Air replaced with Nitrogen. pH 1.0-2.5.  
Storage: Store at controlled room temperature 15°-30°C (59°-86°F). Do not freeze.  
Contents should be dispensed promptly after initial closure puncture.  
Discard unused contents after 4 hours.  
Warning: For IV use only. Must be diluted before use.  
Directions for use: See package insert.  
Contains no more than 5,000 mcg/L of aluminum.  
Manufactured for: Sandoz Inc.  
Princeton, NJ 08540  
Rev. 06-2012



L 2072115  
E 07/17

**L-Cysteine Hydrochloride**  
Injection, USP  
50 mg/mL  
5 x 50 mL Vials  
NDC 66758-005-02

**SANDOZ**

Pharmacy Bulk Package  
Not For Direct Infusion  
For IV Use Only After Dilution

Rx only


78 07-15-15 W 071715

|  |  |   |  |
|--|--|---|--|
| <b>Form Title: Package Insert Record</b> |  | <b>Doc Number: PAL-002-08.03</b>          |  |
| <b>Lot #</b><br>2072115                  | <b>Product</b><br>Cysteine 50mL  | Page 1 of 1                               |  |
| <b>Vial Size</b><br>50mL 20mm            | <b>PI name / part # (see Vial Manufacturing Record page 1)</b><br>Cysteine 50mL/L-028-00 | <b>Form Issue Date</b><br>APR 15 2014     |  |
|  |  | <b>Form Effective Date</b><br>APR 25 2014 |  |

| # of package inserts forecasted | package inserts forecasted by/date | package inserts sample                     |
|---------------------------------|------------------------------------|--|
| 2788                            | EUM 07-21-15                       | Attach a sample of the package insert here |
| 2796                            | EUM 07-21-15                       |  |
| L-028-00-061915                 | L-028-00                           |  |

|  |   |
|--|---|
| <b>Package insert attached by/date</b><br>EUM 07-21-15 | <b>QA package insert approval by/date</b><br>WLG 07-21-15 |
|--|---|

| # placed in cartons  | # of sample package inserts attached to form | # of package inserts discarded | # of package inserts returned to inventory | package inserts returned to inventory by/date |
|--|--|--------------------------------|--|---|
| (A) 2653   | (B) 1  | (C) 2                          | (D) 122                                    | EUM 07-22-15                                  |
| <b>Package Insert Reconciliation</b><br>Used & returned (A - B - C + D) = Total accounted for<br>2653 - 1 - 2 + 122 = 2778 |  |                                |  |   |
| <b>Reconciliation performed by/date</b><br>99.36<br>EUM 07-22-15   |  |                                |  |   |
| <b>Reconciliation checked by/date</b><br>08-11-15  |  |                                |  |   |

|  |
|--|
| <b>Manufacturing Supervisor review by/date</b><br><br>08-11-15 |
|--|





Form Title: Sandoz Shipping Label Record - 50mL Cysteine

Doc Number: PAL-002-12.01

Lot #

Page 1 of 2

Form Issue Date APR 15 2014

2072115

Form Effective Date APR 25 2014

|                    |                   |                         |  |
|--------------------|-------------------|-------------------------|--|
| Label Requirements | Label Type        | White 4" x 1 1/2" label | Obs completed by/date                      |
|                    | Lot #             | 2072115                 | JMA 07-15-15                               |
|                    | Exp. Date (mm/yy) | 07/17                   | Manufacturing Supervisor certified by/date |
|                    | AL Part #         | L-032-00                | ECM 07-21-15<br>ECM 07-21-15               |

|                        |  |                                     |                 |              |
|------------------------|--|-------------------------------------|-----------------|--------------|
| Label template         | QA check the appropriate check boxes when verifying label content  | White 4" x 1 1/2" label             | Lot #           | ECM 07-21-15 |
|                        |  | <input checked="" type="checkbox"/> | Expiration date | 07-21-15     |
|                        |  | <input checked="" type="checkbox"/> | Part #          |              |
| Label Sample           | <p><b>NDC 66758-008-02</b><br/> <b>L-CYSTEINE HCl Injection, USP (50 mg/mL)</b><br/> <b>5 boxes of 5 x 50 mL Vials, Total Quantity 25 Vials</b><br/>         Store at Controlled Room Temperature: 15° - 30°C (59° - 86°F).<br/>         Manufactured for:<br/>         Sandoz Inc.<br/>         Princeton, NJ 08540<br/>         L-032-00</p> <p>Affix sample label here for QA approval</p> <p><b>NDC 66758-008-02</b><br/> <b>L-CYSTEINE HCl Injection, USP (50 mg/mL)</b><br/> <b>5 boxes of 5 x 50 mL Vials, Total Quantity 25 Vials</b><br/>         Store at Controlled Room Temperature: 15° - 30°C (59° - 86°F).<br/>         Manufactured for:<br/>         Sandoz Inc.<br/>         Princeton, NJ 08540<br/>         L-032-00</p> |                                     |                 |              |
| Labels printed by/date | ECM 07-21-15   |                                     |                 |              |



Form Title: Sandoz Shipping Label Record - 50mL Cysteine

Doc Number: PAL-002-12.01

Page 2 of 2

Lot #

2072115

Label Reconciliation

| # of labels printed | # of labels used (including label sample) | # of labels discarded | Reconciliation by date |
|---------------------|---|-----------------------|------------------------|
| 560                 | 532                                       | 28                    | EUM 08-10-15           |

| Inspection                 | Inspected by | Inspected by date/time | # of shipping packages checked | Labels correspond with approved sample                              |
|----------------------------|--------------|------------------------|--------------------------------|---|
| 1 <sup>st</sup> inspection | SP           | 08-10-15 3:31pm        | 10                             | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| 2 <sup>nd</sup> inspection | SP           | 08-10-15 4:00pm        | 10                             | <input type="checkbox"/> Yes <input type="checkbox"/> No            |
| 3 <sup>rd</sup> inspection | SP           | 08-10-15 4:15pm        | 10                             | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| Additional inspection      |              |                        |                                | <input type="checkbox"/> Yes <input type="checkbox"/> No            |
| Additional inspection      |              |                        |                                | <input type="checkbox"/> Yes <input type="checkbox"/> No            |
| Additional inspection      |              |                        |                                | <input type="checkbox"/> Yes <input type="checkbox"/> No            |


Comments

L 08.10.15 SP

Manufacturing Supervisor review by/date

08.10.15

7/2 07-15-15 0807-175

|   |  |   |
|---|--|---|
|  | <b>Form Title: Calculation of Percent Yields for Bulk Solution and Final Containers of Sterile Drug Products</b> | <b>Doc Number: MFG-057-24.02</b>  |
|   | <b>Lot #: 2072115</b><br><b>Product: Cysteine 50mL</b>   | Page 1 of 2<br>Form Issue Date: <b>MAR 27 2014</b><br>Form Effective Date: <b>APR 02 2014</b> |

|               |                                     |  |               |            |
|---------------|-------------------------------------|--|---------------|------------|
| Calculation 1 | Actual amount of bulk solution used | # of weigh check vials from FAF-017-01 or FAF-033-01 (include the initial weigh check vials) | (A) 124       | g          |
|               |                                     | Total filled vials discarded from filling operations (from vial manufacturing record)        | (B) 20        |            |
|               |                                     | Total filled vials discarded from capping operations (from vial manufacturing record)        | (C) 3         |            |
|               |                                     | Total inspected vials filled (A) - (B) - (C) = (D) = (E)                                     | (D) 13301     | 13738      |
|               |                                     | Target fill weight from FAF-017-01 or FAF-033-01   | (E) 13448     | 13885      |
|               |                                     | Actual amount of bulk solution used (E) = (F) = (G)  | (F) 52.27     | g          |
|               |                                     |  | (G) 707926.46 | 725768.45g |

|               |  |  |             |   |
|---------------|--|--|-------------|---|
| Calculation 2 | Theoretical amount of bulk solution used | Initial batch size (from pg 1 of BMR)  | (H) 7620kg  | g |
|               |  | Amount used - amount per vial from mixing tank plus leftover solution from the fill pass (A) | (I) 31.656  | g |
|               |  | Theoretical amount of bulk solution used (H) - (I) = (J)                                     | (J) 730.344 | g |

|               |                                |  |               |           |
|---------------|--------------------------------|--|---------------|-----------|
| Calculation 3 | Percent yield of bulk solution | Answer to calculation 1 (G)                          | (K) 102926.46 | 725768.45 |
|               |                                | Answer to calculation 2 (J)                          | (L) 730.344   |           |
|               |                                | Percent yield of bulk solution (K) / (L) * 100 = (M) | (M) 96.25     | 99.37 %   |

⓪ Entry error at D leading to calculation errors. Corrections made 08-12-15 ELM



Form Title: Calculation of Percent Yields for Bulk Solution and Final Containers of Sterile Drug Products

Doc Number: MFG-057-24.02

Page 2 of 2


Lot #: 2072115

|   |   |   |  |  |
|---|---|---|--|--|
| Calculation 4   | Percent yield for the number of vials prepared and # of vials labeled and packaged (including test samples) | $\frac{\text{# of vials labeled and packaged (including labeled testing vials) (D) from PAE-002-01}}{\text{# of unlabeled vials submitted for testing (do not include AQL vials from vial manufacturing record)}} \times 100$ | (N) 13361  | Substrate from (Q) for (S) calculation |
|   |   |   | (O) 0  | Add to (Q) for (S) calculation         |
| Calculation 5   | Percent yield for the number of vials prepared and # of vials labeled and packaged (including test samples) | $\frac{\text{# of vials processed (do not include AQL vials from vial manufacturing record)}}{\text{# of vials received from pg. 1 of VIK}} \times 100$   | (P) 13301  | (Ra)                                   |
|   |   |   | (Q) 13940  | (Rb)                                   |
| Calculation 6   | Percent yield for calculations 3 or 4 below 90% or above 100%   | $\frac{\text{# of vials used in manufacture of (Q) (Ra) = (S) of (Q) - (Rb) - (S)}}{\text{# of vials added to file for (P) - (S) - (T)}} \times 100$  | 0  | 0                                      |
|   |   |   | 0  | 0                                      |
| Are the percent yields for calculations 3 or 4 below 90% or above 100%?   |   |   | (S) 13940  | (T) 95.42 %                            |
| Number of vials placed into quarantine (N) (# of testing vials labeled and unlabeled) - # of vials placed into quarantine |   |   | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, explain in comments. |  |

13265

N/A EUM 07-22-15

By/Date: EUM 07-22-15  
 Review by/Date: [Signature] 08-11-15


|   |  |  |  |
|---|--|--|--|
|  | Form Title: <b>Gelman Acro 50, 0.2µ Filter Integrity Testing</b> |  | Doc Number: <b>QC-076-01.00</b>                    |
|   | QC Test#: <b>QC-C-3004</b>                                       | QA/QC assigned by/date: <b>MA 07-23-15</b>     |  |
|   | Product: <b>L-Lysteine</b>                                       | Page 1 of 1                                    |  |
|   | Lot #: <b>2072115</b>  | Form Issue Date (stamp):<br><b>NOV 15 2013</b> |  |
|   |  |  | Form Effective Date (stamp):<br><b>NOV 15 2013</b> |

|                         |                |                  |                                  |
|-------------------------|----------------|------------------|----------------------------------|
| Equipment and Materials | Pressure Gauge | ID#: <b>0337</b> | Calibration Due: <b>04-09-16</b> |
|                         | Methanol Lot # | <b>7056</b>      | Expiration Date: <b>02-16</b>    |

| Vent Filter Lot #   | Type of filter to test (check one)   | Type of integrity test (check one)   | PSI Bubble Point Limit: NLT 13psi w/methanol | Integrity test passed? (if bubble point fails notify QA)         |
|---|--|--|--|--|
| <input checked="" type="radio"/> MA 07-23-15<br><b>207 21862850</b> | <input checked="" type="radio"/> Filling Vessel<br><input type="radio"/> L-1 In-Line (monthly)<br><input type="radio"/> L-1 Purging (monthly)<br><input type="radio"/> L-2 Purging (monthly) | <input type="radio"/> Pre-bubble point<br><input checked="" type="radio"/> Post bubble point | <b>19</b>                                    | <input checked="" type="radio"/> Yes<br><input type="radio"/> No |
| <input type="checkbox"/> N/A<br><b>21862850</b>                     | <input checked="" type="radio"/> Filling Vessel<br><input type="radio"/> L-1 In-Line (monthly)<br><input type="radio"/> L-1 Purging (monthly)<br><input type="radio"/> L-2 Purging (monthly) | <input type="radio"/> Pre-bubble point<br><input checked="" type="radio"/> Post bubble point | <b>18</b>                                    | <input checked="" type="radio"/> Yes<br><input type="radio"/> No |

|            |  |
|------------|--|
| QC Analyst | Testing performed by/date:<br><b>MA 07-23-15</b> |
|------------|--|

|  |                                       |
|--|---------------------------------------|
| Quality Assurance/<br>Quality Control Review | Review by/date:<br><b>JW 07-24-15</b> |
|--|---------------------------------------|

|   |   |                                  |                                  |
|---|---|----------------------------------|----------------------------------|
|  | Form Title: Method: Fill Volume                     |                                  | Doc Number: QC-066-01.01         |
|   |   |                                  | Page 1 of 1                      |
|   | QC Test #: QC- <del>E-8</del> C-3001<br>MA 07-23-15 | QA assigned by/date: MA 07-23-15 | Form Effective Date: MAR 14 2013 |
|   | Lot number: 2072115                                 |                                  |                                  |
| Product: L-cysteine   |   |                                  |                                  |

| Fill Volume Results            |   |              |   |        |                          |
|--------------------------------|---|--------------|---|--------|--------------------------|
| Fill volume                    | 50 mL   |              |   |        |                          |
| Serial # of Graduated Cylinder | MA MA 07-24-15  |              |   |        |                          |
| Balance Equipment ID#          | 0393  |              |   |        |                          |
| Number of Vials Tested         | 1   |              | <input type="checkbox"/> Pooled<br><input checked="" type="checkbox"/> Tested Individually* |        |                          |
| Individual Results (mL)        | Vial 1<br>50.88 mL  | Vial 2<br>NA | Vial 3  | Vial 4 | Vial 5<br>MA<br>07-24-15 |
| Total of vial 1 - 5 (mL)       | 50.88 mL  |              |   |        |                          |
| Average of vial 1 - 5 (mL)     | 50.88 mL  |              |   |        |                          |
| Specification                  | ≥ 50 mL   |              |   |        |                          |
| Final Result (check one)       | <input checked="" type="checkbox"/> Pass<br><input type="checkbox"/> Fail |              |   |        |                          |

Calculation if determining by weight:

$$\text{Volume of Injection, mL} = \frac{\text{Injection weight, g}}{\text{Injection density, (g/mL)}}$$


**Specification:**  
Avg of Vials ≥ Labeled Vol.

- If the volume of each container is 10mL or more, select one (1) or more containers.
- \* Unless otherwise specified, one (1) vial is used.
- If the volume of each container is more than 3mL and less than 10mL, select three (3) containers.
- If the volume of each container is 3mL or less, select five (5) containers.

|          |   |                |
|----------|---|----------------|
| Comments | $\text{Vol} = \frac{\text{mass}}{\text{density}}$ $\text{L-cysteine density} = 1.015 \text{ g/mL}$ $\text{weight} = 51.648 \text{ g}$ $\text{Vol} = \frac{51.648 \text{ g}}{1.015 \text{ g/mL}} = 50.88 \text{ mL}$ | MA<br>07-24-15 |
|----------|---|----------------|

|                   |             |
|-------------------|-------------|
| Performed By/Date | MA 07-24-15 |
|-------------------|-------------|

|                        |             |
|------------------------|-------------|
| QA/QC Reviewed By/Date | JW 07-24-15 |
|------------------------|-------------|

|   |  |  |  |  |
|---|--|--|--|--|
|  | Form Title: <b>Particulate Matter Test</b> |  | Doc Number: <b>QC-073-01.02</b>            |  |
|   |  |  | Page 1 of 1                                |  |
|   | QC Test #:<br><b>QC-C-3003</b>             | QA assigned by/date:<br><i>MA 07-23-15</i>     | Form Issue Date:<br><br><b>DEC 11 2014</b> |  |
|   | Product:<br><i>L-Cysteine</i>              | Form Effective Date:<br><br><b>DEC 12 2014</b> |  |  |
|   | Lot #:<br><i>2072115</i>                   |  |  |  |
| Fill volume:<br><i>50mL</i>   |  |  |  |  |

|  |                 |
|--|-----------------|
| Lighthouse particulate counter ID# 0276 Cal. due | <i>07-27-15</i> |
|--|-----------------|

| Test Results   |  |  |                   |   |  |
|--|--|--|-------------------|---|--|
| Number of vials tested   | S  | Particle Count                             | Count * Fill Vol. | <input checked="" type="checkbox"/> Pooled<br><input type="checkbox"/> Tested Individually* |  |
| <b>Results</b><br>(Four samples taken - the first discarded)<br><br>Data attached: | $\geq 10\mu\text{m}$<br>Specification: $< 6,000$ | 1) <i>3.8</i>                              | <i>190</i>        | Average:<br><br><i>190</i>  | <input checked="" type="checkbox"/> Pass <input type="checkbox"/> Fail |
|  |  | 2) <i>4.2</i>                              | <i>210</i>        |   |  |
|  |  | 3) <i>3.4</i>                              | <i>170</i>        |   |  |
|  |  | 4) <input checked="" type="checkbox"/> N/A |                   |   |  |
|  | $\geq 25\mu\text{m}$<br>Specification: $< 600$   | 1) <i>0.2</i>                              | <i>10</i>         | Average:<br><br><i>10</i>   | <input checked="" type="checkbox"/> Pass <input type="checkbox"/> Fail |
|  |  | 2) <i>0.4</i>                              | <i>20</i>         |   |  |
|  |  | 3) <i>0.0</i>                              | <i>0</i>          |   |  |
|  |  | 4) <input checked="" type="checkbox"/> N/A |                   |   |  |

\*For vials with a volume <25mL, the contents of at least 10 units are combined in a 100mL sterile empty vial to obtain a volume of not less than 25 mL.  
 Vials with a volume of 25-100mL may be tested individually. A total of four vials must be tested individually in this case.

|   |
|---|
| <b>Calculation:</b><br>$(\text{Fill Volume} * \text{Particle Count}) = \text{Particle Count per Vial Volume}$ |
|---|

|          |                       |
|----------|-----------------------|
| Comments | <i>NA MA 07-27-15</i> |
|----------|-----------------------|

|            |  |
|------------|--|
| QC Analyst | Testing performed by/date:<br><i>MA 07-27-15</i> |
|------------|--|

|              |  |
|--------------|--|
| QA/QC Review | Reviewed by/date:<br><i>Jhw 07-28-15</i> |
|--------------|--|

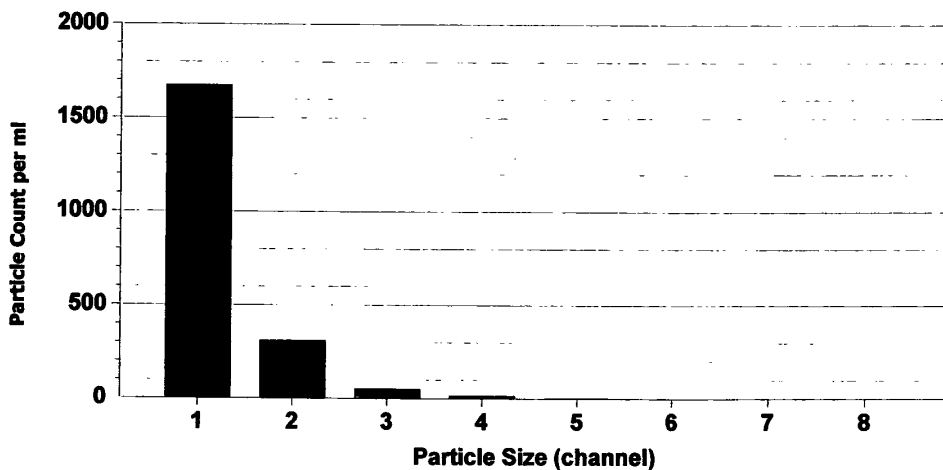


Particle Counter: LIGHTHOUSE LS-20  
 Serial Number: 100548001  
 Channel Sizes: 1.0/2.0/5.0/7.0/10.0/15.0/25.0/50.0  
 User Name: Anton  
 Lot ID: 2072115  
 Batch ID: L-Cysteine  
 Samples: 4  
 Recipe Name: Sample.rcp  
 User Entry: QC-C-3003  
 Discard First Sample

Sample Size: 5 ml  
 Location: 01  
 Syringe: 25 ml  
 Tare: 0.2 ml  
 Flow Rate: 20 ml/min  
 Dilution: 1  
 View Volume: 100%  
 LS-20 Software: V 1.5.2  
 Last Calibrated: 14-Jul-2015

| SAMPLE DATA TABLE(CUML PER ML) |          |        |       |       |      |      |      |      |      |
|--------------------------------|----------|--------|-------|-------|------|------|------|------|------|
| DATE                           | TIME     | 1.0    | 2.0   | 5.0   | 7.0  | 10.0 | 15.0 | 25.0 | 50.0 |
| 2015/07/27                     | 13:57:54 | 1693.0 | 322.4 | 55.2  | 17.2 | 3.8  | 1.0  | 0.2  | 0.0  |
| 2015/07/27                     | 13:58:10 | 1662.6 | 308.0 | 52.8  | 19.6 | 4.2  | 1.0  | 0.4  | 0.0  |
| 2015/07/27                     | 13:58:31 | 1671.2 | 304.0 | 51.8  | 18.8 | 3.4  | 0.6  | 0.0  | 0.0  |
| Total:                         |          | 5026.8 | 934.4 | 159.8 | 55.6 | 11.4 | 2.6  | 0.6  | 0.0  |
| Average:                       |          | 1675.6 | 311.5 | 53.3  | 18.5 | 3.8  | 0.9  | 0.2  | 0.0  |


CUMULATIVE AVERAGES HISTOGRAM



Reviewed by: MA Date: 07-27-15

Reviewed by: JW Date: 07-28-15



|   |   |                                    |  |
|---|---|------------------------------------|--|
|  | Form Title: <b>Extract, Diluent, Sterile Drug Product Bioburden Sample Form</b> |                                    | Doc Number: <b>QC-002-02.01</b>  |
|   | Corresponding SOP(s): <b>QC-002</b>   |                                    | Page 1 of 1  |
|   | QC test #: <b>QC-M-5644</b>   | Issued by/date: <b>LT 07-23-15</b> | Form Effective Date:<br><del>TM 06-25-13</del><br><del>JUN 26 13</del>                       |
|   | Product: <b>L-Cysteine 50 mL</b>  | Lot #: <b>2072115</b>              | Form Effective Date:<br><del>TM 06-25-13</del><br><del>JUN 26 13</del><br><b>JUN 26 2013</b> |

|  |  |   |                               |
|--|--|---|-------------------------------|
| Media plate lot: <b>7197 (15148)</b>         | Media plate expiration: <b>08-26-15</b>      | Inc. ID #: <b>0395</b>                  | Calibration due: <b>11-15</b> |
| Date placed in incubator: <b>07-24-15</b>    | Time placed in incubator: <b>11:12 am</b>    | Plates read by/date: <b>TT 07-27-15</b> |                               |
| Date removed from incubator: <b>07-27-15</b> | Time removed from incubator: <b>10:25 am</b> |   |                               |

| Product category               | # of CFU/mL                | Alert level | Action limit |
|--------------------------------|----------------------------|-------------|--------------|
| Allergenic Extracts            |                            | 222 CFU/mL  | 333 CFU/mL   |
| Diluting Solutions             | <del>N/A TT 07-27-15</del> | 1 CFU/mL    | 3 CFU/mL     |
| 50 % Glycerin Extraction Soln. | <del>N/A TT 07-27-15</del> | 1 CFU/mL    | 3 CFU/mL     |
| Sterile Drug Product           | <b>0</b>                   | 3 CFU/mL    | 5 CFU/mL     |
| Media Fill                     | <del>N/A TT 07-27-15</del> | 144 CFU/mL  | 216 CFU/mL   |

| Dilution level of original sample                  | Vol. of sample or prior dilution | Vol. of PBS or SCD (mL) | Vol. plated (mL) | Date/time placed in incubator/<br>Date/time removed from incubator | CFU/mL |
|--|----------------------------------|-------------------------|------------------|--|--------|
| 1:10 <sup>1</sup>                                  |                                  |                         |                  |  |        |
| 1:10 <sup>2</sup>                                  |                                  |                         |                  |  |        |
| 1:10 <sup>3</sup>                                  |                                  |                         |                  |  |        |
| 1:10 <sup>4</sup>                                  |                                  |                         |                  |  |        |
| 1:10 <sup>5</sup>                                  |                                  |                         |                  |  |        |
| 1:10 <sup>6</sup>                                  |                                  |                         |                  |  |        |
| Dilution performed by/date: <b>N/A TT 07-27-15</b> |                                  |                         |                  | Plates read by/date: <b>TT 07-27-15</b>                            |        |

|  |   |
|--|---|
| <b>Table 3</b><br>Dilution formula:<br>$\text{Plate count} \times \text{Dilution factor} = \# \text{ CFU/mL in stock solution}$<br>_____ X _____ = _____ Record in Table 1 | Dilution Factor:<br>1:10 <sup>1</sup> = 10<br>1:10 <sup>2</sup> = 100<br>1:10 <sup>3</sup> = 1000<br>1:10 <sup>4</sup> = 10000<br>1:10 <sup>5</sup> = 100000<br>1:10 <sup>6</sup> = 1000000 |
|--|---|

Alert level reached:  Yes  No If Yes, notify QA.  
 Action limit reached:  Yes  No If Yes, notify QA to issue a PACAR.

|         |                             |
|---------|-----------------------------|
| Analyst | By/date: <b>TT 07-27-15</b> |
|---------|-----------------------------|

|  |                                    |
|--|------------------------------------|
| Quality Assurance/Quality Control Review | Review by/date: <b>JW 07-27-15</b> |
|--|------------------------------------|



|  |                                       |  |
|--|---------------------------------------|--|
| Form Title: <b>Sterility Test Form</b>                   |                                       | Doc Number: <b>QC-118-01.00</b>            |
| QC Test #<br><b>QC-M-5642</b>                            | Issued By/Date:<br><b>CH 07-23-15</b> | Page 1 of 1                                |
| Product Name/Potency:<br><b>L-Cysteine</b>               | Lot #:<br><b>2072115</b>              | Form Issue Date:<br><b>JUN 27 2014</b>     |
| Fill Volume: <input type="checkbox"/> NA<br><b>50 mL</b> | Vial Size:<br><b>50/20</b>            | Form Effective Date:<br><b>JUL 01 2014</b> |

| Membrane Filtration Testing         |  |                   |                                    |                      |                     |                   |                    |
|-------------------------------------|--|-------------------|------------------------------------|----------------------|---------------------|-------------------|--------------------|
| Number of vials tested:             | <b>20</b>  |                   | Total pre-wet volume:              | <b>100 mL</b>        |                     |                   |                    |
| Amount of rinse fluid added to SEV: | <input checked="" type="checkbox"/> NA<br><input type="checkbox"/> Up to vial neck<br><input type="checkbox"/> Half the vial |                   | Number of rinses:                  | <b>2</b>             | Total rinse volume: | <b>200 mL</b>     |                    |
| Filter Vendor:                      | <b>Sartorius</b>   | Catalog #:        | <b>16466 G80</b>                   | Lot #:               | <b>7010</b>         | Exp. Date:        | <b>03-17</b>       |
| Rinse Fluid:                        | <b>A</b>   | Lot #:            | <del>07-28-15</del><br><b>7141</b> | Exp. Date:           | <b>09-27-15</b>     | Release Date:     | <b>04-20-15</b>    |
| TSB Lot #:                          | <b>7176</b>  | Exp. Date:        | <b>05-06-18</b>                    | Release Date:        | <b>06-17-15</b>     |                   |                    |
| TH Lot #:                           | <b>7148</b>  | Exp. Date:        | <b>10-11-15</b>                    | Release Date:        | <b>05-22-15</b>     |                   |                    |
| RODAC Lot #:                        | <b>7172</b>  | Exp. Date:        | <b>08-27-15</b>                    | Release Date:        | <b>05-25-15</b>     |                   |                    |
| 20-25°C Incubator #:                | <b>0021</b>  | Calibration Date: | <b>11-15</b>                       | 30-35°C Incubator #: | <b>0025</b>         | Calibration Date: | <b>11-15</b>       |
| Tested By / Date:                   |  |                   |                                    |                      |                     |                   | <b>TT 07-28-15</b> |


| Sample Description   | TH<br>Incubated at 30-35°C |                    |                    | TSB<br>Incubated at 20-25°C |                    |                    |
|----------------------|----------------------------|--------------------|--------------------|-----------------------------|--------------------|--------------------|
|                      | Results                    |                    |                    | Results                     |                    |                    |
|                      | Day 3, 4, or 5             | Day 7 or 8         | NET 14 days        | Day 3, 4, or 5              | Day 7 or 8         | NET 14 days        |
| Product              | —                          | —                  | —                  | —                           | —                  | —                  |
| Negative Rinse Fluid | —                          | —                  | —                  | —                           | —                  | —                  |
| Read By / Date       | <b>CH 07-31-15</b>         | <b>CH 08-04-15</b> | <b>TT 08-11-15</b> | <b>CH 07-31-15</b>          | <b>CH 08-04-15</b> | <b>TT 08-11-15</b> |

| Environmental Monitoring<br>Incubated at 20-25°C for 72-120 hours and then 30-35°C for 48-96 hours |          |                        |          |
|--|----------|------------------------|----------|
| Isolator Surface Left  | <b>0</b> | Isolator Surface Right | <b>0</b> |
| Glove Fingers Left   | <b>0</b> | Glove Fingers Right    | <b>0</b> |
| Read By / Date:  |          | <b>CH 08-04-15</b>     |          |

Comments: **N/A TT 08-11-15**

Test Results: **PASS** FAIL

|               |  |
|---------------|--|
| QA/QC Review: | Reviewed by/date:<br><b>jlw 08-11-15</b> |
|---------------|--|

|   |  |                                     |
|---|--|-------------------------------------|
|  | Form Title: <b>Endotoxin Test Record for Product Release</b> | Doc Number: <b>QC-011-02.02</b>     |
|   |  | Page 1 of 1                         |
|   | QC issued by/date:<br><br>CH 07-23-15                        | Form Issue Date:<br>JAN 22 2014     |
|   |  | Form Effective Date:<br>JAN 23 2014 |

| Results of Controls and Samples (+) = pyrogenic (gel formed) (-) = non-pyrogenic (no gel formed) |   |         |                        |          |                |                |                |                |
|--|---|---------|------------------------|----------|----------------|----------------|----------------|----------------|
| QC Test#<br>(if applicable)  | Sample  | Lot #   | Lysate Sensitivity (λ) | Dilution | Sample tube #1 | Sample Tube #2 | Sample Tube #3 | Sample tube #4 |
|  |   |         |                        |          | Un-spiked      | Un-spiked      | Spiked to 2λ   | Spiked to 2λ   |
| N/A  | Control Water<br>(positive and negative controls) | 7100    | 0.063                  | 1:1      | -              | -              | +              | +              |
| M-5643   | L-Cysteine  | 2072115 | 0.031                  | 1:1      | -              | -              | +              | +              |

| Equipment/Reagents Used          |                           |                                     |                        |
|----------------------------------|---------------------------|-------------------------------------|------------------------|
| Pipettor                         | Equipment ID#: 0065       | Calibration due: 02-16-16           |                        |
| Oven/Water Bath                  | Equipment ID#: 0363       | Calibration due: N/A<br>CH 07-24-15 |                        |
| Thermometer                      | Equipment ID#: 0443       | Calibration due: 03-10-16           |                        |
| Timer                            | Equipment ID#: 0368       | Calibration due: 02-26-16           |                        |
| Pipette Tips                     | Lot #: N/A<br>CH 07-24-15 | Expiration date: N/A                |                        |
| Pyrogen-free Tubes               | Lot #: AL0071-14          | Expiration date: N/A                |                        |
| Pyrogen-free Water               | Lot #: 7100               | Expiration date: 11-17              |                        |
| LAL Reagent                      | Lot #: 6657               | Expiration date: 11-16              | Release Date: 02-19-14 |
| Control Standard Endotoxin (CSE) | Lot #: 6870               | Expiration date: 12-17              | Release Date: 08-08-14 |

| Test Time and Water Bath Temperature |  |                          |                      |  |
|--------------------------------------|--|--------------------------|----------------------|--|
| Incubation start time:               | <input type="checkbox"/> A.M.            | Initial Incubation Temp: | Incubation end time: | <input type="checkbox"/> A.M.            |
| 1:52                                 | <input checked="" type="checkbox"/> P.M. | 36.3 °C                  | 2:53                 | <input checked="" type="checkbox"/> P.M. |
|                                      |  |                          |                      | Final Incubation Temp:                   |
|                                      |  |                          |                      | 37.7 °C                                  |

|                       |                                     |
|-----------------------|-------------------------------------|
| <b>Test Performed</b> | Test performed by/date: CH 07-24-15 |
|-----------------------|-------------------------------------|

|  |                              |
|--|------------------------------|
| <b>Quality Assurance/<br/>Quality Control Review</b> | Review by/date: Jlw 07-24-15 |
|--|------------------------------|

# KABS

Quality Assurance Department

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

**Certificate No: 125353**

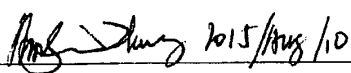
Purchase Order No: 20150727      Sample Code: N. App.  
 Issuing Date: 2015/Aug/10      Sample Lot No.: 2072115

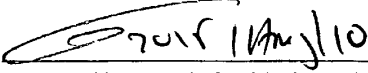
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                | Specifications  | Results  |
|---------------------------------|------------------------|---|--|
| Appearance of Product           | Visual                 | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                 | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                 | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                 | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>           | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231> Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03       | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 98.7 % LC <sup>1</sup><br>(49.3 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>           | NMT 5000 ppb  | 17 ppb   |

08-11-15  
 Revis  
 Reviewed By  
 mt 08-11-15

<sup>1</sup> Label Claim: 50 mg/mL  
<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

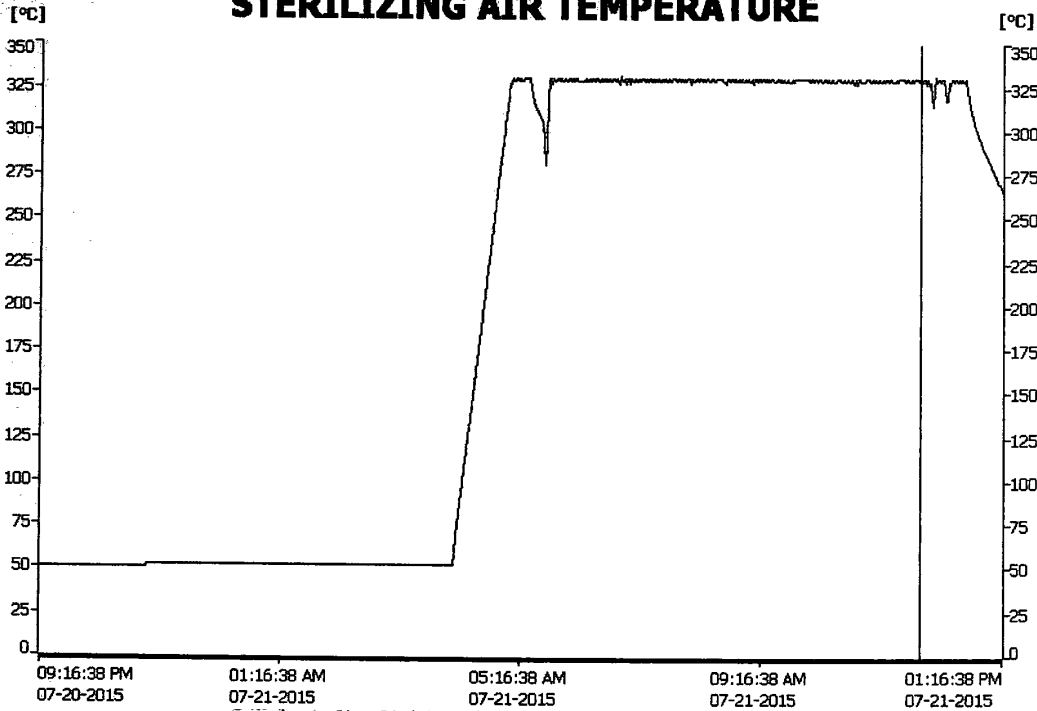
Verified by:  2015/Aug/10  
 Ning-Min Zhang, B.Sc.  
 Analyst, Quality Assurance

Approved by:  2015/Aug/10  
 Karim Mtalsi, Ph.D., Chemist  
 Director, R & D Department



|           |              |              |                      |
|-----------|--------------|--------------|----------------------|
| User:     | almas        | 3            | 07-21-2015           |
| Format:   | G-16 or G-38 |              | 01:16:46 PM          |
| Batch ID: | 2072115      |              |                      |
| Mode:     | Night Mode   | Alarm Active | T038_Tun_SterAirTemp |

### STERILIZING AIR TEMPERATURE



Print Screen

Export to PDF

Save to USB Pen

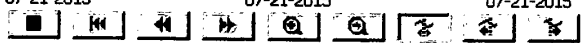
CMDS

Audit Trail

Historical Data

Data out

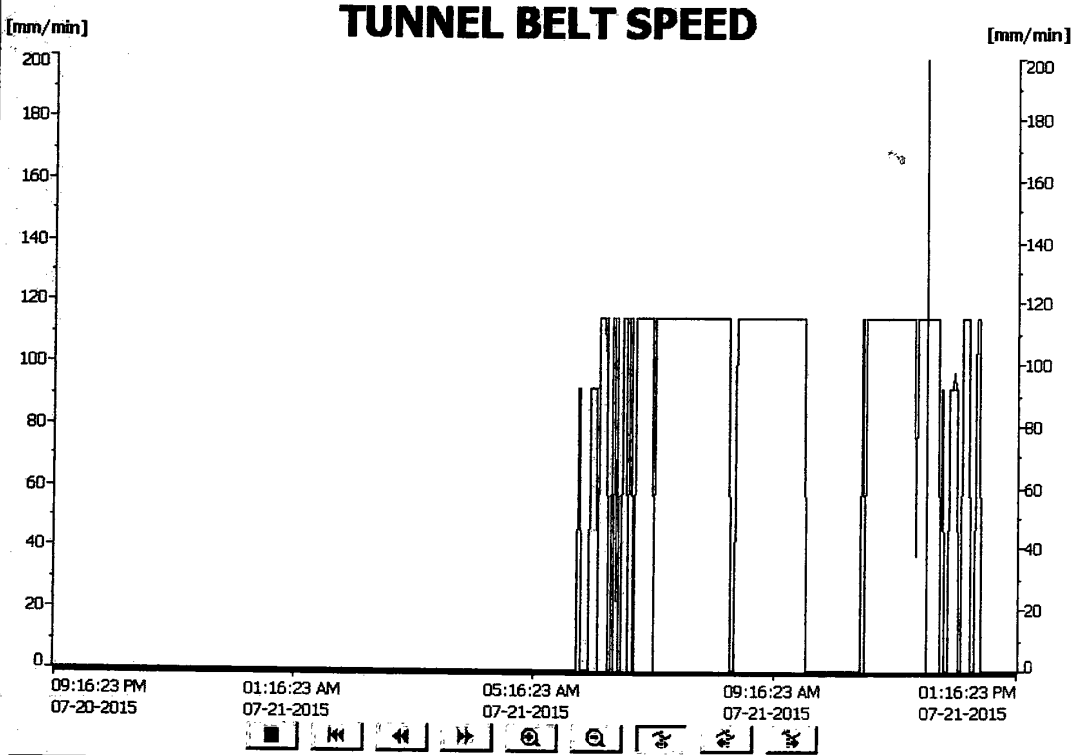
Main Page



| Trend                                       | Value | Date/Time             |
|---|-------|-----------------------|
| Sterilizing Air Temperature Log             | 329   | 07-21-2015 11:55:3... |
| Sterilizing Air Temperature - Process Value | 266.0 |                       |



|           |              |              |                   |
|-----------|--------------|--------------|-------------------|
| User:     | alma         | 3            | 07-21-2015        |
| Format:   | G-16 or G-38 |              | 01:16:30 PM       |
| Batch ID: | 2072115      |              |                   |
| Mode:     | Night Mode   | Alarm Active | T030_TunBeltSpeed |



Print Screen

Export to PDF

Save to USB Pen

CMDS

Audit Trail

Historical Data

Data out

Main Page

| Trend                             | Value | Date/Time             |
|-----------------------------------|-------|-----------------------|
| Tunnel Belt Speed Log             | 115   | 07-21-2015 11:47:3... |
| Tunnel Belt Speed - Process Value | 0     |                       |

**BATCH REPORT**

Line: ST6 - DEPYROGENATION TUNNEL

Batch Name: 2072115  
Batch Number: 2072115  
Product Name: 50ml-20mm  
Product Number: G-16 or G-38  
Format Name: G-16 or G-38  
Date: 07-21-2015

Batch start time: 07-21-2015 05:47:54 AM

Logged user at batch start: alma

**PROCESS PARAMETERS**

Tunnel - Conveyor Belt Speed [mm/min]: 115  
Tunnel - Steril Air Temperature [°C]: 330.0  
Tunnel - Cooling Air Temperature [°C]: 20.0  
Tunnel - Inlet Air Speed [m/s]: 0.60  
Tunnel - Sterilizing Air Speed [m/s]: 0.72  
Tunnel - Cooling Air Speed [m/s]: 0.75  
Tunnel - Inlet chamber/Env. DP [Pa]: 20.0  
Tunnel - Cooling chamber/Env. DP [Pa]: 22.0  
Tunnel - Doors Positions [mm]: 76

Author: 9  
Version: 09-27-2011 03:27:22 PM

**ALLARM PARAMETERS**

Conveyor Speed Range [mm/min]: 10  
Inlet Air Speed Range [m/s]: 0.02  
Sterilizing Air Speed Range [m/s]: 0.02  
Cooling Air Speed Range [m/s]: 0.02  
Inlet Chamber/Env. dP Range [Pa]: 5.0  
Cooling Chamber/Env. dP Range [Pa]: 5.0  
Doors Position Range [mm]: 2  
Steriliz. Air Min Temp. Range [°C]: 5.0  
Steriliz. Air Max Temp. Range [°C]: 10.0  
Cooling Air Min. Temp. Range [°C]: 5.0  
Cooling Air Max. Temp. Range [°C]: 10.0  
Exhaust Air Max. Temperature Range [°C]: 60.0

**OPERATOR NOTE AT BATCH START**

"2072115 50ml-20mm"

**EVENTS**

| TIME STAMP             | EV.ID.          | EVENT DESCRIPTION                                |
|------------------------|-----------------|--|
| 07-21-2015 05:48:12 AM | Ev_id: 1001     | Signed: Batch file - 2072115 - recording started |
| 07-21-2015 05:52:10 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 05:53:13 AM | Ev_id: 1013     | User Logout                                      |
| 07-21-2015 05:58:45 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 06:04:14 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 06:09:48 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 06:20:56 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 06:35:21 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 06:47:29 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 07:16:16 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 07:21:23 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 07:55:53 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 08:00:58 AM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 11:54:55 AM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 11:59:04 AM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 11:59:49 AM | Ev_id: 9564     | START CYCLE PRESSED by 7                         |
| 07-21-2015 12:02:51 PM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 12:06:10 PM | Ev_id: 9564     | START CYCLE PRESSED by 7                         |
| 07-21-2015 12:07:08 PM | Mode: Selection | Night mode selected by 7                         |
| 07-21-2015 12:12:48 PM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 12:16:57 PM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 12:17:07 PM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 12:19:46 PM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 12:19:59 PM | Ev_id: 9564     | START CYCLE PRESSED by 7                         |
| 07-21-2015 12:25:35 PM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 12:34:11 PM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 12:38:47 PM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 12:44:47 PM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 12:51:58 PM | Ev_id: 1013     | User '7' logged on with group 'Administrator'.   |
| 07-21-2015 12:52:35 PM | Ev_id: 1013     | User Logout                                      |
| 07-21-2015 01:02:31 PM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 01:06:14 PM | Ev_id: 9560     | TUN - RESET CYCLE PRESSED by 7                   |
| 07-21-2015 01:07:22 PM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 01:07:50 PM | Ev_id: 1050     | USER 7 has logged on local HMI                   |
| 07-21-2015 01:08:15 PM | Ev_id: 1051     | USER Logoff on local HMI                         |
| 07-21-2015 01:08:28 PM | Ev_id: 1050     | USER 9 has logged on local HMI                   |

07-21-2015 01:08:52 PM Ev\_id: 1051 USER Logoff on local HMI  
 07-21-2015 01:09:05 PM Ev\_id: 1050 USER alma has logged on local HMI  
 07-21-2015 01:15:50 PM Ev\_id: 1013 User 'alma' logged on with group 'Operator'.  
 07-21-2015 01:15:54 PM Ev\_id: 1003 Batch file - 2072115 - recording stopped

ALARMS MESSAGES

| TIME STAMP             | EV.ID.    | DESCRIPTION                       |
|------------------------|-----------|-----------------------------------|
| 07-21-2015 06:15:51 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:15:55 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:15:56 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:22:07 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:22:28 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:23:18 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:23:23 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:23:31 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:23:37 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:23:44 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:23:45 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:23:47 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:23:48 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:23:54 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:24:00 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:24:10 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:24:13 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:25:39 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:26:03 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:27:07 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - In    |
| 07-21-2015 06:27:22 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - Out   |
| 07-21-2015 06:27:24 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:27:31 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:27:42 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:27:56 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:28:57 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - In    |
| 07-21-2015 06:30:42 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - Out   |
| 07-21-2015 06:30:54 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - In    |
| 07-21-2015 06:31:17 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - Out   |
| 07-21-2015 06:31:46 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - In    |
| 07-21-2015 06:32:28 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - Out   |
| 07-21-2015 06:33:07 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:33:08 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:33:14 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:33:17 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:33:21 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:33:28 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:33:32 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:33:36 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:34:34 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - In    |
| 07-21-2015 06:35:34 AM | Alarm_094 | TUNNEL INLET MINIMUM LOAD - Out   |
| 07-21-2015 06:36:15 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:36:16 AM | Alarm_086 | DOORS IN MANUAL MODE - In         |
| 07-21-2015 06:36:47 AM | Alarm_086 | DOORS IN MANUAL MODE - Out        |
| 07-21-2015 06:36:57 AM | Alarm_027 | 4.th DOOR JAMMED - In             |
| 07-21-2015 06:36:58 AM | Alarm_022 | 3.rd DOOR IN WRONG POSITION - In  |
| 07-21-2015 06:37:06 AM | Alarm_086 | DOORS IN MANUAL MODE - In         |
| 07-21-2015 06:37:16 AM | Alarm_086 | DOORS IN MANUAL MODE - Out        |
| 07-21-2015 06:37:20 AM | Alarm_022 | 3.rd DOOR IN WRONG POSITION - Out |
| 07-21-2015 06:37:20 AM | Alarm_027 | 4.th DOOR JAMMED - Out            |
| 07-21-2015 06:37:20 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:37:20 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:37:25 AM | Alarm_027 | 4.th DOOR JAMMED - In             |
| 07-21-2015 06:37:25 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:37:30 AM | Alarm_086 | DOORS IN MANUAL MODE - In         |
| 07-21-2015 06:37:43 AM | Alarm_027 | 4.th DOOR JAMMED - Out            |
| 07-21-2015 06:37:51 AM | Alarm_086 | DOORS IN MANUAL MODE - Out        |
| 07-21-2015 06:37:57 AM | Alarm_027 | 4.th DOOR JAMMED - In             |
| 07-21-2015 06:38:17 AM | Alarm_027 | 4.th DOOR JAMMED - Out            |
| 07-21-2015 06:38:20 AM | Alarm_022 | 3.rd DOOR IN WRONG POSITION - In  |
| 07-21-2015 06:38:27 AM | Alarm_022 | 3.rd DOOR IN WRONG POSITION - Out |
| 07-21-2015 06:38:47 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:38:53 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:38:59 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:39:03 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:39:06 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:39:07 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:39:11 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In    |
| 07-21-2015 06:39:15 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out   |
| 07-21-2015 06:39:32 AM | Alarm_085 | TUNNEL BELT MANUAL STOP - In      |
| 07-21-2015 06:40:21 AM | Alarm_086 | DOORS IN MANUAL MODE - In         |
| 07-21-2015 06:40:35 AM | Alarm_085 | TUNNEL BELT MANUAL STOP - Out     |
| 07-21-2015 06:40:35 AM | Alarm_086 | DOORS IN MANUAL MODE - Out        |
| 07-21-2015 06:40:36 AM | Alarm_085 | TUNNEL BELT MANUAL STOP - In      |
| 07-21-2015 06:40:36 AM | Alarm_086 | DOORS IN MANUAL MODE - In         |
| 07-21-2015 06:40:52 AM | Alarm_023 | 4.th DOOR IN WRONG POSITION - In  |











|                        |           |                                       |
|------------------------|-----------|---------------------------------------|
| 07-21-2015 11:38:16 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:39:57 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:40:18 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:41:05 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:41:18 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:41:51 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:41:53 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:42:48 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:43:12 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:49:03 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:49:23 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:50:15 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:50:16 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:52:43 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:53:00 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:53:32 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:53:34 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:54:21 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:54:35 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:54:48 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - In        |
| 07-21-2015 11:55:13 AM | Alarm_095 | TUNNEL INLET MAXIMUM LOAD - Out       |
| 07-21-2015 11:59:16 AM | Alarm_026 | 3.rd DOOR JAMMED - In                 |
| 07-21-2015 11:59:16 AM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 11:59:26 AM | Alarm_026 | 3.rd DOOR JAMMED - Out                |
| 07-21-2015 12:02:27 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:02:32 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:03:24 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:03:28 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:04:53 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 12:04:58 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 12:04:58 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:04:59 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 12:04:59 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:05:06 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 12:05:06 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:05:07 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 12:05:07 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:05:11 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:05:16 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:05:42 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:05:50 PM | Alarm_026 | 3.rd DOOR JAMMED - In                 |
| 07-21-2015 12:05:53 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:06:00 PM | Alarm_026 | 3.rd DOOR JAMMED - Out                |
| 07-21-2015 12:06:00 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 12:06:00 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:06:01 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 12:06:01 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:06:22 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 12:07:17 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:07:23 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:16:59 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:19:09 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 12:20:00 PM | Alarm_027 | 4.th DOOR JAMMED - In                 |
| 07-21-2015 12:20:14 PM | Alarm_027 | 4.th DOOR JAMMED - Out                |
| 07-21-2015 12:20:14 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 12:28:43 PM | Alarm_021 | 2.nd DOOR IN WRONG POSITION - In      |
| 07-21-2015 12:34:13 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:34:18 PM | Alarm_021 | 2.nd DOOR IN WRONG POSITION - Out     |
| 07-21-2015 12:38:54 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:39:04 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:39:31 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 12:39:37 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 12:40:49 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |
| 07-21-2015 01:02:32 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 01:02:46 PM | Alarm_027 | 4.th DOOR JAMMED - In                 |
| 07-21-2015 01:02:53 PM | Alarm_027 | 4.th DOOR JAMMED - Out                |
| 07-21-2015 01:02:53 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - Out |
| 07-21-2015 01:02:57 PM | Alarm_027 | 4.th DOOR JAMMED - In                 |
| 07-21-2015 01:03:13 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 01:05:38 PM | Alarm_027 | 4.th DOOR JAMMED - Out                |
| 07-21-2015 01:05:38 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 01:05:39 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 01:06:02 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 01:06:08 PM | Alarm_086 | DOORS IN MANUAL MODE - In             |
| 07-21-2015 01:06:27 PM | Alarm_086 | DOORS IN MANUAL MODE - Out            |
| 07-21-2015 01:08:57 PM | Alarm_083 | COOLING CHAMBER TEMPERATURE LOW - In  |

Batch stop time: 07-21-2015 01:15:54 PM

Logged user at batch stop: alma

Batch total time: 7 [h]- 28 [min]- 0 [s]

SIGNATURES

A) Operator: Alma Delia Hernandez 07-21-15

B) Supervisor: [Signature] 07-22-15

C) Quality Assurance: [Signature] 07-27-15

Results : 20 Samplings

| Point         | Type      | Personnel            | Method | Area | Alert          | Action         | Bacteria | Fungi and Yeast | Count | Result     | Exceeding | Date               | Deviations | Batch       | Sampling plan           | Department | Microorganisms | LAL Alert | LAL Action | LAL Test | Types of Control  |
|---------------|-----------|----------------------|--------|------|----------------|----------------|----------|-----------------|-------|------------|-----------|--------------------|------------|-------------|-------------------------|------------|----------------|-----------|------------|----------|-------------------|
| Chest         | Personnel | Salas Junior         |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JS-1 JS Personnel 1   | Line 2     |                |           |            |          | During Production |
| Left Finger   | Personnel | Salas Junior         |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JS-1 JS Personnel 1   | Line 2     |                |           |            |          | During Production |
| Left Forearm  | Personnel | Salas Junior         |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JS-1 JS Personnel 1   | Line 2     |                |           |            |          | During Production |
| Right Finger  | Personnel | Salas Junior         |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JS-1 JS Personnel 1   | Line 2     |                |           |            |          | During Production |
| Right Forearm | Personnel | Salas Junior         |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JS-1 JS Personnel 1   | Line 2     |                |           |            |          | During Production |
| Chest         | Personnel | Quintero Juan Carlos |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JCQ-1 JCQ Personnel 1 | Line 2     |                |           |            |          | During Production |
| Left Finger   | Personnel | Quintero Juan Carlos |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JCQ-1 JCQ Personnel 1 | Line 2     |                |           |            |          | During Production |
| Left Forearm  | Personnel | Quintero Juan Carlos |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JCQ-1 JCQ Personnel 1 | Line 2     |                |           |            |          | During Production |
| Right Finger  | Personnel | Quintero Juan Carlos |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JCQ-1 JCQ Personnel 1 | Line 2     |                |           |            |          | During Production |
| Right Forearm | Personnel | Quintero Juan Carlos |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 10:00:00 |            | L- Cysteine | P-JCQ-1 JCQ Personnel 1 | Line 2     |                |           |            |          | During Production |
| Chest         | Personnel | Salas Junior         |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 12:42:00 |            | L- Cysteine | P-JS-2 JS Personnel 2   | Line 2     |                |           |            |          | End of Production |
| Left Finger   | Personnel | Salas Junior         |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 12:42:00 |            | L- Cysteine | P-JS-2 JS Personnel 2   | Line 2     |                |           |            |          | End of Production |
| Left Forearm  | Personnel | Salas Junior         |        |      | >= 2 cfu/site  | >= 3 cfu/site  | 0        | 0               | 0     | Acceptable |           | 7/21/2015 12:42:00 |            | L- Cysteine | P-JS-2 JS Personnel 2   | Line 2     |                |           |            |          | End of Production |
| Right Finger  | Personnel | Salas Junior         |        |      | >= 1 cfu/glove | >= 2 cfu/glove | 0        | 0               | 0     | Acceptable |           | 7/21/2015 12:42:00 |            | L- Cysteine | P-JS-2 JS Personnel 2   | Line 2     |                |           |            |          | End of Production |

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|               |           |                      |                   |                   |   |   |            |                       |                |                                  |        |  |  |  |                   |
|---------------|-----------|----------------------|-------------------|-------------------|---|---|------------|-----------------------|----------------|----------------------------------|--------|--|--|--|-------------------|
| Right Forearm | Personnel | Salas Junior         | >= 2<br>cfu/site  | >= 3<br>cfu/site  | 0 | 0 | Acceptable | 7/21/2015<br>12:42:00 | L-<br>Cysteine | Personnel<br>2                   | Line 2 |  |  |  | End of Production |
| Chest         | Personnel | Quintero Juan Carlos | >= 2<br>cfu/site  | >= 3<br>cfu/site  | 0 | 0 | Acceptable | 7/21/2015<br>12:50:00 | L-<br>Cysteine | P-JCQ-2<br>Personnel<br>2        | Line 2 |  |  |  | End of Production |
| Left Finger   | Personnel | Quintero Juan Carlos | >= 1<br>cfu/glove | >= 2<br>cfu/glove | 0 | 0 | Acceptable | 7/21/2015<br>12:50:00 | L-<br>Cysteine | P-JCQ-2<br>JCQ<br>Personnel<br>2 | Line 2 |  |  |  | End of Production |
| Left Forearm  | Personnel | Quintero Juan Carlos | >= 2<br>cfu/site  | >= 3<br>cfu/site  | 0 | 0 | Acceptable | 7/21/2015<br>12:50:00 | L-<br>Cysteine | P-JCQ-2<br>JCQ<br>Personnel<br>2 | Line 2 |  |  |  | End of Production |
| Right Finger  | Personnel | Quintero Juan Carlos | >= 1<br>cfu/glove | >= 2<br>cfu/glove | 0 | 0 | Acceptable | 7/21/2015<br>12:50:00 | L-<br>Cysteine | P-JCQ-2<br>JCQ<br>Personnel<br>2 | Line 2 |  |  |  | End of Production |
| Right Forearm | Personnel | Quintero Juan Carlos | >= 2<br>cfu/site  | >= 3<br>cfu/site  | 0 | 0 | Acceptable | 7/21/2015<br>12:50:00 | L-<br>Cysteine | P-JCQ-2<br>JCQ<br>Personnel<br>2 | Line 2 |  |  |  | End of Production |



## Results : 26 Samplings

| Point                  | Description                                     | Type Class   | Method              | Area                       | Alert                  | Action                 | Bacteria | Fungi and Yeast Count | Result Type | Exceeding | Date               | Deviations | Batch       | Sampling plan                      | Department | Microorganisms | LAL Alert | LAL Action Test |
|------------------------|---|--------------|---------------------|----------------------------|------------------------|------------------------|----------|-----------------------|-------------|-----------|--------------------|------------|-------------|------------------------------------|------------|----------------|-----------|-----------------|
| Production Set-up      | Fill machine base                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 06:30:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-1 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 06:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| Filling Turntable      | AA on filling turntable                         | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 07:04:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| Stopper Unit           | AA Stopper Bowl/Chute                           | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 07:09:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-2 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 07:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| Filling Turntable B2   | On the floor, and beneath the intervention area | Air 100      | Settle Plate        | Filling and Capping Line 2 | >= 1 cfu/plate/4 hours | >= 2 cfu/plate/4 hours | 0        | 0                     | Acceptable  |           | 7/21/2015 08:36:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| Filling Machine B2     | On the floor by the filling machine             | Air 100      | Settle Plate        | Filling and Capping Line 2 | >= 1 cfu/plate/4 hours | >= 2 cfu/plate/4 hours | 0        | 0                     | Acceptable  |           | 7/21/2015 08:36:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| Stopper Bowl B2        | On the floor, beneath stopper bowl              | Air 100      | Settle Plate        | Filling and Capping Line 2 | >= 1 cfu/plate/4 hours | >= 2 cfu/plate/4 hours | 0        | 0                     | Acceptable  |           | 7/21/2015 08:36:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-3 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 08:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-4 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 09:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-5 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 10:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| During Filling AA-B2-6 | AA during filling                               | Air 100      | Active Air Sampling | Filling and Capping Line 2 | >= 1 cfu/290L          | >= 1 cfu/290L          | 0        | 0                     | Acceptable  |           | 7/21/2015 11:55:00 |            | L- Cysteine | Air-L2-Daily Viable Air Monitoring | Line 2     |                | N.A.      | N.A.            |
| 7 (1B)                 | Fill Turntable                                  | Surfaces 100 | Contact Plate       | Filling and Capping Line 2 | >= 2 cfu/plate         | >= 4 cfu/plate         | 0        | 0                     | Acceptable  |           | 7/21/2015 12:50:00 |            | L- Cysteine | S-L2-Tuesday                       | Line 2     |                | N.A.      | N.A.            |
| 8 (1C)                 | SW corner                                       | Surfaces 100 | Contact Plate       | Filling and Capping Line 2 | >= 2 cfu/plate         | >= 4 cfu/plate         | 0        | 0                     | Acceptable  |           | 7/21/2015 12:50:00 |            | L- Cysteine | S-L2-Tuesday                       | Line 2     |                | N.A.      | N.A.            |
| 9 (2B)                 | In front of                                     | Surfaces 100 | Contact             | Filling                    | >= 2 cfu/plate         | >= 4 cfu/plate         | 0        | 0                     | Acceptable  |           | 7/21/2015          |            | L- Cysteine | S-L2-Tuesday                       | Line 2     |                | N.A.      | N.A.            |

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|                           | filler  | Surfaces | 100 | Contact Plate | Plate and Capping Line 2   | >= 2 cftu/plate | >= 4 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
|---------------------------|---|----------|-----|---------------|----------------------------|-----------------|-----------------|---|------------|--------------------|---------------------|--------|----------------|
| 10 (2C)                   | Behind filler                                 | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 4 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 11 (3B)                   | In front of conveyor                          | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 4 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 12 (3C)                   | Behind conveyor                               | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 4 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 6 (Filling Turntable 2A)  | Filling Turntable                             | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 1 (Filling Machine S)     | Base of top surface, S side                   | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 3 (Inside Stopper Bowl)   | Inside Stopper Bowl                           | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 1 cftu/plate | >= 1 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 13 (Turntable #2)         | Turntable #2                                  | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 2 (Filling Machine N)     | Base of top surface, N side                   | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 5 (Conveyor)              | Conveyor leading onto filler                  | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 4 (Stopper Chute)         | Surface of stopper chute where stoppers pass. | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |
| 16 (Filling Turntable 2B) | On filling turntable, opposite of 2A          | Surfaces | 100 | Contact Plate | Filling and Capping Line 2 | >= 2 cftu/plate | >= 3 cftu/plate | 0 | Acceptable | 7/21/2015 12:50:00 | Cysteine L2 Tuesday | Line 2 | N.A. N.A. N.A. |











| Time              | Data            | Value               | Alarm Status | Quality | Origin |
|-------------------|-----------------|---------------------|--------------|---------|--------|
| 07/21/15 12:15:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:16:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:17:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:18:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:19:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:20:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:21:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:22:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:23:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:24:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:25:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:26:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:27:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:28:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:29:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:30:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:31:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:32:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:33:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:34:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:35:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:36:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:37:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:38:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:39:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:40:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:41:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:42:49 | RPC-2120-01 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |













| Time              | Data            | Value               | Alarm Status | Quality | Origin |
|-------------------|-----------------|---------------------|--------------|---------|--------|
| 07/21/15 12:15:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:16:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:17:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:18:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:19:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:20:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:21:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:22:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:23:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:24:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:25:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:26:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:27:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:28:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:29:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:30:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:31:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:32:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:33:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:34:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:35:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:36:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:37:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:38:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:39:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:40:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:41:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:42:48 | RPC-2120-02 0.5 | 0 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |













| Time              | Data            | Value                | Alarm Status | Quality | Origin |
|-------------------|-----------------|----------------------|--------------|---------|--------|
| 07/21/15 12:15:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:16:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:17:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:18:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:19:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:20:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:21:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:22:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:23:08 | RPC-2120-03 0.5 | 1 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:24:08 | RPC-2120-03 0.5 | 1 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:25:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:26:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:27:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:28:08 | RPC-2120-03 0.5 | 2 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:29:08 | RPC-2120-03 0.5 | 3 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:30:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:31:08 | RPC-2120-03 0.5 | 5 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:32:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:33:08 | RPC-2120-03 0.5 | 5 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:34:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:35:08 | RPC-2120-03 0.5 | 5 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:36:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:37:08 | RPC-2120-03 0.5 | 1 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:38:08 | RPC-2120-03 0.5 | 20 p/ft <sup>3</sup> | Normal       | Valid   | I/O    |
| 07/21/15 12:39:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:40:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:41:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |
| 07/21/15 12:42:08 | RPC-2120-03 0.5 | 0 p/ft <sup>3</sup>  | Normal       | Valid   | I/O    |

78 07-15-15 0707175

Form Title: **Retention Sample Form for Sandoz Inc. (ID# 714503) Drug Products**

Doc Number: **MFG-037-01.02**

Form Issue Date: **JUN 27 2014**

Form Effective Date: **AUG 26 2014**

Lot #: **2072115**

|  |                                |     |
|--|--------------------------------|-----|
| <input type="checkbox"/> L-Cysteine HCl Injection, USP, 10 mL in a 10mL 22mm 13mm vial       | minimum # of vials to retain = | 64  |
| <input checked="" type="checkbox"/> L-Cysteine HCl Injection, USP, 50 mL in a 50mL 20mm vial | minimum # of vials to retain = | 58  |
| <input type="checkbox"/> Ephedrine Sulfate Injection, USP, 1 mL in a 2mL 13mm vial           | minimum # of vials to retain = | 158 |
| <input type="checkbox"/> Phenylephrine HCl Injection, USP, 5 mL in a 5mL 22mm 13mm vial      | minimum # of vials to retain = | 68  |
| <input type="checkbox"/> Phenylephrine HCl Injection, USP, 10 mL 10mL 22mm 13mm vial         | minimum # of vials to retain = | 56  |

**Product (check one)**

L-Cysteine HCl Injection, USP, 10 mL in a 10mL 22mm 13mm vial    minimum # of vials to retain = 64

L-Cysteine HCl Injection, USP, 50 mL in a 50mL 20mm vial    minimum # of vials to retain = 58

Ephedrine Sulfate Injection, USP, 1 mL in a 2mL 13mm vial    minimum # of vials to retain = 158

Phenylephrine HCl Injection, USP, 5 mL in a 5mL 22mm 13mm vial    minimum # of vials to retain = 68

Phenylephrine HCl Injection, USP, 10 mL 10mL 22mm 13mm vial    minimum # of vials to retain = 56

---

**Retention sample preparation and storage**

Actual number of vials retained: **25**    Middle: **25**    End: **60**    Total: **60**

Label Retention Samples with the items listed below: **25 07-15**

Prepared By/Date: **25 07-15**

Retention samples labeled with:

- Retention sample     Yes     No
- Product     Yes     No
- Product lot number     Yes     No
- Expiration date     Yes     No
- Quantity     Yes     No

Retention samples stored properly?  Yes     No

Stored by/dt/c: **8-17-15**

## **Exhibit B**



# CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

Certificate No: **113622**

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20140127    | Sample Code:    | N. App. |
| Issuing Date:      | 2014/Feb/12 | Sample Lot No.: | 2012114 |

Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                | Specifications  | Results  |
|---------------------------------|------------------------|---|--|
| Appearance of Product           | Visual                 | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                 | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 36                 | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 36                 | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 36 <791>           | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 36 <231> Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC           | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 102.3 % LC <sup>1</sup><br>(51.2 mg/mL)                          |
| Aluminum Content <sup>2</sup>   | USP 36                 | NMT 5000 ppb  | 61 ppb   |

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA.

Verified by: **Ning-Min Zhang, B.Sc.**  
 Analyst, Quality Assurance

Approved by: **Karim Mtalsi, Ph.D.**  
 Director, R&D Department



# CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

|                        |               |
|------------------------|---------------|
| <b>Certificate No:</b> | <b>113621</b> |
|------------------------|---------------|

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20140127    | Sample Code:    | N. App. |
| Issuing Date:      | 2014/Feb/12 | Sample Lot No.: | 2012214 |

Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                          | Specifications  | Results  |
|---------------------------------|----------------------------------|---|--|
| Appearance of Product           | Visual                           | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                           | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 36                           | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 36                           | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 36 <791>                     | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 36 <231><br><i>Method II</i> | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC                     | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 98.8 % LC <sup>1</sup><br>(49.4 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 36                           | NMT 5000 ppb  | 37 ppb   |

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA.

2014/Feb/12  
 Verified by: **Ning-Min Zhang, B.Sc.**  
 Analyst, Quality Assurance

2014/12/5/12  
 Approved by: **Karim Mtalsi, Ph.D.**  
 Director, R&D Department



# KABS

www.kabs.com

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

Certificate No: **125353**

Purchase Order No: 20150727 Sample Code: N. App.

Issuing Date: 2015/Aug/10 Sample Lot No.: 2072115

Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

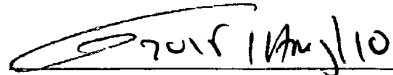
| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 98.7 % LC <sup>1</sup><br>(49.3 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 17 ppb   |

08-11-15  
Reviewed By  
mt 08-11-15

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

Verified by:  2015/Aug/10  
Ning-Min Zhang, B.Sc.  
Analyst, Quality Assurance

Approved by:  2015/Aug/10  
Karim Mtalsi, Ph.D., Chemist  
Director, R & D Department

F-0014-0022-Rev-E01  
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# KABS

PHARMACEUTICALS, INC. GREENVILLE, NC

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

Certificate No: **125354**

Purchase Order No: 20150727 Sample Code: N. App.  
Issuing Date: 2015/Aug/10 Sample Lot No.: 2072215

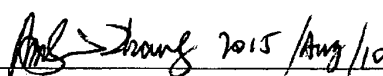
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

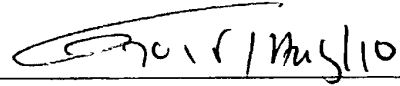
| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 98.5 % LC <sup>1</sup><br>(49.3 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 18 ppb   |

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

Reviewed By  
MA08-11-15

Verified by:  2015 Aug/10  
Ning-Min Zhang, B.Sc.  
Analyst, Quality Assurance

Approved by:   
Karim Mtalsi, Ph.D., Chemist  
Director, R & D Department

F-0014-0022-Rev-E01  
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## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

|                 |               |
|-----------------|---------------|
| Certificate No: | <b>125929</b> |
|-----------------|---------------|

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20150827    | Sample Code:    | N. App. |
| Issuing Date:      | 2015/Sep/10 | Sample Lot No.: | 2081915 |

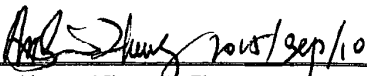
Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

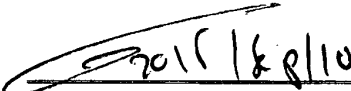
| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 96.4 % LC <sup>1</sup><br>(48.2 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 50 ppb   |

*Reviewed By*  
MA-09-15-15

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

Verified by:   
Ning-Min Zhang, B.Sc.  
Analyst, Quality Assurance

Approved by:   
Karim Mtalsi, Ph.D., Chemist  
Director, R & D Department



# CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

|                 |               |
|-----------------|---------------|
| Certificate No: | <b>125930</b> |
|-----------------|---------------|

|                    |             |                 |                |
|--------------------|-------------|-----------------|----------------|
| Purchase Order No: | 20150827    | Sample Code:    | N. App.        |
| Issuing Date:      | 2015/Sep/10 | Sample Lot No.: | <b>2082015</b> |

Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 - 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 - 105.0 %<br>(47.5 - 52.5 mg/mL)<br><br>Action limit: 85.0 - 115.0 %<br>(42.5 - 57.5 mg/mL) | 96.4 % LC <sup>1</sup><br>(48.2 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 54 ppb   |

*Reviewed By*  
*MA09-15-15*

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

Verified by: **Ning-Min Zhang, B.Sc.**  
Analyst, Quality Assurance

Approved by: **Karim Mtalsi, Ph.D., Chemist**  
Director, R & D Department



## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

**Certificate No: 125931**

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20150827    | Sample Code:    | N. App. |
| Issuing Date:      | 2015/Sep/10 | Sample Lot No.: | 2082115 |

Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 96.2 % LC <sup>1</sup><br>(48.1 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 46 ppb   |

*Reviewed By  
MA09-15-15*

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

Verified by: Ning-Min Zhang, B.Sc.  
Analyst, Quality Assurance

Approved by: Karim Mtalsi, Ph.D., Chemist  
Director, R & D Department

F-0014-0022-Rev-E01  
CONFIDENTIAL

(450) 656-4404 / kabs@kabs.com  
4500, de Tonnancour, St-Hubert (Québec) Canada J3Y 9G2  
www.kabs.com

Page 1 of 1

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

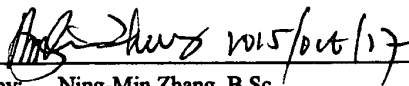
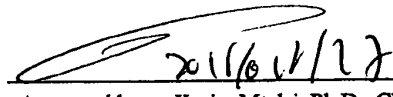
|                        |               |
|------------------------|---------------|
| <b>Certificate No:</b> | <b>126842</b> |
|------------------------|---------------|

|                    |   |                 |                |
|--------------------|---|-----------------|----------------|
| Purchase Order No: | 20151013  | Sample Code:    | N. App.        |
| Issuing Date:      | 2015/Oct/27   | Sample Lot No.: | <b>2093015</b> |
| Product:           | <b>50 mL L-Cysteine HCl Injection, USP (50 mg/mL)</b> |                 |                |

| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 97.1 % LC <sup>1</sup><br>(48.5 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 47 ppb   |

<sup>1</sup> Label Claim: 50 mg/mL  
<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

*Reviewed By*  
*MA 10-28-15*

|  |  |
|--|--|
| <br>Verified by: <b>Ning-Min Zhang, B.Sc.</b><br>Analyst, Quality Assurance | <br>Approved by: <b>Karim Mtalsi, Ph.D., Chemist</b><br>Director, R & D Department |
|--|--|

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

|                        |               |
|------------------------|---------------|
| <b>Certificate No:</b> | <b>126843</b> |
|------------------------|---------------|

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20151013    | Sample Code:    | N. App. |
| Issuing Date:      | 2015/Oct/27 | Sample Lot No.: | 2100115 |

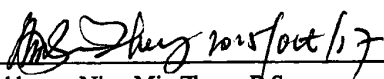
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 97.9 % LC <sup>1</sup><br>(49.0 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | 48 ppb   |

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

*Reviewed By*  
*ma 10-28-15*

  
\_\_\_\_\_  
Verified by: **Ning-Min Zhang, B.Sc.**  
Analyst, Quality Assurance

  
\_\_\_\_\_  
Approved by: **Karim Mtalsi, Ph.D., Chemist**  
Director, R & D Department

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

|                        |               |
|------------------------|---------------|
| <b>Certificate No:</b> | <b>126844</b> |
|------------------------|---------------|

|                    |             |                 |         |
|--------------------|-------------|-----------------|---------|
| Purchase Order No: | 20151013    | Sample Code:    | N. App. |
| Issuing Date:      | 2015/Oct/27 | Sample Lot No.: | 2100215 |

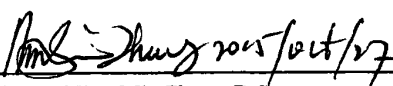
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

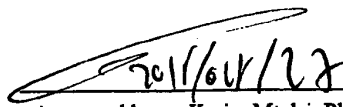
| Test                            | Methods                   | Specifications  | Results  |
|---------------------------------|---------------------------|---|--|
| Appearance of Product           | Visual                    | Clear colorless solution free from visible particulate matter   | Clear colorless solution free from visible particulate matter    |
| Appearance of Container/Closure | Visual                    | No apparent leakage or physical alteration  | No apparent leakage or physical alteration                       |
| Identification A                | USP 38                    | A bluish-gray precipitate is formed   | A bluish-gray precipitate is formed                              |
| Identification B                | USP 38                    | A red-purple color is produced, and it rapidly changes to yellow  | A red-purple color is produced, and it rapidly changes to yellow |
| pH                              | USP 38 <791>              | 1.0 – 2.5   | 1.3  |
| Heavy Metals                    | USP 38 <231><br>Method II | NMT 2 ppm   | < 2 ppm  |
| Assay                           | KABS-1348-LC-V03          | Alert limit: 95.0 – 105.0 %<br>(47.5 – 52.5 mg/mL)<br><br>Action limit: 85.0 – 115.0 %<br>(42.5 – 57.5 mg/mL) | 97.3 % LC <sup>1</sup><br>(48.6 mg/mL)                           |
| Aluminum Content <sup>2</sup>   | USP 38 <206>              | NMT 5000 ppb  | < 43 ppb   |

*Reviewed By  
MA 10-28-15*

<sup>1</sup> Label Claim: 50 mg/mL

<sup>2</sup> Analyses outsourced to Metrics Inc., Greenville, NC, USA

  
 Verified by: **Ning-Min Zhang, B.Sc.**  
 Analyst, Quality Assurance

  
 Approved by: **Karim Mtalsi, Ph.D., Chemist**  
 Director, R & D Department



## **Exhibit C**



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 10 mL

Lot number: 2012114

Vial size: 10ml-22-13mm

Manufacture date: 01/21/2014

Expiration Date: 01 - 2016

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification                                   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification                                   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification                                   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification                                   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification                                   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification                                   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification                                   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 10.0 mL  | Meets Specification                                   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles (≥10µm)/vial<br>NMT 600 particles (≥25µm)/vial                                     | 60.0 particles ≥10µm/vial<br>2.0 particles ≥25µm/vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 – 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 – 57.5mg/mL) | 102.3 %   |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 61 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 02/13/2014 | <b>Release Quantity</b> | 36,800 |
|---------------------|------------|-------------------------|--------|

### Quality Assurance Approval

By / Date

*M. Cobb* 02-14-14

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM021314TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 10 mL

Lot number: 2012214

Vial size: 10ml-22-13mm

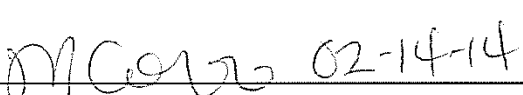
Manufacture date: 01/22/2014

Expiration Date: 01 - 2016

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification                                   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification                                   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification                                   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification                                   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification                                   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification                                   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification                                   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 10.0 mL  | Meets Specification                                   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles (≥10µm)/vial<br>NMT 600 particles (≥25µm)/vial                                     | 48.0 particles ≥10µm/vial<br>1.3 particles ≥25µm/vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 98.8 %  |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 37 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 02/13/2014 | <b>Release Quantity</b> | 37,300 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |  |
|----------------------------|--|
| By / Date                  |  02-14-14 |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM021314TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 50 mL

Lot number: 2072115

Vial size: 50ml-20mm

Manufacture date: 07/21/2015

Expiration Date: 07 - 2017

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 50.0 mL  | Meets Specification   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 190.0 particles $\geq 10\mu\text{m}$ /vial<br>10.0 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 98.7 %  |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 17 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 08/17/2015 | <b>Release Quantity</b> | 13,200 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson</i> 08-17-15 |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM081715TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 50 mL

Lot number: 2072215

Vial size: 50ml-20mm

Manufacture date: 07/22/2015

Expiration Date: 07 - 2017

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 50.0 mL  | Meets Specification   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 173.3 particles $\geq 10\mu\text{m}$ /vial<br>16.7 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 98.5 %  |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 18 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|              |            |                  |        |
|--------------|------------|------------------|--------|
| Release Date | 08/17/2015 | Release Quantity | 13,225 |
|--------------|------------|------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson</i> 08-27-15 |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM081715TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 10 mL

Lot number: 2081915

Vial size: 10ml-22-13mm

Manufacture date: 08/19/2015

Expiration Date: 08 - 2017

| Quality Release Testing           |  |   |  |
|-----------------------------------|--|---|--|
| Test / Parameter                  | Method                                   | Specifications  | Results  |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification  |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification  |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification  |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification  |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification  |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification  |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3  |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification  |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 10.0 mL  | Meets Specification  |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 148.0 particles $\geq 10\mu\text{m}$ /vial<br>2.7 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 96.4 %   |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 50 ppb   |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 09/22/2015 | <b>Release Quantity</b> | 36,760 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson</i> 09-23-15 |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM092315TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 10 mL

Lot number: 2082015

Vial size: 10ml-22-13mm

Manufacture date: 08/20/2015

Expiration Date: 08 - 2017

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 10.0 mL  | Meets Specification   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 68.0 particles $\geq 10\mu\text{m}$ /vial<br>0.7 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 96.4 %  |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 54 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 09/22/2015 | <b>Release Quantity</b> | 36,790 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson</i> 09-23-15 |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

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TLM092315TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 10 mL

Lot number: 2082115

Vial size: 10ml-22-13mm

Manufacture date: 08/21/2015

Expiration Date: 08 - 2017

| Quality Release Testing           |  |   |   |
|-----------------------------------|--|---|---|
| Test / Parameter                  | Method                                   | Specifications  | Results   |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification   |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification   |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification   |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification   |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification   |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification   |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3   |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification   |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 10.0 mL  | Meets Specification   |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 69.0 particles $\geq 10\mu\text{m}$ /vial<br>2.0 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 96.2 %  |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 46 ppb  |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 09/22/2015 | <b>Release Quantity</b> | 36,520 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson</i> 09-23-15 |

Original Certificate

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Fax: (800)811-3389

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Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 50 mL

Lot number: 2093015

Vial size: 50ml-20mm

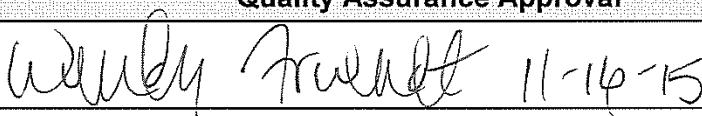
Manufacture date: 09/30/2015

Expiration Date: 09 - 2017

| Quality Release Testing           |  |   |  |
|-----------------------------------|--|---|--|
| Test / Parameter                  | Method                                   | Specifications  | Results  |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification  |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification  |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification  |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification  |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification  |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification  |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3  |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification  |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 50.0 mL  | Meets Specification  |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 103.3 particles $\geq 10\mu\text{m}$ /vial<br>3.3 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 97.1 %   |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 47 ppb   |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|              |            |                  |        |
|--------------|------------|------------------|--------|
| Release Date | 11/12/2015 | Release Quantity | 13,097 |
|--------------|------------|------------------|--------|

| Quality Assurance Approval |   |
|----------------------------|---|
| By / Date                  |  11-14-15 |

Original Certificate

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Oklahoma City, OK 73109

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Fax: (800)811-3389

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Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 50 mL

Lot number: 2100115

Vial size: 50ml-20mm

Manufacture date: 10/01/2015

Expiration Date: 10 - 2017

| Quality Release Testing           |  |   |  |
|-----------------------------------|--|---|--|
| Test / Parameter                  | Method                                   | Specifications  | Results  |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification  |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification  |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification  |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification  |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification  |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification  |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3  |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification  |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 50.0 mL  | Meets Specification  |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles ( $\geq 10\mu\text{m}$ )/vial<br>NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial   | 200.0 particles $\geq 10\mu\text{m}$ /vial<br>3.3 particles $\geq 25\mu\text{m}$ /vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 97.9 %   |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 48 ppb   |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|                     |            |                         |        |
|---------------------|------------|-------------------------|--------|
| <b>Release Date</b> | 02/08/2016 | <b>Release Quantity</b> | 13,000 |
|---------------------|------------|-------------------------|--------|

| Quality Assurance Approval |                              |
|----------------------------|------------------------------|
| By / Date                  | <i>Heidi Wilson 02-08-16</i> |

Original Certificate

1005 S.W. Second Street  
Oklahoma City, OK 73109

Tel: (800)654-3971  
Fax: (800)811-3389

www.AllergyLabs.com  
TLM020816TLM



Allergy Laboratories, Inc.

# Certificate of Analysis

Product: L-Cysteine HCl Injection, USP (50mg/mL)

Manufactured for Sandoz

Volume: 50 mL

Lot number: 2100215

Vial size: 50ml-20mm

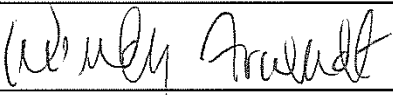
Manufacture date: 10/02/2015

Expiration Date: 10 - 2017

| Quality Release Testing           |  |   |  |
|-----------------------------------|--|---|--|
| Test / Parameter                  | Method                                   | Specifications  | Results  |
| Sterility                         | USP<71> or TEM-3003                      | Sterile (no microbial growth)   | Meets Specification                                    |
| Bacterial Endotoxins              | USP<85> or TEM-3001                      | NMT 0.7 EU/mg L-Cysteine HCl  | Meets Specification                                    |
| Appearance of Product             | Visual or TEM-2005                       | Clear, colorless solution free from particulate matter  | Meets Specification                                    |
| Appearance of Container / Closure | Visual or TEM-2005                       | No apparent leakage or physical alteration  | Meets Specification                                    |
| Identification A                  | USP or TEM-2005                          | A bluish-gray precipitate is formed   | Meets Specification                                    |
| Identification B                  | USP or TEM-2005                          | A red-purple color is produced and it rapidly changes to yellow                                       | Meets Specification                                    |
| pH                                | USP<791> or TEM-1000                     | 1.0 - 2.5   | 1.3  |
| Heavy Metals                      | USP<231>Method II or TEM-2003            | NMT 2 ppm   | Meets Specification                                    |
| Fill Volume                       | USP<1> or TEM-2000                       | To deliver NLT 50.0 mL  | Meets Specification                                    |
| Particulate Matter                | USP<788> or TEM-2035                     | NMT 6000 particles (≥10µm)/vial<br>NMT 600 particles (≥25µm)/vial                                     | 126.7 particles ≥10µm/vial<br>0.0 particles ≥25µm/vial |
| Assay                             | USP, KABS-1348-LC, ARL-AM121 or TEM-2011 | Alert limit: 95.0 - 105.0%<br>(47.5 - 52.5mg/mL)<br>Action limit: 85.0 - 115.0%<br>(42.5 - 57.5mg/mL) | 97.3 %   |
| Aluminum Content                  | USP                                      | NMT 5000 ppb  | 43 ppb   |

This product has been manufactured in accordance with the principles and guidelines of CFR Parts 210 and 211 Current Good Manufacturing Practices and in accordance with the Finished Product Specifications of Allergy Laboratories, Inc. All deviations and out of specifications, if any, have been investigated and closed. This lot is acceptable for release.

|              |            |                  |        |
|--------------|------------|------------------|--------|
| Release Date | 11/12/2015 | Release Quantity | 13,000 |
|--------------|------------|------------------|--------|

| Quality Assurance Approval |  |
|----------------------------|--|
| By / Date                  |  11-16-15 |

Original Certificate

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Oklahoma City, OK 73109

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TLM111615TLM

## **Exhibit D**

**From:** Covert, Evangela [<mailto:Evangela.Covert@fda.hhs.gov>]  
**Sent:** Friday, March 9, 2018 3:35 PM  
**To:** Gold, Lynn <[LGold@camargopharma.com](mailto:LGold@camargopharma.com)>  
**Subject:** NDA 209649: 5% L-Cysteine Hydrochloride Injection, USP: Information Request

Hello Dr. Gold: **Information Request**

Please see the FDA comments below:

### CMC

Based on our preliminary review of your NDA submission, we have identified several deficiencies. The deficiencies outlined below should be addressed in order for the application to be considered complete.

1. You have not submitted the release and stability data for the primary/registration batches of the drug product manufactured at the proposed commercial manufacturing facility, Grand River Aseptic manufacturing (GRAM), Grand Rapids, MI. If this NDA is given a priority review status, a minimum of 9 months long-term and 6 months accelerated stability data from three primary stability batches of drug product manufactured at the proposed commercial manufacturing facility must be provided at time of submission of the NDA with additional 3 months of long-term stability (total 12 months of long-term) to be submitted within 60 days from the filing of the application.
2. You have not provided data for elemental impurities of the drug product as per ICH guidance Q3D for parenteral products.
3. The drug product L-Cysteine Hydrochloride Injection is a small volume parenteral drug product used in TPN. Based on our previous experience with small volume parenteral drug products intended for addition to the TPN, we have determined that the aluminum dose delivered by your drug product, 5% L-Cysteine Hydrochloride Injection, USP, should be limited to  $\leq 0.6$  mcg/kg/day. To comply with this limit, the aluminum content in the final drug product should be controlled to  $\leq 350$  mcg/L. This is calculated based on the clinical dose of 15 mg cysteine free base per gram of amino acid per day. Therefore, the proposed acceptance limit for the aluminum content in the finished drug product specification (3.2.P.5.1) must be revised to  $\leq 350$ mcg/L. The drug product registration batches manufactured at OKC Allergy Supplies, Oklahoma City, OK have not been shown to meet the required acceptance limit for aluminum content.
4. We remind you that due to low pH of the drug product, full assessment of the proposed container closure leachables/extractables (E&L) must be performed. The data should be accompanied with appropriate toxicological evaluations of the detected leachable compounds. Container closure integrity must also be established during accelerated and long-term stability to ensure that it is capable of protecting the drug product from its

external environment and maintaining the drug product sterility throughout the proposed product shelf-life.

5. We acknowledge that you have conducted the stability study of the admixture solution (CPS 2016-0001). We remind you that testing for Particulate Matter must be performed as per USP <788> in the final mixture of Cysteine Hydrochloride Injection and Amino Acid Solutions. Additionally, provide in-use stability data that supports the 24-hour duration of the administration at room temperature.
6. The established name of the drug product is Cysteine Hydrochloride Injection based upon the USP monograph; therefore, the strength in the labelling (Package Insert, Carton and Container Labels) should be expressed as Cysteine Hydrochloride Salt with an equivalency statement to indicate the amount of the free base Cysteine per USP salt policy. See the guidance on Naming of Drug Products Containing Salt Drug Substances: <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM379753.pdf>
7. In future communications, please refer to the product as cysteine hydrochloride and any discussion of the strength or dosing should be in terms of the hydrochloride salt. However, we acknowledge that the label for the approved Hospira product (NDA 19523), the dosing information appears to be based upon cysteine, not cysteine hydrochloride. Also, the published literature predominately discusses dosing based upon cysteine. Therefore, in your communications and submission you may wish to include equivalency statements to ensure there is no misunderstanding of the dose.
8. It is noted that the registration batches were manufactured at the OKC site but the proposed commercial manufacturing facility is the GRAM site. We recommend that you provide the side-by-side comparison of the registration batches of the proposed drug product (5% L-Cysteine Hydrochloride Injection, USP) manufactured at both the OKC and GRAM sites (e.g., description, composition, formulation, pH, osmolality, drug concentration, etc.). Provide justification/assurance that when comparing to the LD product, your proposed final drug product would demonstrate comparable pH, osmolality, and final cysteine concentration in admixtures with amino acids prior to IV administration towards similar *in vivo* pharmacokinetic performance and clinical outcomes.

### Clinical

Our thinking on the approach to this type of NDA submission, which is primarily based on literature, has evolved and additional feedback is provided below on the recommended content of the submission. The data presented in your submission should allow the reviewer(s) to understand all the relevant aspects of the publications, sufficient to permit an understanding of the study results/conclusions without rereading the entire publication.

9. Based on our preliminary review of the published clinical information provided in the submission, we are concerned that the information, as presented, does not provide persuasive evidence to support safety and efficacy in the intended patient population. We are not convinced the plasma levels of cysteine reflect a clinically meaningful outcome. Therefore, you should provide rationale to support that cysteine supplementation is necessary to add into TPN for each of the intended patient populations. You should provide evidence to support that the proposed dose of cysteine is necessary to meet age-appropriate requirements/recommendations for protein intake. Additionally, consider including the following:
  - a. Studies that included short and long-term efficacy analysis such as assessments of growth, and prevention of complications associated with reduction of glutathione (i.e., risk of death, bronchopulmonary dysplasia (BPD), retinopathy of pre-maturity (ROP), necrotizing enterocolitis (NEC), periventricular leukomalacia, and intraventricular hemorrhage).
  - b. Nitrogen balance and or turn over studies.
  - c. Studies that evaluated the integration steps in assimilation of cysteine in to the final product (i.e. AA/protein).
  - d. Provide summary of supportive evidence from literature/clinical studies for the normal/optimal blood amino acid (AA) levels that should be achieved in all age groups.
10. Briefly (in a few paragraphs) summarize the prevailing rationale for adding cysteine to standard parenteral nutrition formulations.
  - a. Include the best available evidence to support that cysteine is essential using information based on animals and humans, the mechanism of action, etc. A claim stating that cysteine is essential in premature infants and other specific patient populations must be supported by studies which substantiate this claim. The literature submitted to date does not clearly support all patient populations represented in the proposed indication.
  - b. It is anticipated that some of this information may come from textbooks (and constitute general medical knowledge); therefore, it does not need to be extensively written/supported.
  - c. This information can be used to write Section 12.1 Mechanism of Action of the label.
11. Summarize the evidence to support the proposed dosing for cysteine in parenteral nutrition. As part of the summary, describe the quality of the efficacy data, strengths and

weaknesses, how persuasive, what are the limitations? What are the uncertainties in the available evidence to support the proposed dosing regimen?

- a. Provide separate tables for each age group.
- b. Include details on the specific ages studied for each cited publication.
- c. Include mention of whether patients were receiving TPN only, TPN plus oral feeds, or TPN with other types of supplementation.
- d. Summarize the current clinical practice guidelines, including but not limited to ASPEN/ESPGHAN, dosing recommendations in adults/pediatrics for cysteine relation to the proposed dosing.
  - i. In a paragraph or two summarize the rationale and basis for the current ASPEN (2015) and ESPGHAN recommendations supported by primary literature references.
  - ii. Discuss any changes to the ASPEN and ESPGHAN recommendations over time and include the primary literature references to support the more recent changes in the recommendations.
  - iii. If societal guidelines are available, other than ASPEN and ESPGHAN, provide a discussion on any points of uncertainty or controversy between the guidelines with regards to best practices.

12. Identify clinical conditions, medical settings, or population subgroups that may require higher or lower doses of cysteine for parenteral nutrition.

- a. Briefly summarize what is known about the cysteine in Renal Impairment, Hepatic Impairment, Geriatric Use, and Pregnancy.

13. Provide a summary of publications related to the efficacy of cysteine. Each table should be based on the efficacy outcome studied [i.e., prevention of deficiency (prophylaxis/maintenance), development of deficiency with suboptimal supplementation, or deficiency that responded to supplementation (treatment)]. The tables should include information on the following:

- a. Study design.
- b. Patient population.
- c. Specify whether cysteine administration was for prevention of deficiency, maintenance, development of deficiency with suboptimal supplementation, or deficiency that responded to supplementation.
- d. Duration of the study.
- e. Daily and total cysteine dose received.
- f. Primary and secondary efficacy criteria: include clinical, laboratory and/or radiological outcomes.
- g. Short and long-term assessment and benefit(s).



h. Whether efficacy criteria were met to support the cysteine dose.  
 A shell table, as shown below, may be considered as a template to create tables.  
 Additional columns may be added to convey the complete information.

Example: Summary of Publications of Cysteine – According to Efficacy Outcome Reported

| <i>Author/Year of Pub/reference #</i> | <i>Study design<sup>1</sup></i> | <i>Study population<sup>2</sup></i> | <i>Dose(s)</i><br><i>Duration of treatment</i><br><i>Other co-administered amino acids, electrolytes and trace elements</i> | <i>Reason for cysteine supplementation</i> | <i>Efficacy Outcome</i><br><i>Include descriptive and/or quantitative information for any of the outcomes provided</i><br><i>Specify clinical, laboratory<sup>3</sup> and/or radiological outcomes</i> | <i>Comments<sup>4</sup></i> |
|---------------------------------------|---------------------------------|-------------------------------------|---|--|--|-----------------------------|
|                                       |                                 |                                     |   |  |  |                             |
|                                       |                                 |                                     |   |  |  |                             |

<sup>1</sup>Study design to include design (RCT or other), number of patients on treatment, number on placebo (if applicable), primary disease.

<sup>2</sup>Study population to include demographics (age [mean ± SD], race, gender, country) and baseline characteristics (other comorbidities, pregnancy/lactation, renal impairment, hepatic impairment, elderly, etc). Number of patients who discontinued.

<sup>3</sup>Laboratory includes both standard chemistries measured during and at the end of study.

<sup>4</sup>The Comments column is a free text column to capture any other relevant information included in the publication.

14. Provide a summary of efficacy (maximum 3-5 pages). Integrate the data in the efficacy tables with the other available evidence to summarize the efficacy, considering the totality of the evidence. Describe the quality of the efficacy data, strengths and weaknesses, persuasiveness of the findings, and limitations of the studies.

15. Provide a summary of publications related to the safety of cysteine, using a similar format to the shell efficacy table.

- a. Provide separate tables for each age group.
- b. Describe toxicities or adverse events associated with cysteine when used for parenteral nutrition.
- c. Include any available evidence from the literature.

Example: Summary of Publications of Cysteine – According to Safety or Toxicity  
Outcome Reported

| <i>Author/Year of Pub/reference #</i> | <i>Study design<sup>1</sup></i> | <i>Study population<sup>2</sup></i> | <i>Dose(s)</i><br><i>Duration of treatment</i><br><i>Reason for cysteine supplementation</i><br><i>Other co-administered amino acids, electrolytes and trace elements</i> | <i>Safety Outcome</i><br><i>Include descriptive and/or quantitative information for any of the outcomes provided</i><br><i>Specify clinical, laboratory<sup>3</sup> and/or radiological outcomes</i> | <i>Comments<sup>4</sup></i> |
|---------------------------------------|---------------------------------|-------------------------------------|---|--|-----------------------------|
|                                       |                                 |                                     |   |  |                             |

<sup>1</sup> Study design to include design (RCT or other), number of patients on treatment, number on placebo (if applicable), primary disease.

<sup>2</sup> Study population to include demographics (age [mean ± SD], race, gender, country) and baseline characteristics (other comorbidities, pregnancy/lactation, renal impairment, hepatic impairment, elderly, etc). Number of patients who discontinued.

<sup>3</sup> Laboratory includes both standard chemistries measured during and at the end of study.

<sup>4</sup> The Comments column is a free text column to capture any other relevant information included in the publication.

16. Provide the summary of safety (maximum 3-5 pages). Integrate the data in the safety tables to describe the quality of the safety data, strengths and weaknesses, persuasiveness of the data, and any limitations. Discuss the uncertainties in the available evidence to support the proposed indication and dosing.
17. Provide a summary of the overall risk/benefit assessment using the available evidence and any uncertainties about the quality/strength of the evidence presented in the efficacy and safety tables and summaries. Provide rationale to support the addition of cysteine to TPN for each of the intended populations in the proposed label. You should also consider the risk of deficiency vs. toxicity for cysteine, and which one drives the overall assessment.

Kind Regards,

**Evangelina Covert, BS**  
Regulatory Health Project Manager  
Division of Gastroenterology and Inborn Errors Products

Office of Drug Evaluation III  
Office of New Drugs  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue  
Silver Spring, MD 20993 - *Use zip code 20903 if shipping via United States Postal Service (USPS)*  
Bldg. 22, Room 5245  
office: 301-796-4075  
fax: 301-796-9904  
[Evangela.Covert@fda.hhs.gov](mailto:Evangela.Covert@fda.hhs.gov)

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