

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 filling 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.

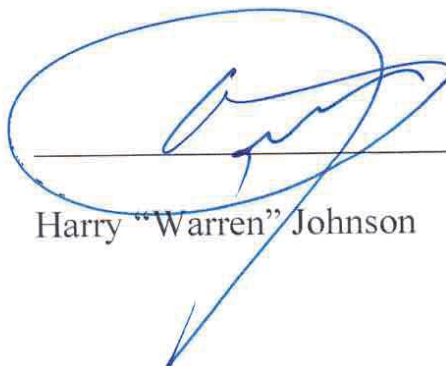
22. In response, AL Pharma amended the aluminum specification to  $\leq 350$  mcg/L ( $\leq 350$  ppb) and submitted additional information demonstrating compliance

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

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

Document/Process	Document
<input checked="" type="checkbox"/> Routine Intervention Log completed and approved by QA	Form #: QA-006-03
<input checked="" type="checkbox"/> QA-006-02 "Corrective Intervention Log - Line 1 & 2 Aseptic Products" completed and approved by QA	
<input checked="" type="checkbox"/> Batch Manufacturing Record completed and approved by the Prod. Supervisor	Form #: BMR-010
<input checked="" type="checkbox"/> Vial Manufacturing Record completed and approved by the Prod. Supervisor	Form #: 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	Form #: 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)	Form #: 08-12-15

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 #: 2072115

Product: Cysteine 50mL

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Document Present? (Circle One)	Document (Reference any Deviations, OOS or CAPA Investigations in the investigations section [page 3])	Results (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>BiZed</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)		Recorded 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>Ernie</i> 08-14-15				



Form Title: Lot Release Approval for Customer 714503

Doc Number: QA-032-01.02

Lot #:

Product: Cysteine 50mL

Page 4 of 4

By/Date: Heidi Wilson 08-12-15	
By/Date: [Signature] 8/12/15	
Do the investigations support the release of this product? (Circle One)	Yes No <input checked="" type="radio"/> N/A (If No, provide comment)
Is the product acceptable for release? (Circle One)	<input checked="" type="radio"/> Yes No (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
Document Present and Complete		
Material Safety Data Sheet (MSDS) (one per pallet) revision # N/A TH 08-17-15	<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> N/A	By/Date: [Signature] 08-17-15
MFG-037-01 "Retention Sample Form for Sandoz Inc. (ID# 714503) Drug Products" (last form in batch record)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A	By/Date: [Signature] 08-17-15
Allergy Laboratories, Inc. Certificate of Analysis	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A	By/Date: [Signature] 08-17-15



2/14 07-15-15 07-07-15

<b>Form Title: Routine Intervention Log - Line 2 Aseptic Products</b>	
<b>Doc Number: QA-006-03.01</b>	Page 1 of 1
<b>Lot #: 2072115</b>	<b>Product Name: Cysteine 50mL</b>
<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): MAY 05 2015</p>	
<p>Form Effective Date (stamp): MAY 06 2015</p>	

Area	Count	Notes
Glass/Inert (Glass) 3 Doors Fill Machine (FM) 2 Doors Stopper/Evaporator (SE) 6 Doors	1	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	
Filter Vials Caps/Plugs/Stop (top stains) Outlets/Taps/Rib On/Over/Up Int. Plates	0	

<b>Before Break</b> Time: 6:47 AM - 9:57 AM Date: 07-21-15 By: JS	<b>After Break</b> Time: 10:47 AM - 12:47 PM Date: 07-21-15 By: JS
0 1/2 5.21.15 SD	Jeff 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]*

Batch Size: 750L/762.0kg

Qty manufactured: 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/mL	Qty Required	By	Exp. Date	Quantity	Date	Dispensed	Checked
1. EX-10000	Water for Injection USP	0.90mL	686.0kg	N/A	N/A	686.0kg	07-20-15	<i>[Signature]</i>	<i>[Signature]</i>
2. AP-10000	Cysteine HCl Monohydrate	50mg	37.5kg	6947-4 6947-5	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	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 #	Page 2 of 6
F1000	Cysteine HCl Injection 50mg/mL	Sandoz Inc.	2072115	

PRE-VENTILATING				
Equipment	ID#	Document with full certification (ID#)	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) (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: <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 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. Record the tank weight <u>387.3</u> kg. Label the tank as QUARANTINE. Proceed to tare the scale.				
4.	Add 686.0 kg of USP WFI (item #1) to the tank. Record results on Page 1 of the batch record. WFI source (✓one): <input type="radio"/> 2130 <input checked="" type="radio"/> 2130HE <input type="radio"/> 2131 When using WFI source 2130HE refer to the instruction in FAE-004 for operation of the heat exchanger. Allow WFI to cool between the temperatures of 20°C-32°C.				
5.	Temperature of WFI: <u>29.0</u> °C Verify that the temperature measuring device ID# <u>0267</u> is within calibration.				
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. Record mixing speed: <u>260</u> rpm.				
7.	Check the raw materials for the correct name, item code and quantity. Record results on Page 1 of this form.				

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 4 of 6	

<p>Step 8: MANUFACTURING PROCESS</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>Step 9: 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>Step 10: 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>Step 11: 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	

SOP: 001-001-001 MANUFACTURING PROCESSES		BATCH: 2072115		DATE: 07/20/15																									
12.	<p>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 07-20-15		52 57.20.15																								
13.	<p>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). Add slowly and mix 15 min before retest.</p> <table border="0"> <tr> <td></td> <td>1</td> <td>2</td> <td>3</td> </tr> <tr> <td>pH Before</td> <td>_____</td> <td>_____</td> <td>_____</td> </tr> <tr> <td>pH After</td> <td>_____</td> <td>_____</td> <td>_____</td> </tr> <tr> <td>Time start</td> <td>_____</td> <td>_____</td> <td>_____</td> </tr> <tr> <td>Time finish</td> <td>_____</td> <td>_____</td> <td>_____</td> </tr> <tr> <td>Total mixing time</td> <td>_____</td> <td>_____</td> <td>_____</td> </tr> </table> <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>		1	2	3	pH Before	_____	_____	_____	pH After	_____	_____	_____	Time start	_____	_____	_____	Time finish	_____	_____	_____	Total mixing time	_____	_____	_____	QA/QC:			
	1	2	3																										
pH Before	_____	_____	_____																										
pH After	_____	_____	_____																										
Time start	_____	_____	_____																										
Time finish	_____	_____	_____																										
Total mixing time	_____	_____	_____																										



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

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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> 07-20-15	<u>[Signature]</u> 07-20-15
15.	Remove a 10mL sample into a cleaned container and submit to QA/QC for pH testing.	<u>[Signature]</u> 07-20-15	<u>[Signature]</u> 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: <u>MA</u> 07-20-15	<u>[Signature]</u> 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> 07-20-15	<u>[Signature]</u> 07-20-15
18.	<p>Time cleaned: <u>4:22pm</u></p> <p>QA/QC RELEASE: Prior to filling operation, identify the tank as being released and include product name, lot number, volume, initials and date.</p>	QA/QC: <u>MA</u> 07-20-15	<u>[Signature]</u> 07-20-15
19.	<p>Close the lid on the tank.</p> <p>Process completion time: <u>4:24pm</u> (Filling must commence within 24 hours*)</p> <p>(* indicates Critical Process Parameter)</p>	<u>[Signature]</u> 07-20-15	<u>[Signature]</u> 07-20-15

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

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

Document Review and Approval: [Signature]

017175

**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      07-15-15

Originator/date: *Thad V. Blum 01-28-14*

Department Approval/date: *Justin 1/28/14*

QA Approval/date: *cl - 2/28 01-28-14*

Customer Approval/date: *See attached page 1 for customer approval. MC01-29-14*

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	<i>SE 07-20-15</i>	750.344kg	Quantity discarded: 27.2kg - Tank - 07-21-15 4.45kg - Labware - 07-21-15	
2.	G-16	50mL 20mm Clear Glass Vial	G-16-012115	1	13940	<i>ADH 07-21-15</i>	13940	0	<i>SD</i>
3.	ST-07	20mm Rubber Stopper	ST-07-041114	1	15000	<i>SEM 07-17-15</i>	15000	0	<i>SD</i>
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-018-01-062615	1			See PAL-002-01 for vial labeling operations.		
7.	L-023-XX (current version)	Vial Tray	L-023-01-121913 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>01.28.14</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 (Controllable)	Pre-Manufacturing	Calibrator/Probe	Checked By	Date
Vial washer	0239	N/A		SS	07.20.15
Steam sterilizing autoclave(s)	0237 & 0238	12.15		SS	07.20.15
Depyrogenating tunnel	0242	12.15		SS	07.20.15
Vial filling and stoppering machine	0336	N/A		SS	07.20.15
Vial capping machine	0250	N/A		SS	07.20.15
Weight scale (Range: 0.000-310.000g) (Steps 12 & 13)	0262	8.15		SS	07.20.15
Weight scale (Range: 0.000-35.000kg) (Step 20)	0263	8.15		SS	07.20.15
Floor scale (Range: 0.0-2,250.0kg) (Step 20)	0245	8.15		SS	07.20.15
Floor scale (Range: 0.0-2,250.0kg) (Step 20)	0244	8.15		SS	07.20.15
Vial labeling machine	<input checked="" type="checkbox"/> 0257 <input type="checkbox"/> 0295 <input type="checkbox"/> 0153	N/A		SS	07.20.15
Carton printing machine	<input type="checkbox"/> 0120 <input type="checkbox"/> 0289 <input checked="" type="checkbox"/> 0391	N/A		SS	07.20.15
Shrink wrap machine	<input checked="" type="checkbox"/> 0261 <input type="checkbox"/> 0215	N/A		SS	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.

Checklist ID	Date	Checked By
1.	ELM 07-17-15	ELM 07-17-15
2.	ELM 07-17-15	ELM 07-17-15
3.	ELM 07-17-15	ELM 07-17-15
4.	ELM 07-17-15	ELM 07-17-15
5.	ADH/07-21-15	ADH/07-21-15

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")

- Obtain depyrogenated rubber stoppers for the lot.
- Record the stopper lot number and the number of stoppers received on page 1, Item 3.
- Sterilize the stoppers\* according to the instructions in FAE-026 "Operation of the Getinge Steam Sterilizers, ID#s 0237 and 0238."
- 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.
- At cycle completion, transfer the sterilized stoppers to the aseptic support room # 2119.

Prepare equipment required for the production run according to MFG-044 "Equipment Preparation for SEV and Sterile Filled Vials, Building 2."

Filling surge tank:	Autoclave Cycle #* 0238-071715-2 ELM 07-17-15 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

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.

Place all prepared equipment and components in the Aseptic Support Room ID# 2119.

\*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"> <tr> <td>Lot</td> <td>G-16-011215</td> </tr> <tr> <td>Run #</td> <td>N/A AMH/07-21-15</td> </tr> <tr> <td>Batch/Run on the tunnel computer?</td> <td>2072115</td> </tr> <tr> <td>Verified? * <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</td> <td></td> </tr> <tr> <td>(A) 205</td> <td></td> </tr> <tr> <td>(B) 68</td> <td></td> </tr> <tr> <td>(C) 705</td> <td></td> </tr> <tr> <td>(D) 13940</td> <td></td> </tr> <tr> <td>(E) 0</td> <td></td> </tr> <tr> <td>(F) 13940</td> <td></td> </tr> <tr> <td>Lot number:</td> <td>2072115</td> </tr> <tr> <td>Weight of bulk product (kg):</td> <td>762.0 kg</td> </tr> </table>							Lot	G-16-011215	Run #	N/A AMH/07-21-15	Batch/Run on the tunnel computer?	2072115	Verified? * <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		(A) 205		(B) 68		(C) 705		(D) 13940		(E) 0		(F) 13940		Lot number:	2072115	Weight of bulk product (kg):	762.0 kg
Lot	G-16-011215																													
Run #	N/A AMH/07-21-15																													
Batch/Run on the tunnel computer?	2072115																													
Verified? * <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No																														
(A) 205																														
(B) 68																														
(C) 705																														
(D) 13940																														
(E) 0																														
(F) 13940																														
Lot number:	2072115																													
Weight of bulk product (kg):	762.0 kg																													
<p>8. Prior to filling operations, the release of the bulk product must be verified.</p> <p>Product: L-Cysteine Release date: 07-20-15</p>																														

\*Critical Process Parameter

Doc Number: VMR-014.00

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\*This page shall be copied onto autoclavable paper.

50mL Cysteine HCl Injection Vial Manufacturing Record - Line 2	
Cysteine HCl Injection 50mg/mL	CYS-002
2072115	07/17

Vial filling

Step	Manufacturing Process	By Date	Checked By Date
9.	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")	JS 07-21-15	EUH 07-21-15
10.	Set-up filling and stoppering machine according to FAE-033 "Operation of the Bosch Fill Machine, ID # 0336."	JS 07-21-15	
11.	Record sterilizing filter pressure* Initial Filtration Time: 6:45AM Final Filtration Time: 12:38PM Total Filtration Time: 5 hrs 53 min (not to exceed 6 hrs 0 min)*	JS 07-21-15	
12.	Set fill volume according to FAE-033 "Operation of the Bosch Fill Machine, ID # 0336." Use scale ID# 0262 to set the fill volume. Minimum limit 50.0mL Target fill: 51.5mL Maximum limit: 53.0mL Weight (g) 50.79g 52.27g 53.80g Calculation of fill weight: Formula: Density (g) x fill volume (mL) = fill weight (g) L-Cysteine HCl 50mg/mL density=1.015g	JS 07-21-15	EUH 07-21-15
13.	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. Filling start time: 6:47AM Is start time within 24 hours of completion of the batch manufacturing process? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No Fill end time: 12:41PM Total fill time: 5 HRS 54 MIN.	JS 07-21-15	
14.	Transfer all filled and stoppered vials to the vial capping machine.	JS 07-21-15	EUH 07-21-15
15.	Approximate # of empty vials discarded during filling and stoppering: 40 Approximate # of filter vials discarded during filling and stoppering: 20		
16.	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."	EUH 07-21-15	EUH 07-22-15

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 Date
17.	Record filter lot #s and perform bubble point testing* according to the instructions FAE-033 "Operation of the Bosch Fill Machine, ID # 0336."		
	Nitrogen purging Acro 50 0.2µ filter (PN 4250) lot #:	JS	07-21-15
	Acro 50 0.2µ vent filter #1 (PN 4250) lot #:		644
	Acro 50 0.2µ vent filter #2 (PN 4250) lot #:		07-21-15
	Millipore Opticap 4" 0.22µ sterilizing filter (catalog #: KVGLS04HHB) lot #:		AMM
	Sterilizing filter post-fill bubble point (alt 50 psi)*:		08-11-15
	Vent filter #1 post-fill bubble point (alt 13 psi w/methanol): Submit vent filter to QC and log onto QC-038-01 "Sample Log and Quality Control Analytical Results Tracking."		See QC-076-01 "Gelman Acro 50 0.2µ Filter Integrity Testing" for documentation
	Vent filter #2 post-fill bubble point (alt 13 psi w/methanol): Submit vent filter to QC and log onto QC-038-01 "Sample Log and Quality Control Analytical Results Tracking."		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 *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 07-21-15	EWY 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."	LS 7-21-15	
20.	Approximate # of vials that disintegrated during capping 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."	EUJ 07-21-15	EUJ 07-21-15
	A stopper reconciliation will be performed by manufacturing personnel.		
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)		
	Approximate # of stoppers used during production $[(A) - (B)] = (C)$		
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	EUJ 07-21-15
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.	<p>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.</p> <p>Sterility = 20 vials (7 from beginning, 6 from middle, 7 from end)                      Particulate Matter = 4 vials (2 from beginning, 1 from middle, 2 from end)                      Bacterial Endotoxin = 2 vials (1 from beginning, 1 from end)                      Fill Volume = 1 vial (1 from beginning)                      Contract Testing = 7 vials (2 from beginning, 3 from middle, 2 from end)                      Aluminum = 1 vial (1 from middle)                      Total = 35 vials                      Other requirements (# of vials):                      NA 7th 08-17-15</p>	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 07-21-15	EU 07-21-15
32.	Place a package insert (Item 8) within each tray.	D.L.G 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 07-21-15	EU 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 07-21-15	SO 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 07-21-15	SO 07-21-15
36.	Place 5 shrink-wrapped trays in applicable shipping box (Item 9).	EU 08-10-15	SO 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 07-21-15	SO 08-10-15
38.	Apply the approved shipping box labels (Item 10) to each shipping box.	EU 08-10-15	SO 08-10-15
39.	Load finished product onto carts or pallets and transfer to quarantine area.	EU 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 07-22-15	SO 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

507-21-5 \* STOPPERS FOR BREAK 51-12-05

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

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

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

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

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

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

10:00AM	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

11:00AM	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

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

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

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

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

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

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

12:10PM	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

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

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



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
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5	6	7	8
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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9	10	11	12
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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9	10	11	12
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<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Handwritten notes: **2072115** and **2072115** with arrows pointing to the tables.

Reviewed by/date: **S** 08.12.15  
**S** 08.12.15

2/15 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 time/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	Specifications		Acceptance	Initials	Date	Time
		Reading at white background	Reading at black background				
Area 1	6200	3600	4200	<input checked="" type="radio"/> Yes <input type="radio"/> No, notify Supervisor	EUM	07-21-15	6:24am
Area 2	5200	3600	4200	<input checked="" type="radio"/> Yes <input type="radio"/> No, notify Supervisor	EUM	07-21-15	6:24am
Area 3	8400	3600	4200	<input checked="" type="radio"/> Yes <input type="radio"/> No, notify Supervisor	EUM	07-21-15	6:24am
Area 4	9200	3600	4200	<input checked="" type="radio"/> Yes <input type="radio"/> No, notify Supervisor	EUM	07-21-15	6:25am

IBH: 0294  
Calibration Due: 03-25-2016

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/date	Times of inspection (time-time)	Inspected by/date	Times of inspection (time-time)
EUM 07-21-15	9:20am 9:51am	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	10:49am 12:00pm	AR 07-21-15	10:53am 11:15pm
AR 07-21-15	12:25pm 12:45pm	AR 07-21-15	11:07am
AR 07-21-15		AR 07-21-15	



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 07-21-15	AR 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 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 07-22-15
# of labeled vials discarded (E) from PAE-002-01	(E) 5	
# of labeled and packaged vials (F) from PAE-002-01	(F) 13301	
# of unlabelled vials discarded during labeling (G) from PAE-002-01	(G) 0	
# of inspected unlabeled vials submitted for QC 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 ( $\leq 1.2\%$ ) Acceptable <input type="checkbox"/> Alert ( $> 1.2$ and $\leq 1.7\%$ )* Acceptable <input type="checkbox"/> Action ( $> 1.7\%$ ** Not Acceptable	ELM 07-22-15	AKR 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 ( $\leq 2.4\%$ ) Acceptable <input type="checkbox"/> Alert ( $> 2.4$ and $\leq 3.4\%$ )* Acceptable <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 ( $\leq 3.6\%$ ) Acceptable <input type="checkbox"/> Alert ( $> 3.6$ and $\leq 5.1\%$ *** Acceptable <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

Comments	✓ 8.11.15
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Manufacturing Supervisor Review	Review by/date:  08.11.15
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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: **NI** Date: **07-22-15** Time: **11:55 am**  
 Performed By: **NI** 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 Describe defect(s) here	N/A  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 NJ 07-22-15
VOC Reviewed	Initials/Date 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

QA recorded by/date  
JNA 07-15-15  
Manufacturing Supervisor verified by/date  
ECM 07-21-15  
Performed by/date/time  
JNA 07-21-15  
7:33 AM  
Checked by/date/time  
AR 07-21-15  
7:33am

QA recorded by/date  
JNA 07-15-15  
Manufacturing Supervisor verified by/date  
ECM 07-21-15

Label Information	Label Information (Check this box if you are using a pre-printed label)
Lot # 2072115	<input checked="" type="checkbox"/> Lot #
Fill volume 50 mL	<input checked="" type="checkbox"/> Fill volume
Expiration date 07/17	<input checked="" type="checkbox"/> Expiration date
Type of diluent/drug solution Cysteine	<input checked="" type="checkbox"/> Type of diluent/drug solution
Company Sandoz	<input checked="" type="checkbox"/> Company

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  
 SA 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  
 Sandoz

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 3 of 5

Lot #: 2072115

(A)	5	(for sample) label on form
(B)	80	available labels (only) on hand
(C)	5	of labels not discarded
(D)	13,301	of labels and vials used
(E)	13,391	of vials used
(F)	0	of vials used
(G)	2,590	of vials used
(H)	15,981	of vials used
(I)	99.8 %	Must be within 98-102%
		Reconciliation <input checked="" type="checkbox"/> Pass <input type="checkbox"/> Fail If fail, request a CAPA for investigation

07-22-15

07-22-15

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

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

Vials labeled by/date  
 07-21-15

Comments  
 N/A  
 07-21-15

① DOCUMENTS ON 08.19.15. 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> Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution 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>07-21-15</p>
<p>Roll # 3</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b> Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution 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>07-21-15</p>
<p>Roll # 4</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b> Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution 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>L.M.07-21-15</p>
<p>Roll # 5</p> <p>Approval by/date</p> <p>Rx only NDC 66758-005-01</p> <p><b>L-Cysteine</b> Hydrochloride Injection, USP</p> <p>PHARMACY BULK PACKAGE NOT FOR DIRECT INFUSION</p> <p>50 mg/mL</p> <p>For IV Use Only After Dilution 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> <p>AL07-21-15</p>

Handwritten notes: R/A, 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 Approval by/date	Roll # 14 Approval by/date
Roll # 11 Approval by/date	Roll # 15 Approval by/date
Roll # 12 Approval by/date	Roll # 16 Approval by/date
Roll # 13 Approval by/date	Roll # 17 Approval by/date

*Handwritten notes:*  
- In the cell for Roll # 11: M/A  
- In the cell for Roll # 12: A, 07-21-15  
- A large diagonal line is drawn across the entire table area.

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

Form Issue Date: APR 15 2014

Form Effective Date: APR 25 2014

Lot # 2072115

Product: Cysteine 50mL

Vial size: 50mL 20mm

Printed container name/part # (see Vial Manufacturing Record page 1): Cysteine / L-023-01

Printed Container Request and Check-Out	# of printed containers requested: 2788	Requested by/date: U07-1715	Attach a sample of the printed container to the back of this form
	Total # of printed containers issued: 3055	Issued by/date: U07-1715	
	Printed container part # L-023-01	Printed container ID: L-023-01-121913 (1105) L-023-01-070215 (1950)	

Print Contents	Lot or L: 2072115	Sample container printed by: U071715	By/date: U071715
	Exp or E: 07 / 17 (format: mm/yy)	QA approval (insert printed sample contained):	By/date: 07-17-15
Carton Codes Used	AL ID #: 0391		By/date: U071715

Pre-Packaging Line Clearance

Performed by/date/time: EUM07-21-15 7:22am

Checked by/date/time: AR07-21-15 7:22am

Printed Container Reconciliation	(A) 2655	(B) 1	(C) 119	(D) 279	Printed containers returned to inventory by date: U07-21-15
	# used & returned (A+B+C+D) = Total # accounted for: 3054				
	# cartons issued (100) = 99.97				
Reconciliation performed by/date: EUM07-22-15					Calculations checked by/date: 08/11/15



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)

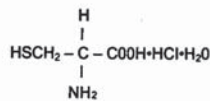
PHARMACY BULK PACKAGE  
NOT FOR DIRECT INFUSION

## 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> 2072115	<b>Product</b> Cysteine 50mL	Page 1 of 1	
<b>Vial Size</b> 50mL 20mm	<b>PI name / part # (see Vial Manufacturing Record page 1)</b> Cysteine 50mL/L-028-00	<b>Form Issue Date</b> APR 15 2014	
		<b>Form Effective Date</b> APR 25 2014	

# of package inserts forecasted	package inserts forecasted by/date	package insert 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> EUM 07-21-15	<b>QA package insert approval by/date</b> WLG 07-21-15
--	---

(A) # placed in cartons	(B) # of sample package inserts attached to form	(C) # of package inserts discarded	(D) # of package inserts returned to inventory	package inserts returned to inventory by/date
2653	1	2	122	EUM 07-22-15
<b>Package Insert Reconciliation</b> Used & returned (A - B - C + D) = Total accounted for 2653 - 1 - 2 + 122 = 2778				
<b>Reconciliation</b> (F) Must be within 98-102% 99.36				
<b>Reconciliation performed by/date</b> EUM 07-22-15			<b>Reconciliation checked by/date</b> 08-11-15	

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





Form Title: Sandoz Shipping Label Record - 50mL Cysteine

Doc Number: PAL-002-12.01

Page 1 of 2

Form Issue Date APR 15 2014

Form Effective Date APR 25 2014

Lot #

2072115

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 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>  <b>L-CYSTEINE HCl Injection, USP (50 mg/mL)</b>  <b>5 boxes of 5 x 50 mL Vials, Total Quantity 25 Vials</b>          Store at Controlled Room Temperature: 15° - 30°C (59° - 86°F).          Manufactured for:          Sandoz Inc.          Princeton, NJ 08540          L-032-00</p> <p>Affix sample label here for QA approval</p> <p><b>NDC 66758-008-02</b>  <b>L-CYSTEINE HCl Injection, USP (50 mg/mL)</b>  <b>5 boxes of 5 x 50 mL Vials, Total Quantity 25 Vials</b>          Store at Controlled Room Temperature: 15° - 30°C (59° - 86°F).          Manufactured for:          Sandoz Inc.          Princeton, NJ 08540          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>Product: Cysteine 50mL</b>	Page 1 of 2
<b>Lot #: 2072115</b>	<b>Form Issue Date: MAR 27 2014</b>	
	<b>Form Effective Date: APR 02 2014</b>	

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

Initial batch size (from pg. 1 of BMR)	(H) 7620kg	g
Amount used (from pg. 1 of BMR) Amount used - amount per vial (filling quantity plus overflow solution from the fill pass)	(I) 31.656	g
Theoretical amount of bulk solution used (H) - (I) = (J)	(J) 730.344	g

Answer to calculation 1 (C)	(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	<p>Percent yield for the number of vials prepared and # of vials labeled and packaged (including test samples)</p> <p>Change in the number of vials prepared</p> <p>Percent yield for the number of vials prepared and # of vials labeled and packaged (including test samples)</p>	<p>(N) 13361</p> <p>(O) 0</p> <p>(P) 13301</p> <p>(Q) 13940</p> <p>(Ra) 0</p> <p>(Rb) 0</p> <p>(S) 13940</p> <p>(T) 95.42 %</p>
Are the percent yields for calculations 3 or 4 below 90% or above 100%?	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, explain in comments.	

Number of vials placed into quarantine: (N) # of testing vials labeled and unlabeled = # of vials placed into quarantine

13265

Comments


N/A EUM 07-22-15

Calculations Performed By: EUM 07-22-15

By/Date: EUM 07-22-15

Manufacturing Supervisor Review: EUM 08-11-15

Review by/Date: EUM 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): <b>NOV 15 2013</b>	
			Form Effective Date (stamp): <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 <b>207 21862850</b>	<input checked="" type="radio"/> Filling Vessel <input type="radio"/> L-1 In-Line (monthly) <input type="radio"/> L-1 Purging (monthly) <input type="radio"/> L-2 Purging (monthly)	<input type="radio"/> Pre-bubble point <input checked="" type="radio"/> Post bubble point	<b>19</b>	<input checked="" type="radio"/> Yes <input type="radio"/> No
<input type="checkbox"/> N/A <b>21862850</b>	<input checked="" type="radio"/> Filling Vessel <input type="radio"/> L-1 In-Line (monthly) <input type="radio"/> L-1 Purging (monthly) <input type="radio"/> L-2 Purging (monthly)	<input type="radio"/> Pre-bubble point <input checked="" type="radio"/> Post bubble point	<b>18</b>	<input checked="" type="radio"/> Yes <input type="radio"/> No

QC Analyst	Testing performed by/date: <b>MA 07-23-15</b>
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Quality Assurance/ Quality Control Review	Review by/date: <b>JW 07-24-15</b>
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	Form Title: Method: Fill Volume		Doc Number: QC-066-01.01
			Page 1 of 1
	QC Test #: QC- <del>E-8</del> C-3001 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 <input checked="" type="checkbox"/> Tested Individually*		
Individual Results (mL)	Vial 1 50.88 mL	Vial 2 NA	Vial 3	Vial 4	Vial 5 MA 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 <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 07-24-15
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Performed By/Date	MA 07-24-15
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QA/QC Reviewed By/Date	JW 07-24-15
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	Form Title: <b>Particulate Matter Test</b>		Doc Number: <b>QC-073-01.02</b>	
			Page 1 of 1	
	QC Test #: <b>QC-C-3003</b>	QA assigned by/date: <i>MA 07-23-15</i>	Form Issue Date:  <b>DEC 11 2014</b>	
	Product: <i>L-Cysteine</i>	Form Effective Date:  <b>DEC 12 2014</b>		
	Lot #: <i>2072115</i>			
Fill volume: <i>50mL</i>				

Lighthouse particulate counter ID# 0276 Cal. due	<i>07-27-15</i>
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Test Results						
Number of vials tested	S	Particle Count	Count * Fill Vol.	<input checked="" type="checkbox"/> Pooled <input type="checkbox"/> Tested Individually*		
<b>Results</b> (Four samples taken - the first discarded)  Data attached:	$\geq 10\mu\text{m}$ Specification: <6,000	1) <i>3.8</i>	<i>190</i>	Average:  <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				
	$\geq 25\mu\text{m}$ Specification: <600	1) <i>0.2</i>	<i>10</i>	Average:  <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> $(\text{Fill Volume} * \text{Particle Count}) = \text{Particle Count per Vial Volume}$
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Comments	<i>NA MA 07-27-15</i>
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QC Analyst	Testing performed by/date: <i>MA 07-27-15</i>
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QA/QC Review	Reviewed by/date: <i>Jhw 07-28-15</i>
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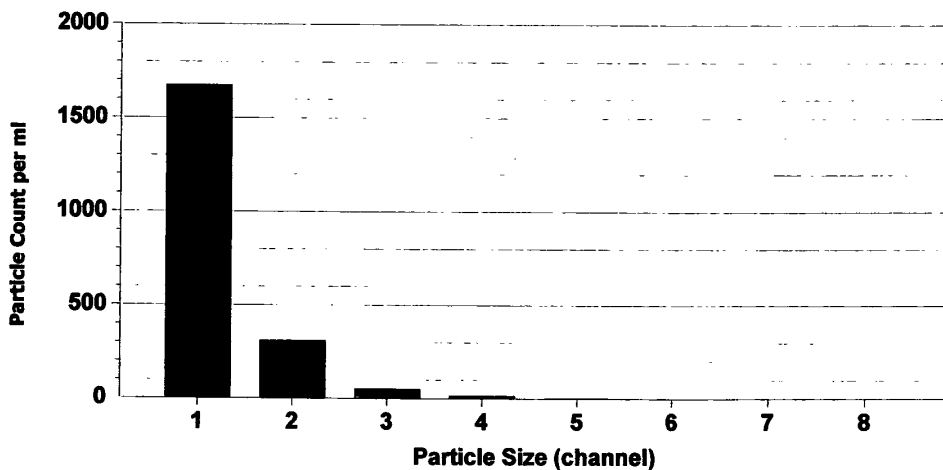


Particle Counter: LIGHTHOUSE LS-20  
 Serial Number: 100548001  
 Channel Sizes: 1.0/2.0/5.0/7.0/10.0/15.0/25.0/50.0  
 User Name: Anton  
 Lot ID: 2072115  
 Batch ID: L-Cysteine  
 Samples: 4  
 Recipe Name: Sample.rcp  
 User Entry: QC-C-3003  
 Discard First Sample

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>CH 07-23-15</b>	Form Effective Date: <del>TM 06-25-13</del> <del>JUN 26 13</del>
	Product: <b>L-Cysteine 50mL</b>		<b>TM 06-25-13</b> <del>JUN 26 13</del> <b>JUN 26 2013</b>
	Lot #: <b>2072115</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.		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/ 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: <del>N/A TT 07-27-15</del>				Plates read by/date:	

<b>Table 3</b> Dilution formula: $\text{Plate count} \times \text{Dilution factor} = \# \text{ CFU/mL in stock solution}$  $\text{_____} \times \text{_____} = \text{_____}$ Record in Table 1	Dilution Factor: 1:10 <sup>1</sup> = 10 1:10 <sup>2</sup> = 100 1:10 <sup>3</sup> = 1000 1:10 <sup>4</sup> = 10000 1:10 <sup>5</sup> = 100000 1:10 <sup>6</sup> = 1000000
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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>
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Quality Assurance/Quality Control Review	Review by/date: <b>JW 07-27-15</b>
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Form Title: <b>Sterility Test Form</b>		Doc Number: <b>QC-118-01.00</b>
QC Test # <b>QC-M-5642</b>	Issued By/Date: <b>CH 07-23-15</b>	Page 1 of 1
Product Name/Potency: <b>L-Cysteine</b>	Lot #: <b>2072115</b>	Form Issue Date: <b>JUN 27 2014</b>
Fill Volume: <input type="checkbox"/> NA <b>50 mL</b>	Vial Size: <b>50/20</b>	Form Effective Date: <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 <input type="checkbox"/> Up to vial neck <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>
Rinse Fluid:	<b>A</b>	Lot #:	<b>07-28-15 7141</b>	Exp. Date:	<b>09-27-15</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>
Tested By / Date:		<b>TT 07-28-15</b>			


Sample Description	TH Incubated at 30-35°C			TSB 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 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>	Isolator Surface Center	<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: <b>jlw 08-11-15</b>
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	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:  CH 07-23-15	Form Issue Date: JAN 22 2014
		Form Effective Date: JAN 23 2014

Results of Controls and Samples (+) = pyrogenic (gel formed) (-) = non-pyrogenic (no gel formed)								
QC Test# (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 (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 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 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
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<b>Quality Assurance/ Quality Control Review</b>	Review by/date: Jlw 07-24-15
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# KABS

Pharmaceutical Quality Systems, Inc.

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

**Certificate No: 125353**

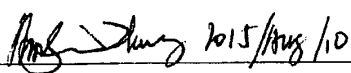
Purchase Order No: 20150727      Sample Code: N. App.  
Issuing Date: 2015/Aug/10      Sample Lot No.: 2072115

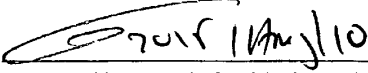
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

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 % (47.5 – 52.5 mg/mL) Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	98.7 % LC <sup>1</sup> (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

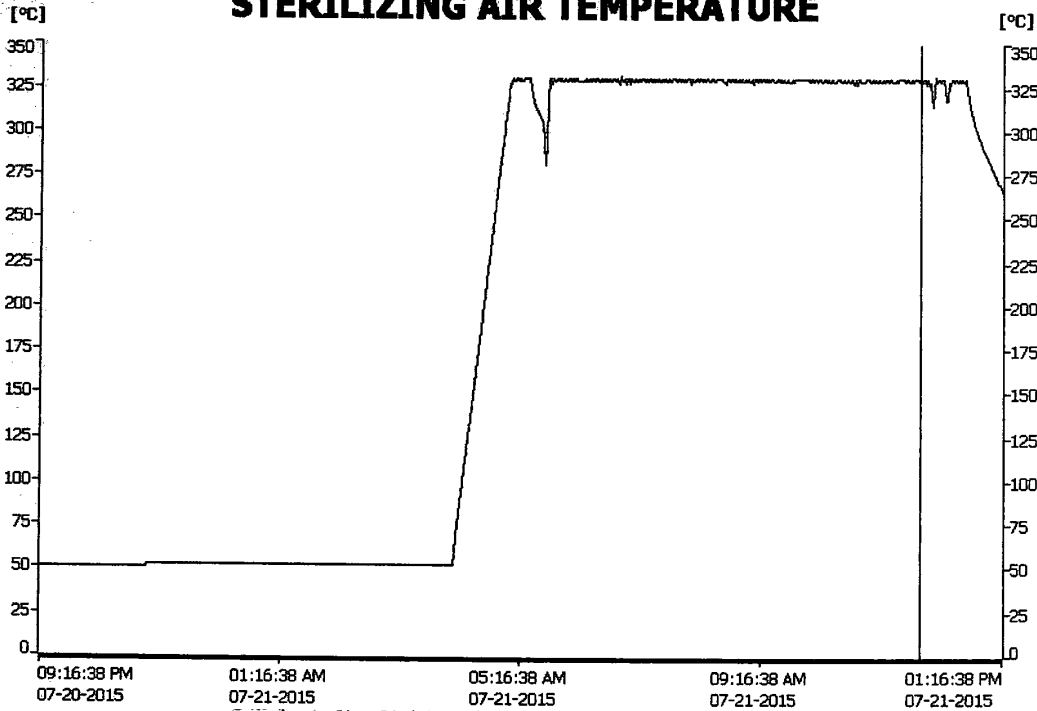
Verified by:  2015/Aug/10  
Ning-Min Zhang, B.Sc.  
Analyst, Quality Assurance

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



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

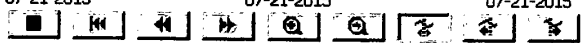
CMDS

Audit Trail

Historical Data

Data out

Main Page

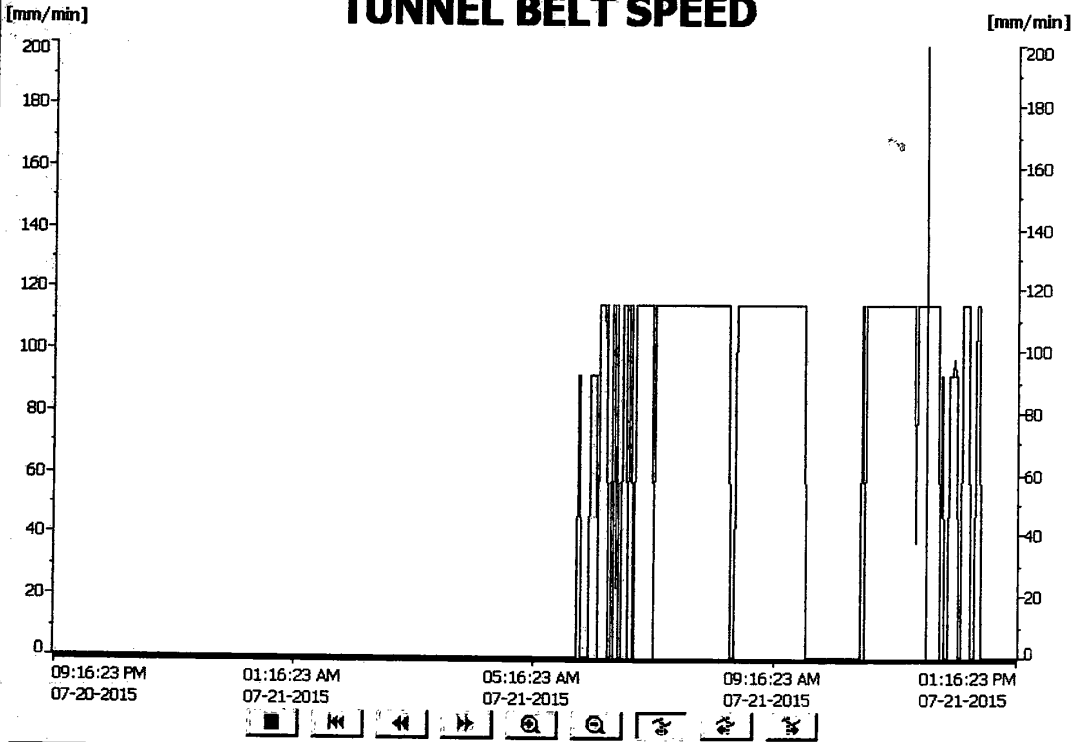


Trend	Value	Date/Time
Sterilizing Air Temperature Log	329	07-21-2015 11:55:3...
Sterilizing Air Temperature - Process Value	266.0	



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

## TUNNEL BELT SPEED



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

data:text/html;charset=utf-8,%3Cp%20style%3D%22font-family%3A%20Verdana%3B%20font-size%3A%2010pt%3B%20color%3A%20000000%3A%20font-weight%3A%20bold%3B%20fo... 1/2

Right Forearm	Personnel	Salas Junior	>= 2 cfu/site	>= 3 cfu/site	0	0	Acceptable	7/21/2015 12:42:00	L- Cysteine	Personnel 2	Line 2				End of Production
Chest	Personnel	Quintero Juan Carlos	>= 2 cfu/site	>= 3 cfu/site	0	0	Acceptable	7/21/2015 12:50:00	L- Cysteine	P-JCQ-2 Personnel 2	Line 2				End of Production
Left Finger	Personnel	Quintero Juan Carlos	>= 1 cfu/glove	>= 2 cfu/glove	0	0	Acceptable	7/21/2015 12:50:00	L- Cysteine	P-JCQ-2 JCQ Personnel 2	Line 2				End of Production
Left Forearm	Personnel	Quintero Juan Carlos	>= 2 cfu/site	>= 3 cfu/site	0	0	Acceptable	7/21/2015 12:50:00	L- Cysteine	P-JCQ-2 JCQ Personnel 2	Line 2				End of Production
Right Finger	Personnel	Quintero Juan Carlos	>= 1 cfu/glove	>= 2 cfu/glove	0	0	Acceptable	7/21/2015 12:50:00	L- Cysteine	P-JCQ-2 JCQ Personnel 2	Line 2				End of Production
Right Forearm	Personnel	Quintero Juan Carlos	>= 2 cfu/site	>= 3 cfu/site	0	0	Acceptable	7/21/2015 12:50:00	L- Cysteine	P-JCQ-2 JCQ Personnel 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 Plate	Filling	>= 2 cfu/plate	>= 4 cfu/plate	0	0	Acceptable		7/21/2015		L- Cysteine	S-L2-Tuesday	Line 2		N.A.	N.A.

data:text/html;charset=utf-8,%3Cp%20style%3D%22font-family%3A%20Verdana%3B%20font-size%3A%2010pt%3B%20color%3A%20000000%3B%20font-weight%3A%20bold%3B%20fo... 1/2

10 (2C)	filler	Surfaces	100	Contact Plate	Filling and Capping Line 2	>= 2 cftu/plate	>= 4 cftu/plate	0	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	N.A.	N.A.
12 (3C)	Behind conveyor	Surfaces	100	Contact Plate	Filling and Capping Line 2	>= 2 cftu/plate	>= 4 cftu/plate	0	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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	0	Acceptable	7/21/2015 12:50:00	Cysteine Tuesday L2	Line 2	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: **EM 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: **Jul 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 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	102.3 % LC <sup>1</sup> (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> <i>Method II</i>	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	98.8 % LC <sup>1</sup> (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)**

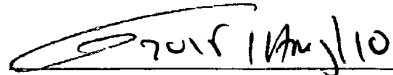
Test	Methods	Specifications	Results
Appearance of Product	Visual	Clear colorless solution free from visible particulate matter	Clear colorless solution free from visible particulate matter
Appearance of Container/Closure	Visual	No apparent leakage or physical alteration	No apparent leakage or physical 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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	98.7 % LC <sup>1</sup> (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

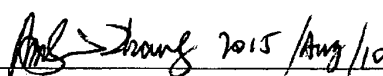
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

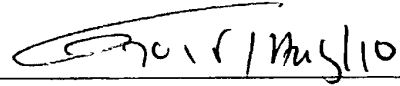
Test	Methods	Specifications	Results
Appearance of Product	Visual	Clear colorless solution free from visible particulate matter	Clear colorless solution free from visible particulate matter
Appearance of Container/Closure	Visual	No apparent leakage or physical alteration	No apparent leakage or physical 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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL) Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	98.5 % LC <sup>1</sup> (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  
CONFIDENTIAL

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Eton Ex. 1022  
106 of 131

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

Certificate No:	<b>125929</b>
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Purchase Order No:	20150827	Sample Code:	N. App.
Issuing Date:	2015/Sep/10	Sample Lot No.:	2081915

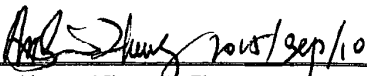
Product: **10 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

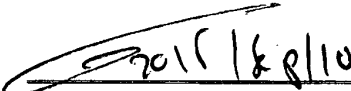
Test	Methods	Specifications	Results
Appearance of Product	Visual	Clear colorless solution free from visible particulate matter	Clear colorless solution free from visible particulate matter
Appearance of Container/Closure	Visual	No apparent leakage or physical alteration	No apparent leakage or physical 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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	96.4 % LC <sup>1</sup> (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>
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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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 - 105.0 % (47.5 - 52.5 mg/mL)  Action limit: 85.0 - 115.0 % (42.5 - 57.5 mg/mL)	96.4 % LC <sup>1</sup> (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:	<b>125931</b>
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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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	96.2 % LC <sup>1</sup> (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

## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

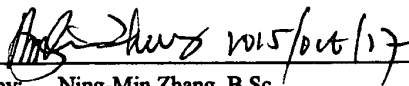
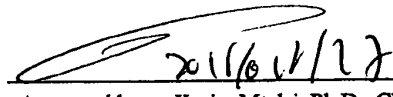
**Certificate No: 126842**

Purchase Order No:	20151013	Sample Code:	N. App.
Issuing Date:	2015/Oct/27	Sample Lot No.:	2093015
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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	97.1 % LC <sup>1</sup> (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*

<p style="text-align: center;">                  Verified by: <b>Ning-Min Zhang, B.Sc.</b>                  Analyst, Quality Assurance</p>	<p style="text-align: center;">                  Approved by: <b>Karim Mtalsi, Ph.D., Chemist</b>                  Director, R &amp; D Department</p>
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## CERTIFICATE OF ANALYSIS

For: **ALLERGY LABORATORIES INC.**

<b>Certificate No:</b>	<b>126843</b>
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Purchase Order No:	20151013	Sample Code:	N. App.
Issuing Date:	2015/Oct/27	Sample Lot No.:	2100115

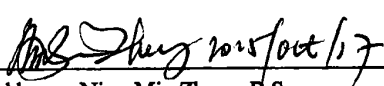
Product: **50 mL L-Cysteine HCl Injection, USP (50 mg/mL)**

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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	97.9 % LC <sup>1</sup> (49.0 mg/mL)
Aluminum Content <sup>2</sup>	USP 38 <206>	NMT 5000 ppb	48 ppb

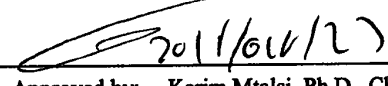
<sup>1</sup> Label Claim: 50 mg/mL

<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>
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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> Method II	NMT 2 ppm	< 2 ppm
Assay	KABS-1348-LC-V03	Alert limit: 95.0 – 105.0 % (47.5 – 52.5 mg/mL)  Action limit: 85.0 – 115.0 % (42.5 – 57.5 mg/mL)	97.3 % LC <sup>1</sup> (48.6 mg/mL)
Aluminum Content <sup>2</sup>	USP 38 <206>	NMT 5000 ppb	< 43 ppb

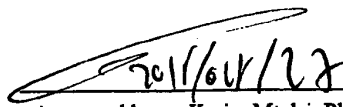
*Reviewed By*  
*MA 10-28-15*

<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 NMT 600 particles (≥25µm)/vial	60.0 particles ≥10µm/vial 2.0 particles ≥25µm/vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 – 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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Quality Assurance Approval	
By / Date	<i>M. Cobb</i> 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

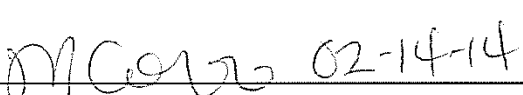
Manufacture date: 01/22/2014

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 ( $\geq 10\mu\text{m}$ )/vial NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial	48.0 particles $\geq 10\mu\text{m}$ /vial 1.3 particles $\geq 25\mu\text{m}$ /vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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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 (≥10µm)/vial NMT 600 particles (≥25µm)/vial	190.0 particles ≥10µm/vial 10.0 particles ≥25µm/vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 – 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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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 NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial	173.3 particles $\geq 10\mu\text{m}$ /vial 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% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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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 (≥10µm)/vial NMT 600 particles (≥25µm)/vial	148.0 particles ≥10µm/vial 2.7 particles ≥25µm/vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 – 52.5mg/mL)  Action limit: 85.0 - 115.0% (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
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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 NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial	68.0 particles $\geq 10\mu\text{m}$ /vial 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% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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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: 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 (≥10µm)/vial NMT 600 particles (≥25µm)/vial	69.0 particles ≥10µm/vial 2.0 particles ≥25µm/vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 – 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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Quality Assurance Approval	
By / Date	<i>Heidi Wilson</i> 09-23-15

Original Certificate

1005 S.W. Second Street  
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: 2093015

Vial size: 50ml-20mm

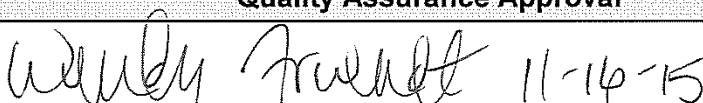
Manufacture date: 09/30/2015

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 NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial	103.3 particles $\geq 10\mu\text{m}$ /vial 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% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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
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Quality Assurance Approval	
By / Date	 11-14-15

Original Certificate

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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 NMT 600 particles ( $\geq 25\mu\text{m}$ )/vial	200.0 particles $\geq 10\mu\text{m}$ /vial 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% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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.

Release Date	02/08/2016	Release Quantity	13,000
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Quality Assurance Approval	
By / Date	<i>Heidi Wilson 02-08-16</i>

Original Certificate

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

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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

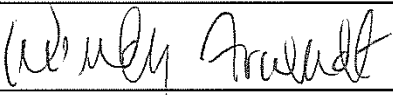
Manufacture date: 10/02/2015

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 NMT 600 particles (≥25µm)/vial	126.7 particles ≥10µm/vial 0.0 particles ≥25µm/vial
Assay	USP, KABS-1348-LC, ARL-AM121 or TEM-2011	Alert limit: 95.0 - 105.0% (47.5 - 52.5mg/mL) Action limit: 85.0 - 115.0% (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.

<b>Release Date</b>	11/12/2015	<b>Release Quantity</b>	13,000
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Quality Assurance Approval	
By / Date	 11-16-15

Original Certificate

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

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

www.AllergyLabs.com  
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>  <i>Duration of treatment</i>  <i>Other co-administered amino acids, electrolytes and trace elements</i>	<i>Reason for cysteine supplementation</i>	<i>Efficacy Outcome</i>  <i>Include descriptive and/or quantitative information for any of the outcomes provided</i>  <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> <i>Duration of treatment</i> <i>Reason for cysteine supplementation</i> <i>Other co-administered amino acids, electrolytes and trace elements</i>	<i>Safety Outcome</i> <i>Include descriptive and/or quantitative information for any of the outcomes provided</i> <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

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Office of New Drugs  
Center for Drug Evaluation and Research  
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Silver Spring, MD 20993 - *Use zip code 20903 if shipping via United States Postal Service (USPS)*  
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