AUDIT CONDUCTED AND PREPARED BY:
LABTOPIA, INC.

FOR

UNIVAR USA, INC.

AUDIT REPORT

Company A
Anytown, USA

Dates of Audit: July 8-9, 2012

Date of Report: August 28, 2012

Date of Final Report: September 16, 2012

1. AUDIT EXECUTIVE SUMMARY

Company A produces liquid Product A and Product B and crystalline Product B which are sold as USP grade products. Therefore, the purpose of the audit was to ascertain the degree of compliance to International Pharmaceutical Excipient Council (IPEC:PQG) Good Manufacturing Practices for Pharmaceutical Excipients in the manufacture, handling, storage and testing of these products. The scope of the audit encompassed raw material receipt to initial finished product distribution at a contracted off-site warehouse owned and operated by Warehouse Company X. The assessment included review of procedures, records, and quality control systems established for these operations. This summary indicates the auditor's judgment as to the extent of Company A's compliance with the guidance set forth in the IPEC:PQG GMPs and opportunities for improvement.

The staff at Company A Anytown, USA was knowledgeable and focused in the establishment of an effective quality management system incorporating elements of the IPEC:PQG GMP guidance. The personnel in all areas were co-operative in providing all information requested by the auditor. All questions were completely answered with supporting evidence provided by thorough documentation and records. A number of positive observations were noted.

1. The site has sound programs in place to prevent contamination to excipient products. This includes monitored metal detection systems, enclosed manufacturing facilities, robust pest control programs, sanitation and cleaning procedures and appropriate personnel gowning procedures.
2. The site has a sound change control program based on the IPEC Significant Change guidance which includes customer notification in the event of a significant change.
3. All plant documents were found to be approved and controlled.
4. Management commitment to a quality system based on IPEC:PQG GMPs is evident throughout. This was supported by the Quality Policy, Quality Manual, quality objectives and annual product review.

A summary of deficiencies and Company A's corrective action response with estimated completion dates can be found in Attachment 5. Company A's written audit response is included as an attached document.

This report is the opinion of the auditor only and is based on a sample of Company A's quality system and information presented at the time of the audit.

2. AUDIT INFORMATION

Client Name	Company A
Client Mailing Address	1234 A Street, Anytown, USA 11114
Address of audited location	1234 A Street, Anytown, USA 11114
Primary client contact	Mr. Bob Smith
Telephone	123-456-7890
Fax	123-456-7890
e-mail	Bob.smith@companya.com
Audit guideline used	IPEC:PQG Good Manufacturing Practices for Pharmaceutical Excipients (2006) The IPEC Good Distribution Practices Guide for Pharmaceutical Excipients (2006)

3. LIST OF ATTACHMENTS

Attachment 1	Personnel Participating in the Audit
Attachment 2	Auditor Qualifications
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Attachment 5	Company A's Audit Response

ATTACHMENT 1: PERSONNEL PARTICIPATING IN THE AUDIT

4. AUDIT TEAM MEMBERS

Lead Auditor

NAME	TITLE	ORGANIZATION/ADDRESS
Ms. Gretchen Mc Auliffe	President & Principal Consultant	Labtopia, Inc.

5. CLIENT PERSONNEL

NAME	TITLE	DEPARTMENT
Mr. Bob Smith	Manager QA/QC	Company A
Mr. Mike Jones	Quality Assurance Manger	Company A
Mr. Paul Miller	Process Supervisor	Company A
Mr. Henry Johnson	Senior Plant Accountant	Company A
Mr. Tom Adams	Plant Manager	Company A
Ms. Sue Smith	Customer Service Supervisor	Warehouse Company X
Mr. Bill White	Vice President Warehousing, Home Delivery & Record Storage	Warehouse Company X

ATTACHMENT 2

AUDITOR QUALIFICATIONS

Gretchen McAuliffe, President and Principal Consultant of Labtopia, provides GMP, GLP and ISO support to manufacturers, laboratories, and distributors in regulated industries. During her career, she has managed and conducted domestic and international audits of manufacturers, distributors and laboratories. She has extensive experience in quality management systems, SOP development, document control, and laboratory compliance. Previously, Ms. McAuliffe's was responsible for Quality Assurance, Quality Control and GMP compliance activities, for a global specialty chemical manufacturer. Ms. McAuliffe has a B.S. in Biology from the University of Houston and a M.S. in Biological Sciences from the University of Houston-Clear Lake. She is an American Society for Quality (ASQ) Certified Quality Auditor (CQA), Certified Pharmaceutical GMP Professional, Certified Biomedical Auditor (CBA) and Certified HACCP Auditor (CHA). She is also a certified ISO 9001:2008 lead auditor. She has received training in Good Laboratory Practices, Good Manufacturing Practices and International Pharmaceutical Excipient Council Good Manufacturing Practices for Excipients.

ATTACHMENT 3: AUDIT SUMMARY
COMPANY A
ANYTOWN, USA

BACKGROUND & HISTORY

Company A Specialty Ingredients manufactures liquid and crystalline chemicals at the Anytown, USA facility. The chemicals are sold as liquid Product B USP grade and crystalline Product B (trade name Excipient A®) and USP grade liquid Product A (trade name Excipient B®).

Company B began manufacture of liquid Product B at the facility in 1973. Company B sold the liquid chemicals plant in June 2000 to Company C and Company C sold the plant to Company A in February 2010. The plant operates 24 hours a day, 7 days a week. The liquid chemicals plant size is approximately 30,000 sq. ft.

In September 2011, Company A commissioned a new Product B plant. The plant operates 24 hours a day, 7 days a week. The crystalline Product B plant is approximately 20,000 sq ft. The plant has the capacity to produce 20 MM lbs/yr crystalline Product B using melt crystallization technology. The primary feed stock is USP Product B from the liquid chemicals plant on-site. The plant produces five different products using melt crystallization technology which are differentiated based on particle size. The products are packaged in three different types of containers. The plant is operated by two operators per shift.

Company A does not have any Drug Master Files for any USP grade product produced at the Anytown, USA site. The plant does not have ISO 9001 accreditation.

The Company A site was last audited by the Food and Drug Administration (FDA) in Month Year. No 483s were issued.

4. QUALITY MANAGEMENT SYSTEM-EXCIPIENT QUALITY SYSTEMS

4.1 General Requirements

4.2 Documentation Requirements

Company A has a Corporate Quality Manual that is the top tier document in the quality management system. This manual is reviewed annually. The plant also has a site Quality Manual (effective date mm/dd/yy). The plant has a Document Control Procedure (xx-xx) that outlines the formal control, approval and issuance of documents at the Anytown, USA facility. Documents are stored on a local area network drive for use in the work areas. Operating Areas have hardcopy distribution of applicable Standard Operating Procedures. Documents are required by SOP xx-xx to be reviewed every two years. The approvers for each document are assigned by Quality Assurance. Training must occur on any document updates within 30 days of the document approval.

The Quality Policy is posted and given to every employee. The facility has a GMP Poster posted throughout the facility and in manufacturing areas that outlines the intent to meet basic excipient GMP requirements.

GMPs are applied from the point of raw material unload in the liquid chemicals plant.

Records are retained onsite for 7 years. The record retention procedures are defined in SOP xx-xx.

DEF-1: The laboratory does not control the issuance or retention of laboratory notebooks (IPEC:PQG GMP Guide§4.2.3 and §4.2.4).

Documents Reviewed

XX-xx	Corporate Quality Manual
XX-xx Rev. 2	Document Control Procedure
XX-xx Rev. 1	Data Record & Recording Procedure

4.3 Change Control

The site follows a written Management of Change procedure (XX-xx). This procedure follows the IPEC Significant Change Guide. Quality must approve every site MOC prior to implementation. The products produced at the Mapleton facility do not have a Drug Master File filed with the FDA; therefore, the Management of Change Procedure does not require update of these documents. The management of change procedure does require an evaluation of any existing validation documents for changes made to GMP processes. The procedures requires a notification to customers for all significant changes as defined by the IPEC guidance.

Documents Reviewed

XX-xx Rev. 1	Management of Change Procedure
MOC No. 1	
MOC No. 3	

5. MANAGEMENT RESPONSIBILITY

5.1 Management Commitment

Management commitment is documented in the form of a corporate Quality Policy.

5.2 Customer Focus

Customer requirements are defined and met. The plant hosts approximately 10-12 customer audits per year.

5.3 Quality Policy

The corporate Quality Policy is posted throughout the facility. All employees must sign a business code of conduct yearly which includes the Quality Policy. The Quality Policy supports continual improvement of the quality management system.

5.4 Planning

Plant quality goals are aligned with the corporate goals issued annually by the Senior Director of Quality. The manufacturing site monitors and publishes metrics monthly. These metrics include out-of-specification, customer complaints, COA conformity and first pass compliance. A summary is reviewed annually during the Annual Product Review.

5.5 Responsibility, Authority and Communication

Organizational charts exist to show an independent relationship between Quality and Production. The site QA/QC Manager reports to the Plant Manager and has dotted line responsibility to the Sr. Director of Quality, Safety, and Regulatory Affairs. In addition, the Manager, US Quality Assurance reports directly to the Sr. Director Quality, Safety and Regulatory Affairs. Job descriptions exist for all positions. The Quality Unit's responsibilities are defined within the job descriptions and throughout the Standard Operating Procedures.

The plant QA/QC Manager is responsible for approval of raw material specifications and the Manager, US Quality Assurance is responsible for approval of finished product specifications. The plant QA/QC Manager is responsible for the disposition of all raw materials, in-process, and finished products.

The Sr. Director Quality, Safety and Regulatory Affairs is responsible for dissemination of quality policies, quality objectives and procedures throughout the organization.

Documents Reviewed

	Associate Chemist/Chemist Job Description
	Company A Specialty Ingredients Organizational Charts • Senior Management • Plant Organizational Chart • Quality, Safety and Regulatory Affairs North American Division • Plant QA/QC Department

5.6 Management Review

The management representative, the plant QA/QC Manager, reports on the conformance of the Quality System through an Annual Product Review. The last review was done in January 2012 and covered product produced in 2011. This process is defined in SOP XX-xx.

6. RESOURCE MANAGEMENT

6.1 Provision of Resources

6.2 Human Resources

Of the 28 employees at the Company A Anytown plant, 20 of them are operators. The operators are members of the "Y" Union. Expected employee performance for each unit operation is defined by collective bargaining agreements. During the start-up of the crystalline Product B plant, employees were trained on standard operating procedures and work instructions. The plant site is in the process of transitioning to a CBT based training called "Training Online".

Training requirements are defined in SOP XX-xx "Employee Training Procedure". Employee GMP training is conducted on-site by the QA/QC Manager every two years. New hires receive approximately one hour of GMP training. The QA/QC Manager attended the IPEA Excipient GMP course in mm/yy. Employees were aware of GMP requirements as they pertained to their job function when interviewed. The plant provided documented evidence of GMP training.

Sanitation and hygiene practices are defined in the procedure SOP XX-xx "GMP Procedure." GMP posters are posted throughout the plant site which define basic hygiene requirements. Appropriate gowning must be worn in packaging areas. Jewelry and loose items are prohibited in manufacturing areas. Buildings are only accessible through site security.

Company A retains an outside consultant to monitor changes in regulatory requirements. The consultant provides a monthly update of changes to the USP-NF, FCC, JP, EP, etc. that affect Company A's products. In addition, the site maintains an up to date copy of the United States Pharmacopoeia.

Documents Reviewed

SOP XX-xx Rev. 1	Employee Training Procedure
	GMP Poster

6.3 Infrastructure

The manufacturing process of liquid chemicals is primarily a closed system consisting of raw material storage tanks, reactors, intermediary storage tanks, an evaporator and bulk storage tanks for finished excipients. Most of the process equipment is in an enclosed building. Raw materials are primarily received through rail cars and are unloaded using dedicated hoses. All hoses were capped at the time of the audit. Finished product is either packaged in an enclosed environment or transferred to raw material feed tanks for the crystalline Product B plant. Non-USP grade product and specialty blends are manufactured using some of the same equipment.

The crystalline Product B manufacturing process consists of an evaporator, extruder, conditioner, hopper, mill, sifters, and product hoppers. Product is monitored for metal contamination using magnets

and metal detectors. The manufacturing process is in an enclosed building. The manufacturing equipment is dedicated to crystalline Product B manufacture. Finished product is packaged in a dedicated, enclosed environment. The crystalline Product B process was commissioned in mm/yy by an outside vendor.

All plant operations use a Type A Distributed Control System. The DCS in the liquid chemicals plant was validated in 2010 and was validated in 2011 for the crystalline plant. The system is not 21 CFR Part 11 compliant. Operators use a general log-in id to access the system. Two persons have authority to make changes in the system. Modifications to the system are maintained in a log with a date/time stamp. Changes to the system are included as part of the Management of Change procedure.

Potable water is used in process areas. Water is tested for coliform quarterly according to SOP XX-xx "Water Testing". Microbial testing is performed in-house every other week.

The analytical laboratory is located in the crystalline Product B building. Finished product is not stored on-site, but is immediately loaded into trailers for transport to the Warehouse Company X warehouse.

6.4 Work Environment

The site has a written program to protect quality critical materials and product from contamination. The program is outlined in SOP XX-xx "Pest Control". The site uses an outside contractor to maintain this program. A site map outlines the required bait stations. The contractor issues an invoice at the time of service which outlines any problems and the corrective action taken. This is reviewed by the site QA/QC Manager. Chemicals are EPA registered and documented at the time of use. Equipment and manufacturing areas are generally enclosed. No pests or vermin were noted during the audit.

Lighting, drainage, and washing and toilet facilities appear adequate. Facilities are available for employees to change clothes. Uniforms are laundered by an outside vendor.

Documents Reviewed

SOP XX-xx	Pest Control

7. PRODUCT REALIZATION

7.1 Planning of Product Realization

The liquid chemicals plant produces USP and non-USP grade product in a semi-continuous process. Reactor batches are fed forward to a feed tank where continuous processing starts. Reactor batches are also assigned sequential lot numbers depending on which of the reactors is used. The crystalline plant produces only NF or FCC grade product in a continuous process. Process flow diagrams exist for the chemicals and crystalline plant.

A lot is defined as one finished product tank for liquid products and one product hopper of crystalline products. Lot numbers from the Anytown, USA site are assigned by the SAP system when a finished product lot is tested. The lot number is a 10 digit number. The first three digits are the plant id code (xxx for Anytown, USA), the next digit is the last number of the current year (i.e. 9), the next three digits are the julian date and the last three digits are the sequential batch number produced on that date. Sampling plans are defined in SOP XX-xx "In-Process Testing".

7.2 Customer-related Processes

Finished product specifications are approved and controlled by the Manager, US Quality Assurance. Raw material specifications are approved and controlled by the plant QA/QC Manager.

7.3 Design and Development

7.4 Purchasing

Raw materials are purchased from approved suppliers according to agreed upon specifications. Raw materials (C and D) for liquid chemical production are supplied by another Company A facility. Hydrogen, catalyst and buffers are purchased. Raw material specifications are approved by the plant QA/QC Manager. Raw materials must be approved either by testing or COA prior to use per SOP XX-xx.

Raw material USP Product B solution for the crystalline Product B plant is verified prior to use.

There is a site procedure SOP XX-xx for supplier audits.

7.5 Production and Service Provision

7.5.1 Control of Production and Service Provision

Operations are performed through approved Standard Operating Procedures. Process parameters are recorded on controlled forms. Shut down and start up procedures are also defined in approved SOPs.

Cleaning is performed between product campaigns in the liquid chemicals plant. Reactor rinses are performed per a documented procedure SOP XX-xx which defines the number of rinses that must occur between product types. Company A used a worst case scenario to validate the cleaning processes. Records are maintained of reactor rinse steps with documented start and finish times on form SOP XX-xx "Rinse Form".

At this time, there are no validated cleaning procedures required for the crystalline Product B plant since the equipment is not multi-purpose.

Product packaging of liquid chemicals and crystalline Product B is done in enclosed areas. Packagers must be appropriately gowned (hair nets, beard cover, sleeves) per SOP XX-xx "GMP Procedure". There is a written procedure (SOP XX-xx) which describes the procedure for Label Control. Labels are printed by the operator based on the pack-out instructions issued by the operations supervisor. Company A uses Easy Label to print product labels. The format of labels is controlled by the corporate logistics department. A label specimen of each lot is retained. Label reconciliation is recorded which includes the record of labels made, who made the labels, number of labels used and who destroyed excess labels.

DEF-2: For product A Lot #1234567890, the drum number (136) on the label specimen was crossed-out and drum number "68" was hand-written on the specimen label (IPEC:PQG GMP Guide §7.5.1.6).

The crystalline packaging room is cleaned daily and documented on form XX-xx. Liquid Product B and Product A share the same packaging line. The lines are cleaned between product changeovers and prior to start-up per work instruction XX-xx. The packaging area is cleaned out weekly according to a Master Cleaning Schedule (XX-xx) and is documented on XX-xx. Bag filters (F-123) are changed weekly.

DEF-3: There is not documented evidence that all previous labels have been removed prior to packaging operations. (IPEC:PQG GMP Guide §7.5.1.6).

Documents Reviewed

Validation Report A Rev 0	Validation Report for Performance of Reactor Rinses
SOP XX-xx	
Product Code 1234 Lot 1234567890	Product B Drum Filling and Pack-out Sheet (2-12-11)
SOP XX-xx	General Operating Parameters (crystalline Product B plant)
SOP XX-xx Rev 001	Metal Detector Readings
SOP XX-xx	Metal Detector Testing Procedure
SOP XX-xx	Dryer Startup Procedure
SOP XX-xx	Product B Storage and Transfer from Liquids Plant Procedure

SOP XX-xx	Evaporator and Readco General Manufacturing Instructions
A-159 Product B USP A-160 Product B USP A-161 Product B USP	Batch Record
Form XX-xx	Rinse Form

7.5.2 Validation of Processes for Production and Service Provision

The site has a Validation Master Plan (XX-xx). Validation of the liquid Product B manufacturing process was complete in February 2011 and the Product A manufacturing process was validated in 2010. An installation qualification and operational qualification was performed on the crystalline Product B manufacturing equipment by an outside vendor as part of the new equipment commissioning process. A total of three lots of two different product codes and one lot of fines were included in the protocol.

DEF-4: Validated operating ranges have not been established for quality critical parameters for the crystalline Product B manufacturing process (IPEC:PQG GMP Guide §7.1 and §7.5.2). Quality critical instruments were identified during the OQ validation phase for the crystalline Product B unit; however, there is not a clear connection between the OQ and the operating parameters assessed during the process validation protocol and translated into ranges for daily operations. Likewise, the actions required for deviating from validated operating parameters have not been defined (IPEC:PQG GMP Guide §7.1) .

Documents Reviewed

SOP XX-xx	IQ Protocol Crystalline Product B
SOP XX-xx	OQ Protocol Crystalline Product B

7.5.3 Identification and Traceability

Product labels contain the manufacturer, lot number, material number, package number, and weight.

DEF-5: During the audit of the Warehouse Company X warehouse, 9 drums of material were found labeled 1162 (for rework). The drums did not contain the name and grade of the excipient, the manufacturer's name, and batch number. (IPEC:PQG GMP Guide 7.5.3.3).

7.5.4 Customer Property

Company A does not use any customer property in the manufacture of excipients.

7.5.5 Preservation of Product

Company A's liquid Product B USP, liquid Product A USP and crystalline Product B USP do not require any special storage conditions. Therefore, records of storage conditions are not maintained.

7.6 Control of Measuring and Monitoring Devices

Scales used in manufacturing areas are calibrated monthly by an outside vendor.

DEF-6; There is not a documented calibration and maintenance program for the four instruments identified as quality-critical during the commissioning and validation of the crystalline Product B unit (IPEC:PQG GMP Guide §7.6). These instruments are Transmitter 1, Transmitter 2, Transmitter 3 and Transmitter 4.

Laboratory instruments are validated prior to use and routinely calibrated according to defined procedures. For example, balances are calibrated every six months by an outside vendor. Weekly internal weight checks are performed over the balance range of use, typically 100g, 10g, 1g, .01g. Weights are certified every six months by an outside vendor. Calibration of pH meters is done daily

with buffers 4 and 7. Calibrations are recorded in laboratory notebooks or the raw instrument data is retained (HPLCs).

DEF-7: Some laboratory equipment and instruments used to perform analytical tests do not have adequate controls to verify the acceptability of the instrument prior to use (IPEC:PQG GMP Guide §7.6). For example,

- *Mettler Toledo Balance S/N abc123, used routinely for particle size analysis, does not have documented weekly weight checks.*
- *There are no defined acceptable tolerance ranges for the weekly weight checks on any analytical balances.*
- *There is not a defined acceptance range for the calibration slope on the pH meter.*

Documents Reviewed

	Calibration certificate for weight set S/N 1234 (10/15/11)
	Maintenance logs for HPLCs
Validation Protocol xx-xx for HPLC	Operational Qualification for HPLC 1, 2, 3 and 4

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.1 General

8.2 Monitoring and Measurement

8.2.1 Customer Satisfaction

Customer complaints are received by corporate customer service and routed to the plant for investigation per Corporate procedure Corp-1 "Customer Complaint Process". Plant customer complaint responses for order processing and transportation are approved by QA/QC Manager. Quality related issues are approved by the Plant Manager prior to issuance to the customer.

8.2.2 Internal Audit

Internal audits are performed quarterly per SOP XX-xx "GMP Compliance Audit Procedure". The last internal audit was performed January 2012.

8.2.4 Monitoring and Measurement of Product

Samples are received in the laboratory and are appropriately labeled with the description of the sample, date sampled and batch number or code. Sample results are recorded in laboratory notebooks. Some calculations are performed in Excel spreadsheets.

Preparation of standards and reagents are recorded in laboratory notebooks and include the name of the solution, date of preparation, and quantities of materials used. Standardization of solutions is also recorded in laboratory notebooks.

DEF-8: Laboratory records do not contain sufficient information to establish full traceability of data (IPEC:PQG GMP Guide §8.2.4.1). For example,

- *The test method number used for analysis is not recorded in the laboratory notebooks.*
- *The Karl Fischer data printouts for water results are not retained as original observations.*
- *Laboratory personnel do not record the weights of solution preparation for pH measurement.*
- *Laboratory personnel do not record the ID of the balance used to prepare solutions or weigh materials or the instrument serial number or ID used for Karl Fischer, color or titration.*
- *Sample preparation data is recorded on the bottle and is not retained.*

Finished product testing is performed on a composite sample from each batch for crystalline Product B and on a tank sample for liquid products and compared to documented specifications within SAP. The composite of the crystalline sample is created during packaging. Manufacturing batch records and analytical data are reviewed by QA/QC prior to release of the excipient lot per SOP XX-xx "Finished Product Release". The certificate of analysis is entered into SAP and reviewed against the raw data in the laboratory notebook(s). If the product is approved, the laboratory will release the material to operations for packaging.

SOP XX-xx "OOS Procedure" describes the program for out of specification events.

Procedure XX-xx defines the sample retention policy. The retained sample size is one pint and is at least twice the amount required to perform all specification testing. Retain samples are stored in a designated retain storage area. Liquid raw material retains are stored for two years, in-process samples are retained for one week , liquid shipments are retained for two years, crystalline composites are retained for two years and tank samples are retained for one month.

The facility has recently reestablished a stability testing program for all USP grade products. The plan includes putting three lots of new product into the stability testing program. Thereafter, one lot per year is entered into the program. From each lot, two original containers are kept in the program. The stability containers are stored at the Warehouse Company X Warehouse in the same storage conditions as marketed product. Stability lots which exceed specifications are required to undergo a formal failure investigation.

Data is collected every three months for each lot. The tests include assay, pH, conductivity, water, microbial and yeast.

Retest dates of one year are assigned to each lot of product. The retest date is printed on the Certificate of Analysis.

Certificates of Analysis are issued for each lot of product. The COAs conform to all the requirements of the IPEC:PQG Certificate of Analysis Guide for Bulk Pharmaceutical Excipients (2000) except that the manufacturing site is not listed on the COA. The manufacturing site can be identified through the product lot number and is labeled on the product container. Statistical testing is performed for some analytical tests and is denoted on the COA. Statistical testing is defined by XX-xx.

DEF-9: Depending on where Certificate of Analyses are generated from the SAP system, the COA may not list the manufacturing site as suggested by the IPEC-Americas® Certficate of Analysis Guide for Bulk Pharmaceutical Excipients (§4.1).

Documents Reviewed

	Acetic acid preparation 4-7-11 (Analyst B) Sodium thiosulfate preparation 3-26-12(Analyst A)
	Various Laboratory Notebooks for daily and weekly records (no control numbers)
SOP XX-xx	Assurance Test Sample for HPLC
SOP XX-xx	Calibration of HPLCs
SOP XX-xx	Qualification of ATS
Material abc123 Lot No. 1234567890	Certificate of Analysis
SOP XX-xx	Statistical Analysis Test Scheme Procedure

8.3 Control of Nonconforming Product

Control of non-conforming work is done and documented per procedure SOP XX-xx "Nonconformance Procedure". Non-conforming material is electronically quarantined in SAP. The site QA/QC Manager is responsible for the final disposition of non-conforming product. The plant does not rework any material per the IPEC:PQG definition of rework. The plant does reprocess material and this is defined in the procedure SOP XX-xx "Finished Product Release."

The site has a “Lot Trace and Mock Recall Procedure” XX-xx and a “Recall Procedure” XX-xx that define how retrieval of an excipient from distribution should be conducted and recorded.

Returned product is handled per XX-xx “Returned Product Disposition.” Returned product disposition is determined by the site QA/QC Manager.

8.4 Analysis of Data

The site performs an annual product review which covers a review of customer plaints, product reviews and internal and external audit results per XX-xx “Annual Product Review.”

8.5 Improvement

Corrective actions are documented per XX-xx “Corrective Action Procedure.” Corrective actions are also documented through the OOS procedure XX-xx “OOC Procedure”.
Preventive actions are monitored per the procedure XX-xx “Preventive Maintenance and Calibration Cycle.”

ATTACHMENT 4: AUDIT SUMMARY
WAREHOUSE COMPANY X
Another Town, USA

BACKGROUND & HISTORY

Company A uses Warehouse Company X for the warehousing and distribution of USP grade products. The local warehouse, located in Another Town was audited for conformance to the IPEC Good Distribution Practices Guide for Pharmaceutical Excipients (2006) as it pertains to the storage and distribution of these products.

Warehouse Company X Warehouse does not perform any direct contact activities with the excipients. Therefore, the scope of the audit pertained to supply chain activities for transportation of packed excipients and warehousing of packed excipients. The audit summary sections below correspond to the appropriate sections of IPEC GDP Guide for Pharmaceutical Excipients (2006).

1. QUALITY MANAGEMENT

Warehouse Company X is not ISO accredited and does not have a documented quality systems in place. The company is registered with the FDA but has not had an FDA inspection. The Warehouse Company X Warehouse was last audited by the State Department of Health in October 2011. No observations were issued. A group from Corporate Company A audits Warehouse Company X Warehouse per a defined schedule.

2. ORGANIZATION AND PERSONNEL (except 2.6)

Employees are given safety training and on-the job training at the start of employment.

DEF-10: Warehouse Company X employees have not been trained in IPEC GDP or IPEC GMPs as they relate to the warehousing and distribution of excipients. Warehouse Company X managers were not aware of the IPEC guidance documents at the time of the audit (IPEC:PQG GMP Guide §6.2.2 and IPEC GDP Guide §2.3).

3. PREMISES (except 3.5)

Adequate areas existed to prevent contamination and mix-up of finished excipients. The buildings are not climate controlled. Lighting fixtures are plastic shielded throughout the warehouse area.

Access to the premises was controlled through visitor sign-in logs. Visitors must be escorted by a Warehouse Company X employee at all times. Access to the warehouse area was controlled through fences and/or gates.

The warehouse has a documented pest control program which is maintained by an outside vendor. The vendor performs on-site service two times per month. The warehouse has inside and outside bait stations. The bait stations are documented on a pest control map. No evidence of pest infestation was noted at the time of the audit.

4. WAREHOUSING AND STORAGE (except 4.8, 4.9, 4.10, 4.11)

Finished product is loaded onto trailers at the Company A plant. Each trailer is sealed with a unique tamper evident seal. The bill of lading accompanies the shipment to the Warehouse Company X Warehouse. When material is received at Warehouse Company X, the Warehouse Company X employee removes the seal and compares the seal number to that on the bill of lading. Each incoming trailer is assigned a tally number, which serves as the unique identifier in the Warehouse Company X inventory system. The unload is inspected, documented (initialed/dated) and reviewed by a supervisor. The material is then received into the Company A' SAP system as received at Warehouse Company X.

In addition, the product is entered into the Warehouse Company X inventory system and tracked via tally number.

6. DOCUMENTATION (except 6.3, 6.4, 6.7, 6,8, 6.9)

Warehouse Company X retains records for five years through their Warehouse Company X Records business unit.

8. COMPLAINTS

10. RETURNED GOODS

11. HANDLING OF NON-CONFORMING MATERIALS

Communication relating to non-conforming materials between the plant and the warehouse typically occurs via email. The plant QA/QC Manager quarantines material in SAP.

Hold stickers are placed on product that is quarantined. The material is quarantined electronically within the SAP and Warehouse Company X inventory system, but is not physically relocated to a quarantine area. Several quarantined lots were challenged and found to be on-hold within the inventory system.

During the audit interview process, a Warehouse Company X employee indicated that damaged labels could be re-created and replaced by Warehouse Company X employees.

Documents Reviewed

Lot abc123abc123	Quarantined material (tally #212170)
Lot abc123abc123	Quarantined material (tally #?) -

12. DISPATCH AND TRANSPORT (except 12.4, 12.5 and 12.7)

Liquid Product B and Product A and crystalline Product B do not require controlled environmental conditions during transport.

Company A' Customer Service department issues delivery documents for each Sales Order. The delivery document specifies the product lot number and ship date. The material is selected on a first in, first out (FIFO) basis, except in the case of special customer requirements. Special customer requirements will be included on the delivery document. Once the delivery document is received by Warehouse Company X, the bill of ladings (BOLs), COA and packing list are created for the shipment. The pick note given to the warehousemen specifies the internal tally number and warehouse location for the product. Product lids are typically wiped before shipment. Shipments are sent in tamper evident sealed trailers. Warehouse Company X employees post the goods as shipped in Company A' SAP system.

Documents Reviewed

BOL #987654 Sales Order #00044455566	Bill of Lading and Sales Order for Company A Lot 1234567890 and Lot abc123abc123

ATTACHMENT 5:
SUMMARY OF AUDIT OBSERVATIONS & CUSTOMER RESPONSE

DEF-1: The laboratory does not control the issuance or retention of laboratory notebooks (IPEC:PQG GMP Guide§4.2.3 and §4.2.4).

Company A' Response: Response 2
Completion Date: mm/dd/yy

DEF-2: For product abc123 Lot #1234567890, the drum number (136) on the label specimen was crossed-out and drum number "68" was hand-written on the specimen label (IPEC:PQG GMP Guide §7.5.1.6).

Company A' Response: Response 3
Completion Date: mm/ddd/yy

DEF-3: There is not documented evidence that all previous labels have been removed prior to packaging operations. (IPEC:PQG GMP Guide §7.5.1.6).

Company A' Response: Response 4
Completion Date: Complete

DEF-4: Validated operating ranges have not been established for quality critical parameters for the crystalline Product B manufacturing process (IPEC:PQG GMP Guide §7.1 and §7.5.2). Quality critical instruments were identified during the OQ validation phase for the crystalline Product B unit; however, there is not a clear connection between the OQ and the operating parameters assessed during the process validation protocol and translated into ranges for daily operations. Likewise, the actions required for deviating from validated operating parameters have not been defined (IPEC:PQG GMP Guide §7.1).

Company A' Response: Response 5
Completion Date: mm/dd/yy

DEF-5: During the audit of the Warehouse Company X warehouse, 9 drums of material were found labeled 1162 (for rework). The drums did not contain the name and grade of the excipient, the manufacturer's name, and batch number. (IPEC:PQG GMP Guide 7.5.3.3).

Company A' Response: Response 6
Completion Date: Complete

DEF-6; There is not a documented calibration and maintenance program for the four instruments identified as quality-critical during the commissioning and validation of the crystalline Product B unit (IPEC:PQG GMP Guide §7.6). These instruments are Transmitter 1, Transmitter 2, Transmitter 3, Transmitter 4.

Company A' Response: Response 7
Completion Date: mm/dd/yy

DEF-7: Some laboratory equipment and instruments used to perform analytical tests do not have adequate controls to verify the acceptability of the instrument prior to use (IPEC:PQG GMP Guide §7.6). For example,

- *Mettler Toledo Balance S/N abc123, used routinely for particle size analysis, does not have documented weekly weight checks.*
- *There are no defined acceptable tolerance ranges for the weekly weight checks on any analytical balances.*
- *There is not a defined acceptance range for the calibration slope on the pH meter.*

Company A' Response: Response 9
Completion Date: 07/30/2012

DEF-8: Laboratory records do not contain sufficient information to establish full traceability of data (IPEC:PQG GMP Guide §8.2.4.1). For example,

- *The test method number used for analysis is not recorded in the laboratory notebooks.*
- *The Karl Fischer data printouts for water results are not retained as original observations.*
- *Laboratory personnel do not record the weights of solution preparation for pH measurement.*
- *Laboratory personnel do not record the ID of the balance used to prepare solutions or weigh materials or the instrument serial number or ID used for Karl Fischer, color or titration.*
- *Sample preparation data is recorded on the bottle and is not retained.*

Company A' Response: Response 10
Completion Date: 07/30/2012

DEF-9: Depending on where Certificate of Analyses are generated from the SAP system, the COA may not list the manufacturing site as suggested by the IPEC-Americas® Certificate of Analysis Guide for Bulk Pharmaceutical Excipients (§4.1).

Company A' Response: Response 14
Completion Date: mm/dd/yy
Auditor's Reply: Reply A

DEF-10: Warehouse Company X employees have not been trained in IPEC GDP or IPEC GMPs as they relate to the warehousing and distribution of excipients. Warehouse Company X managers were not aware of the IPEC guidance documents at the time of the audit (IPEC:PQG GMP Guide §6.2.2 and IPEC GDP Guide §2.3).

Company A' Response: Warehouse Company X Warehouse has been given a Copy of the IPEC guidelines. We will request training records for IPEC GDP and IPEC GMPS.
Completion Date: 08/30/2012

DEF-11: There was no documented evidence that Warehouse Company X employees who are responsible for activities involving returned goods, quarantined material and non-conforming materials are trained in any applicable Company A's quality procedures or any internal procedures relating to the disposition of Company A's excipients, such as MPN-A-QSP-PRC-007 'Storage, Delivery & Distribution Procedure'. (IPEC:PQG GMP Guide §6.2.2 and IPEC GDP Guide §2.4).

Company A' Response: Warehouse Company X employees will be trained on all Company A applicable procedures.
Completion Date: mm/dd/yy