1. Introduction

1.1 History

The founder of Giles Chemical, John L. Giles, came to Waynesville, North Carolina in 1948. His previous ventures were with Morton Salt and prior to World War II, he formed Michigan Chemical, producer of magnesium compounds and bromine.

The Defense Department took over Michigan Chemical and Mr. Giles became a dollar-a-year member of the War Production Board. He was assigned the task of finding magnesium deposits which brought him to Asheville, North Carolina. His search for olivine (20% magnesium) led him to Balsam, North Carolina where, after the war, he purchased an area that had an outcropping of olivine.

This mineral was processed for refractory use and sold to brick manufactures, as well as, the atomic energy project in Oak Ridge, Tennessee.

Michigan Chemical operated a magnesium oxide (MgO) facility in Florida whose purity was 99% MgO, while olivine contained only 20% MgO. The source in Florida displaced the ore from Balsam, North Carolina.

While olivine was selling for $15 per ton, Epsom Salt brought $50 per ton. As a result, Mr. Giles worked out crystallizing techniques for the manufacture of Epsom Salt in Waynesville, where production began in 1950.

His first customers were the tanneries all along the Appalachian Mountains. Rayon manufacturers were next followed by wood pulp producers, resale druggists, animal glue manufacturers and dye divisions of the textile industry.

In 1965, the plant was bought by Howard Split whose 28 years in the industrial chemical distribution helped expand the business.

In 1995, the business was purchased by Richard N. Wrenn, Jr.

On February 27, 2007, Giles Chemical merged with Premier Magnesia, LLC. Premier Magnesia manufactures a wide variety of magnesium oxide and magnesium hydroxide products. Giles Chemical produces Magnesium Sulfate Heptahydrate also known as Epsom salt. Our Repackaging plant packages Epsom salt into cartons and pouches.

Giles Chemical has been a leader in magnesia chemicals for over 30 years. Premier Magnesia is the primary manufacturer of magnesium oxide and magnesium hydroxide and offers more grades of magnesia chemicals than any other supplier.

The end uses have expanded to plastics, rubber, synthetic food sweeteners, animal feeds, agricultural and various other industrial usages as well as pharmaceutical industry products.

1.2 Giles Chemical Production Activities

Activities at Giles Chemical, a division of Premier Magnesia, are the production of magnesium sulfate in both liquid and crystalline form and repackaging operations.

The company's facilities are located as follows:

Giles Chemical
Manufacturing
102 Commerce Street
Waynesville, NC 28786

Giles Chemical
Repackaging
393 Smathers Street
Waynesville, NC 28786

Production Activity at the Manufacturing Facility:

Magnesium Oxide, Sulfuric Acid, and **Water** are used in the manufacture of Magnesium Sulfate Heptahydrate. The principal ingredients are stored in tanks and silos and dispensed from there at prescribed rates to digesters where a chemical reaction occurs, and $MgSO_4$ brine is formed. The brine is filtered and directed to Vacuum Crystallizers where crystal growth is promoted. Next, crystals are separated from residual liquor, dried and packaged for shipment to customers. Liquid product is also produced in which the brine, at specified strength, is shipped direct to customers via liquid transportation. All raw materials arrive in bulk by either rail car or truck. Finished product is shipped out via truck and rail service.

Production Activity at the Repackaging Facility:

Bulk bags of Magnesium Sulfate are brought into the facility to be repackaged into much smaller retail presentations. We are able to provide a finished product ready to display on the store shelf in the following presentations: USP Pouch, USP Carton, and Scented Pouches.

Production Activity at the Greendale Facility:

Magnesium Oxide, Sulfuric Acid, and **Water** are used in the manufacture of Liquid Magnesium Sulfate. The principal ingredients are stored in tanks and silos and dispensed from there at prescribed rates to digesters where a chemical reaction occurs, and $MgSO_4$ brine is formed. The brine is filtered, diluted, and stored in tanks to await shipping to customers.

2.0 Scope

This Quality Manual and the Quality Management System at Giles Chemical, a division a Premier Magnesia, LLC (Giles) have been developed incorporating the recommended elements in International Conference on Harmonization (ICH) Q10 "Pharmaceutical Quality System" and are in compliance with the requirements outlined in the FDA's current Good Manufacturing Practices (cGMP) 21 CFR 210/211.

This Quality Manual applies to the systems supporting the manufacture of the active pharmaceutical ingredient (API) Magnesium Sulfate throughout the product lifecycle. The product lifecycle includes the following technical activities for new and existing products:

- Pharmaceutical Development
  - Process Development
  - Manufacturing of process development and scale-up
  - Analytical method development
- Technology Transfer
  - New product transfers during development through manufacturing
  - Transfer of processes to customers
- cGMP Manufacturing
  - Acquisition and control of materials
  - Provision of facilities, utilities, and equipment
  - Production (including packaging and labeling)
  - Quality control and assurance
  - Release
  - Stability
  - Storage
  - Distribution
- Product Discontinuation
  - Retention of Documentation
  - Sample Retention
  - Continued product assessment and reporting

3.0 Quality Objectives

Achieve Product Realization – To establish, implement and maintain a system that assures the delivery of products with the quality attributes appropriate to meet the needs of our customers (internal and external) and regulatory authorities.

Measurable: Customer Satisfaction Surveys

Customer and Regulatory Audit Results

Establish and Maintain a State of Control – To develop and implement monitoring and control systems for process performance and product quality, thereby providing assurance of continued suitability and process capability using quality risk management to aid in the identification of these systems.

Measurable: Trend Charting
Statistical Process Control (SPC)

Total Quality Improvements – Continuously improving all aspects of the total Quality System facilitated by applying the principals of quality risk management.

Measurable: Customer Returns
Internal Audits
Corrective Actions
Supplier Corrective Actions

Employee Loyalty – Building Long Term Relationships through the power of the "***Our House"*** philosophy and quarterly bonuses propelling improvements by the employee sharing in the gains of increased productivity.

Measurable: Turnover rates

Manufacturing – Implementing world class manufacturing and information systems.

Measurable: Yields and Utilization

4.0 Mission Statement

Giles' mission is to continually improve products and service, to meet the customers' needs and requirements, which will promote growth, improvement, and prosperity, as a business. Giles' will conduct all aspects of its business in an ethically moral and responsible manner.

To support the mission, Giles is committed to:

Servicing customers' needs with quality products which meet or exceed mutually agreed upon specifications and standards.

Continuously improving performance in delivering products to customers in a timely fashion.

Focusing on a total quality approach to processing as a means of preventing non-conformances and constantly improving systems to maintain the production of high quality products.

Protecting the safety and health of employees, the public and the environment by conducting operations in a safe responsible manner.

Building long-term partnerships with customers and suppliers and basing these relationships on mutual trust and respect.

Providing employees with the training and tools required to do their jobs efficiently and effectively, thus allowing them to contribute personally and individually to the achievement of quality.

Creating an atmosphere which encourages all employees to learn and grow professionally throughout their careers, and which allows them to participate in decision-making and problem-solving.

5.0 Management Responsibility

Senior management within Giles has the ultimate responsibility to ensure that an effective pharmaceutical quality system is in place to achieve our quality objectives and those roles, responsibilities and authorities are defined, communicated and implemented throughout the company.

Giles' management demonstrates its commitment by:

- Participating in the design, implementation, monitoring and maintenance of the quality system.
- Providing strong and visible support for the pharmaceutical quality system and ensuring its implementation throughout the organization.
- Ensuring that a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management.
- Defining individual and collective roles, responsibilities, authorities and inter-relationships of all organizational units related to the quality system and ensuring that these interactions are communicated and understood at all levels of the organization.
- Ensuring that independent quality unit exists with the authority to fulfill the requirements for quality systems as defined within applicable regulations.
- Conducting management reviews of the pharmaceutical quality system utilizing performance indicators that measure progress against quality objectives.

Supporting Documentation:

Annual Product Review	Q12-PR-100-007
Management Review	Q13-PR-100-0XX
Internal Quality Audits	Q12-PR-100-008

6.0 Quality Policy

To achieve excellence in all that we do, exceeding the expressed needs and expectations of our customers, focusing on never ending Quality Improvement, using World Class Manufacturing, Engineering, and Information Systems resulting in employee and customer trust within an environment that embodies the philosophy of ***"Do it right the first time, every time."***

Giles' management is committed to the Quality Policy as the cornerstone of our pharmaceutical quality management system. This policy is a living document that guides our strategic quality direction. Giles' Quality Policy is consistent with its organizational goals, the expectations and needs of its customers, complies with applicable regulatory requirements and facilitates continual improvement.

Giles ensures that this policy is understood, implemented and maintained at all levels throughout the company.

This policy is approved and will be reviewed periodically for continuing effectiveness by:

President, Jim Hill
Director of Operations, Matt Haynes
Director of Quality & Safety, Deborah Durbin
Manufacturing Manager, Jason Bumgarner
Repackaging Manager, Monte Plott

7.0 Quality Management System

Giles' has established and implemented a Quality Management System in accordance with the applicable requirements and is dedicated to continual improvement. The Quality Management System includes the following elements:

People:

Giles has in place an adequate organizational structure and sufficient personnel to assure that product is manufactured in accordance with cGMP regulations. All employees have job descriptions and are suitably qualified and trained to carry out their allocated duties.

At Giles, the Quality System is managed by the Quality Assurance unit. The Quality Assurance unit is separate from and independent of Production (Manufacturing/Repackaging).

Supporting Documentation:

Organizational Chart
Job Descriptions

Premises:

All premises and equipment used for the manufacture, repackaging and testing of Magnesium Sulfate are constructed, validated, cleaned and maintained in order to ensure that products are adequately protected, minimizing the possibility of contamination.

Equipment:

All equipment used for manufacturing, repackaging and testing of product is validated, maintained and calibrated to ensure both reliability and reproducibility of operations.

Processes:
All manufacturing and repackaging processes follow specifications agreed upon between the Customer and Giles. All manufacturing and repackaging follow, and are recorded on approved Daily Production Records such that full traceability of all operations and conditions are maintained. Daily Production Records are reviewed and approved by both Production and QA prior to issue and after completion of manufacturing operations.

Products:

The only product that Giles manufactures is bulk Epsom salt. Giles has no repackaged product of its own. Therefore, there is no conflict between Giles' own products and those of its customers.

Procedures:

All cGMP production and testing activities are described in approved procedures and analytical methods. Key quality system procedures include: Training, Validation, Change Control, Deviations, Complaints, Recalls, Vendor Assurance, Quality Agreements, Specifications, Analytical Method Qualification, Out of Specification and Product Release.

Product Release:

All products, bulk or repackaged, are released by appropriately experienced and qualified members of the Quality Unit.

8.0 Quality System Processes

8.1 Documentation System:

Good, detailed, precise, correctly completed and well controlled documentation is key to the successful and compliant manufacture of pharmaceutical products. Giles utilizes a comprehensive system of documentation for all cGMP manufacturing, repackaging and testing activities. All documentation is available for review by employees, customers and regulatory authorities.

Supporting Documentation:

Document Control Procedure	Q12-PR-100-002
Document Numbering Procedure	Q12-PR-100-003
Document Approval Form	Q12-PR-100-F002
Document Review Schedule	Q12-PR-100-005
Document Retention Policy	Q12-PL-100-001
Document Correction and Signature Policy	Q12-PL-100-002
Review, Approval and Archiving of Batch Records	Q12-PR-100-0XX

8.1a Procedures, Policies and Forms:

All cGMP activities are detailed in Procedures, Policies or Forms which have been reviewed and approved by relevant, qualified personnel as being fit for purpose and in compliance with regulatory requirements.

Procedures, Policies and Forms are available for use in the work area. These documents are available as "read only" in electronic format via company intranet. Procedures, Policies and Forms also form the basis for training. To ensure that all documents may be understood and followed, translation to Spanish is available.

Supporting Documentation:

Employee use of Procedures, Policies and Forms on the Giles Document System	Q13-PL-100-0XX

8.2 Training:

A system has been established which ensures employees are trained in quality awareness, occupational safety and health and specific job related functions. All employees engaged in cGMP activities undergo initial training in the principals and practices of cGMP prior to assignment in a cGMP area. Employees also undergo annual refresher training in cGMP.

All employees engaged in cGMP activities are fully trained in the procedures or methods relevant to their activities in accordance with each area's training procedures. Where necessary, employees are certified to perform certain manufacturing or quality procedures and are recertified annually. Additionally, all employees carrying out cGMP batch manufacture or testing are trained in the associated batch manufacturing records, analytical methods and associated documentation prior to the manufacture or testing of the batch. However, bulk product is manufactured via a continuous flow process in which a sampling plan is designed to assure quality through statistical process control.

Supporting Documentation:

New Hire Training Manual	Q12-PR-100-006
Documentation Training Record	Q12-PR-100-F006
Good Manufacturing Practices	Q12-PR-100-009
Good Manufacturing Practices in Spanish	Q12-PR-100-010
Production Quality Control Training and Certification	
Training Check Lists	Q12-PR-100-F006

8.3 Validation:

As a manufacturer of an active pharmaceutical ingredient (API), manufacturing processes and analytical methods are validated. Validation documents, with a high degree of assurance, that the process is controlled and consistently produces a product that meets pre-determined specifications and quality characteristics.

All equipment used for cGMP manufacture and analysis, together with the facilities and utilities associated with these activities, are fully validated, calibrated, and maintained in order to ensure their reliability and fitness for purpose. Validation documentation includes (as appropriate): validation master plans, user requirement specifications, design qualification, installation qualification, operational qualification and performance qualification.

Supporting Documentation:

Validation (Policy, Documentation, Review)	Q12-PR-100-018
Computer System Validation Policy and Guidance	Q12-PR-100-0XX
Cleaning Verification and Validation	Q12-PR-100-0XX
Validation of USP Testing Methods and Equipment	L12-PR-100-035
Validation of Specific Gravity vs. %MgSO4 Reference Chart	

8.4 Nonconforming Product (Out of Specification - OOS):

Giles has established and maintains a documented procedure to ensure that product that does not conform to specified requirements is prevented from unintended use. This control provides for identification, documentation, evaluation, segregation and disposition of nonconforming product, and notification to the entities concerned. Giles does not produce a grade identified as Damaged Product.

QA has the ultimate responsibility to review and authorize the disposition of nonconforming product. Records of these variances, including investigations, inspections, and testing performed shall be maintained.

Possible dispositions are:

a) reprocessed to meet specified requirements
b) accepted without reprocessing by concession
c) regarded for alternative applications
d) shipped to a willing customer by agreement
e) scrapped

Supporting Documentation:

Release of Nonconforming Product	Q12-PR-100-017
Nonconforming Material Release form	Q12-PR-100-F017
Returned Crystal Product, Customer Returns	Q12-PR-100-026
Out of Specification (OOS) Investigation Procedure	L13-PR-100-0XX

8.5 Change Control:

All changes potentially impacting quality relating to Giles' cGMP facility, system, process, method, procedure or equipment are carefully controlled by the use of a formal Change Control System. This ensures that all potential benefits and risks are assessed in a controlled manner prior to a change being implemented. It also defines and tracks the actions required for successful implementation and closure of the change and where appropriate an assessment of the outcome. Pre- and post-change activities are approved by Quality. Depending on the requirements of the quality agreement, customer approval of a change may be required.

The Change Control System ensures continual improvement is undertaken in a timely and effective manner. It provides a high degree of assurance that there are not any unintended consequences of the change. The Change Control System is applied throughout the product lifecycle.

Supporting Documentation:

Management of Change	Q13-PR-100-0XX
Change Control	Q13-PR-100-0XX

8.6 Deviations

Deviations are raised for failures in validated equipment and systems, and where approved procedures, policies or processes have not been met. Deviations are fully investigated in a timely manner in order to determine root causes and the associated actions to prevent recurrence.

Supporting Documentation:

Deviation Authorization	Q12-FM-100-003

8.7 Process Performance and Product Quality Monitoring

Using quality risk management, Giles has identified and planned the production processes which directly affect quality and ensures that these processes are carried out under controlled conditions. Product characteristics are monitored and measured to verify that the product requirements have been met. Where appropriate, procedures are established to identify the required statistical techniques to evaluate data within our operations. This is carried out at appropriate stages of the product realization process.

Appropriate data is collected and analyzed to demonstrate the suitability and effectiveness of the quality management system and to evaluate if improvement of the effectiveness of the quality management system can be made.

Supporting Documentation:

Annual Product Quality Review	Q12-PR-100-007
Internal Quality Audits	Q12-PR-100-008
Daily Quality Audit - Manufacturing	Q12-PR-100-011
Daily Quality Audit - Repackaging	R12-PR-100-001
Calculating Daily MgO Yield	E13-PR-100-00X
Statistical Process Control	E13-PR-100-00X
Methods and Frequency of Monitoring and Control	Q13-PR-100-0XX

8.8 Vendor Assurance and Raw Material Release

The quality of all raw materials and contracted services is appropriately assured depending on the use and criticality of the material or service being employed.

All raw materials are inspected and released by the Quality unit in accordance with the relevant material specification before used in production.

Supporting Documentation:

Critical Vendor Qualification and Evaluation	Q12-PR-100-023
Vendor Assessment Survey	Q12-PR-100-F023c
Vendor Site Quality Audit	Q12-PR-100-F023d
Vendor Reassessment	Q12-PR-100-F023g
Quality Approval of In-coming Raw Materials	Q12-PR-100-015
In-coming Raw Material: Pouch-Carton	R12-PR-100-013
In-coming Raw Material: Fragrance Barrel	R12-PR-100-014
In-coming Raw Material: Magnesium Sulfate	R12-PR-100-015
Approval of Pouches	R12-PR-100-006

8.9 Stability Testing

Product will not be released for consumer use without adequate determination of the product's stability. Stability studies include an evaluation of the product's physical and chemical properties to determine temperature sensitivity and susceptibility to degradation over time. The results of on-going stability testing are used to confirm appropriate storage conditions and expiry dates.

Supporting Documentation:

USP Stability Testing	L12-PR-100-010
USP Stability Testing Worksheet	L12-PR-100-F010

8.10 Product Release

The Manufacturing Facility is a continuous flow process where a sampling plan has been designed to assure quality through statistical process control. Critical processing variables and their effect on performance and quality have been identified with the goal of improving product quality by designing it into the process. Released product is defined by the date/time it was produced. This allows for characterization of the quality attributes of the raw materials and traceability in the event of a recall.

At the Repackaging Facility, final product is tested, retained and released based upon a batch code that will represent the expiry date. Traceability of bulk material is maintained throughout the Repackaging Facility.

The Quality unit is responsible for the appropriate laboratory determination of satisfactory conformance to final specifications and approves/releases or rejects product accordingly.

Supporting Documentation:

Steps for Liquid Load Testing	L12-PR-100-024
Release of Non-conforming Product	Q12-PR-100-017
Release of ARCH Loads	Q12-PR-100-025
Bulk Salt Release	Q12-PR-100-029

8.11 Corrective Action and Preventive Action (CAPA) System

All complaints are dealt with promptly by appropriately experienced members of the Quality unit. A system exists for implementing corrective actions and preventive actions resulting from the investigation of complaints, product rejections, non-conformances, recalls, deviations, audits, regulatory inspections/findings and trends from process performance and product quality monitoring. Our CAPA methodology results in product and process improvements and enhanced product and process understanding. A documented procedure is established to define requirements for:

- Reviewing nonconformities (including customer complaints)
- Determining the causes of nonconformities
- Evaluating the need for action to ensure that nonconformities do not recur
- Determining and implementing action needed
- Recording of the results of any investigation and action taken
- Reviewing corrective action taken and its effectiveness

Supporting Documentation:

CAPA Procedure	Q12-PR-100-014
CAPA Report	Q12-PR-100-F014
Reporting Customer Complaint	Q12-PR-100-019
Procedure for Reporting Serious Adverse Event (SAE)	Q13-PR-100-0XX

8.12 Recalls

It is the responsibility of the Quality unit to approve and coordinate any final decisions and communications involving product recalls. Procedures have been established to define the recall of a product and a mock recall exercise is conducted at least annually.

Supporting Documentation:

Product Recall	Q12-PR-100-013
Quarantine of Product	Q12-PR-100-012

9.0 Appendix

I. Distribution

An updated Master Copy of the Quality Manual is maintained on the Giles Intranet Document System and a hard copy is kept in the Quality Laboratory. All employees are required to read the Quality Manual as part of their new hire training. It will be documented that the employee has read and understood its contents. Thereafter, the Quality Manual is available to all employees for reference either on the Giles intranet or in the Quality Laboratory. Revisions will be communicated to employees during monthly employee meetings.

II. Document Approval

DOCUMENT APPROVAL				
GILES QUALITY MANUAL				2012
Approval Required	**Date**	**Approved**	**Rejected**	**Signature**
President – *Jim Hill*	11/16/12	Yes	NA	Jim Hill
Director of Operations – *Matt Haynes*	11/16/12	Yes	NA	Matt Haynes
Director of Quality – *Deborah Durbin*	11/15/12	Yes	NA	Deborah Durbin
Manufacturing Manager – *Jason Bumgarner*	11/21/12	Yes	NA	Jason Bumgarner
Repacking Manager – *Monte Plott*	11/21/12	Yes	NA	Monte Plott

- **The above approval signatures (on hard copy in QA Lab) indicate review, approval and issue of every page within the attached document or manual. This manual must be re-approved either after 10 revisions have been made or after it has undergone its three year document review.**

III. Revisions List

REVISIONS LIST				
GILES QUALITY MANUAL				2012
DATE	**SECTION / PAGE**	**PARAGRAPH**	**COMMENTS**	**APPROVAL**
02/13/13	NA	NA	Original Quality Manual completely revised to reflect ICH recommendations.	DD
AFTER TEN (10) REVISIONS, THIS MANUAL MUST BE RE-ISSUED				