1.0 Purpose

The purpose of this procedure is to explain how Batch and Lot numbers are assigned and used at Giles. Stability and reserve sampling is based on this Batch / Lot number assignment. Product is released upon issuance of CoAs using Lot numbers as described in this procedure. A well defined Batch / Lot numbering system ensures traceability is maintained from Manufacturing through Repackaging.

2.0 Scope

This procedure applies to both USP and Tech grade products in the Manufacturing and Repackaging facilities.

3.0 Responsibility

Quality Assurance is responsible for proper assignment of Batch and Lot numbers, release of product, and collection of reserve and stability samples.

Production employees are responsible for understanding and following the Batch / Lot numbering system.

4.0 Safety Considerations

PPE required in designated areas shall be donned.

Safety is a condition of employment. Employees are not authorized to work in an unsafe manner and are prohibited from harming the environment of the facility or community.

5.0 Materials/Equipment

N/A

6.0 Procedure

Manufacturing:

The process at Manufacturing is recognized and accepted as a continuous process. Therefore, Batch and Lot designations are defined by time. The product produced during the timeframe between discontinuation or change of flow, equipment cycles, interruptions, shut down, etc. are examples.

- *Batch #* - is assigned for bulk product produced during the time period between annual shut downs; annual shut down typically occurs in September. The Batch number designation represents the year in which shut down occurs (similar to an academic school year). Since Giles is currently using the #XX13 on CoAs, Batch # 013 will be in remain in effect until annual shut down 2014. At that time the new Batch number will be # 014. Thereafter, a Batch will consist of approximately one year of product produced between annual shut downs.

- *Lot #* - is assigned for bulk product produced during the time period between weekly clean days when production is idled for several hours; weekly clean days typically occur on Thursdays. The Lot number designation represents approximately the number of weeks since annual shut down and consists of approximately one week's worth of product. If the system is stopped for anything else before the next scheduled clean day, a new Lot number will be assigned using the same numerical designation but with a letter after it. For example, #1413*a* represents the 14th week since annual shut down 2013; however, something occurred in the system during week 14 that required the issuance of another CoA. Note: since this numbering system did not go into effect until several months after shut down 2012, the number of weeks currently does not represent the actual number of weeks since shut down but the next sequential number available at Lot change. The Lot # designation will be representative of the weeks post shut down beginning with annual shut down 2014.

- *Daily Affirmation Lot #* - is assigned for bulk product produced during an approximate 24 hour time period (7 am to 7 am – morning shift change). This number designation represents the number of days since clean day. Clean day is designated as 01. Therefore, if clean day occurs on Thursday, Thursday is 01, Friday is 02, Saturday is 03…….. Wednesday is 07 and the next Thursday starts over with 01. The affirmation Lot number changes daily and is printed on product with the Lot number whereas the Lot number changes weekly and is used on the CoA.

Example: Daily affirmation Lot # on product would appear as **05 1513**.

05 = fifth day of week since clean day, 05 should be Monday; this is the ***affirmation Lot*** number

15 = fifteen weeks since annual shut down; this with the batch number is the weekly ***Lot*** number

13 = annual shut down 2013; this is the annual ***Batch*** number

Whereas, the Lot# on the CoA would appear as **1513.**

- *Release of Lots* – Two USP samples are collected on clean day for weekly Lot change from each packaging line that is running; one at the beginning and one at the end of the weekly production cycle. One sample (affirmation sample for the previous Lot) is collected just before idling the plant for weekly clean day and the second sample (new Lot) is collected when flow resumes and the process has stabilized. Samples are collected by QA in the morning and taken to the QA Lab to begin testing using the USP monograph. The new Lot number is assigned to product when production resumes; however, product is not released until USP testing has been successfully completed and a CoA issued by QA. Announcement of release is made electronically and the CoA is available on the Doc System.

  The daily affirmation Lot sample is collected from the sampling port every day at 7:00 am (shift change) and the affirmation Lot number is changed on product at this time. Product is not held pending daily USP results because it is released based on the weekly Lot USP testing results and CoA. This is only an affirmation of the weekly USP test results from the continuous process.

  In the event that product fails a USP test, the *Out of Specification Investigation* procedure *(Q13-PR-100-025)* will be followed.

- *Stability Requirements* – Upon introduction to this new numbering system, supplemental data to current stability data will be gathered by conducting stability on three Lots from the current Batch (013). Thereafter, data will be gathered by conducting stability on annual Batches. The samples will be collected at annual shut down (upon start up) for real time and accelerated studies. Accelerated stability samples must be kept at the correct temperature and humidity in a calibrated, temperature mapped chamber (T=40±2 and H=75± 5%). Industry practice defines 3 months of accelerated stability studies to be equivalent to 2 years and 6 months to 4 years. (See *USP Stability L12-PR-100-010*)

- *Reserve Sample Requirements* – Reserve samples are only required to be collected for each Lot (weekly). However, reserve samples will continue to be collected daily by QA. Reserve samples

will be securely stored by QA for at least one year beyond the three year expiration date (or 4 years). (See *Reserve Samples -Manufacturing L13-PR-100-042*)

Repackaging:

The process at Repackaging fits more of the traditional definition of a Batch /Lot process. The process starts every morning and shuts down every night, a definitive starting and end point.

- *Batch #* - Repackaging retains the same annual Batch number as Manufacturing; Batches are not mixed within final product.
- *Lot #* - Repackaging assigns daily Lot numbers based on the Julian day + year. Daily Lot number assignment is required because packaging lines actually shut down and start up daily. Using this scheme allows for more than one Manufacturing Lot to be used in Repackaging final product. However, different Manufacturing Batches may not be combined in Repackaging final product.
- *Release of Lots* – Three samples are collected for each daily Lot from each packaging line that is running USP product; one at the beginning, one in the middle, and one at the end of the day. Samples (pouch, carton, etc.) are collected at the end of the day (Lot affirmation samples) before the lines are shut down and then again in the morning after the lines have started and stabilized (new Lot samples). The actual number of samples depends on which packaging lines are running on a particular day. Samples are picked up by QA in the morning and taken to the QA Lab to begin USP testing on the beginning and end samples. The middle sample will be kept as a reserve sample and tested later if deemed necessary. The Lot number will have already been assigned at start-up based on the Julian date. Product will not be released until USP testing has been successfully completed and a CoA issued by QA. However, product will be released "at risk" to Aaron Industries (see contract) until USP test results are available and the CoA issued by QA. Announcement of release is made electronically and the CoA is available on the Doc System.
- *Stability Requirements* – Only one stability study per Batch is required. Therefore, one of each representative packaging (pouch, carton, etc.) per year (Batch) will be collected to put on stability. However, initial studies will be conducted first for three Lots as described above.
- *Reserve Samples Requirements* – Reserve samples are collected for each Lot (daily). The reserve samples are collected in the middle of the day and consist of each representative packaging

(pouch, carton, etc.). This sample serves as the 'middle of a Lot' sample required for the beginning-middle-end sampling strategy. (See *Reserve Samples - Repackaging R12-PR-100-008*)

7.0 Reference Documents

USP Stability	*(L12-PR-100-010)*
Out of Specification Investigation	*(Q13-PR-100-025)*
Reserve Samples - Manufacturing	*(L13-PR-100-042)*
Reserve Samples - Repackaging	*(R12-PR-100-008)*

8.0 Change Information

New document