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## MOPS BIO EXCIPIENT GRADE 2020 REAL-TIME STABILITY REPORT

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## 1. OVERVIEW:

The purpose of this report is to analyze the data obtained from the long-term stability of MOPS Bio Excipient Grade material manufactured at BioSpectra's Stroudsburg, PA facility. Samples were placed on the stability testing program in February of 2020 to fulfil the requirements of placing one lot of manufactured material per year on the stability testing program. Testing intervals are designated by  $T_n$ , where  $n$  represents the number of months on stability. Testing is performed every three months for the first year, every six months for the second year, and annually for each subsequent year for a total of three years. Analysis has been conducted for a total of thirty-six months in order to assure that the manufactured product remains stable under the specified conditions and for the specified interval of time. The analysis of the compiled data may be used to re-evaluate the retest period for future lots of manufactured MOPS Bio Excipient Grade material.

This long-term stability report assesses the stability of one lot of MOPS Bio Excipient Grade material, lot MP3200-254-0220. The study includes the following analyses: Absorbance (0.1M), Appearance and Color, Assay (Dried), Loss on Drying, Water (by KF) and Solutions Test. Results from all analyses are summarized in Table 2 and 3, and shelf-life plot determinations have been created for all quantitative analyses. Shelf-life plots determine the point in time at which the slope would exceed the acceptance criteria. As long as the slope has a statistically significant difference from zero using a 95% confidence limit, an estimated time in months can be established at which the acceptance criteria will no longer be met, i.e. the predicted shelf-life. This allows BioSpectra to ensure that the product will be stable over the time period in which it is part of the Stability Testing Program. The following product codes are commercially available.

- MOPS-3220
- MOPS-3201
- MOPS-4220
- MOPS-5220
- MOPS-7201

## 2. REFERENCES:

- 2.1. BSI-SOP-0136, Stability Testing Program
- 2.2. BSI-SOP-0146, Stability Inventory
- 2.3. Current USP
- 2.4. ICH Q1E

## 3. SAMPLE DESIGNATION:

Samples placed on the stability testing program consisted of one lot of MOPS Bio Excipient Grade material. Stability samples from this batch were placed into two packaging configurations, P/P and Labline. These samples were packaged in accordance with the Stability Inventory SOP. Reference Table 1, below, for the packaging configuration and its description. The type of packaging utilized in this stability study was based on BioSpectra final packaging offered to the customer.

**TABLE 1: PACKAGING DETAILS**

Packaging Configuration	Packaging Description
Poly/Poly (P/P)	Samples are packaged into small poly bags and sealed with a zip tie. All individual samples are then placed into a poly drum.
Labline	Samples are packaged into a HDPE Lab Screw-Top Bottle.

**4. STORAGE:**

Samples were placed on stability in BioSpectra’s Stroudsburg, PA facility stability area, located in the quarantine area of the warehouse. Although there are no storage requirements for MOPS Bio Excipient Grade material, storage conditions were continuously monitored and recorded utilizing MadgeTech data loggers for temperature (specification 15-30°C), humidity (specifications: monitor) and Mean Kinetic Temperature (all ≤ 25°C). The samples were stored in the Stroudsburg warehouse from February 2020 through February 2023. The maximum temperature of the warehouse during this time was 28.24°C and the minimum temperature of the warehouse during this time was 11.73°C. The average mean kinetic temperature was 20.48°C. See Section 5 for the discrepancy investigations initiated for temperature excursions.

**5. INVESTIGATIONS:**

- 5.1. **SDI20-33** was initiated for four MadgeTech loggers in use past the calibration due date. This had no impact on the MOPS stability samples, as the next time point, T<sub>36</sub>, was pulled and tested and all lots met specification.
- 5.2. **SDI20-107** was initiated for MadgeTech loggers August temperature and humidity assessment not complete due to missing data. This had no impact on the MOPS stability samples as some data from six out of the seven data loggers was auto downloaded on the software. The data still available was used to perform a partial assessment of the Stroudsburg warehouse for 08/03/20-09/02/20.
- 5.3. **SDI21-27** was initiated because one of the Madge Tech data loggers failed to download correctly resulting in missing data. All data from 3/8/21 to 4/1/21 is missing. This had no impact on the MOPS stability samples, as the next time point was pulled and tested and all lots met specification.
- 5.4. **SDI21-35** was initiated because one of the Madge Tech data loggers malfunctioned and failed to collect data. This had no impact on the MOPS stability samples as the other six data loggers did not fall outside the specified temperature range of 15 – 30°C during the missing time.
- 5.5. **SDI21-88** was initiated for a MadgeTech logger that was calibrated and found to be out of specification whith respect to relative humidity. This had no impact on the MOPS stability samples although the data logger was found to be out of specifications the warehouse relative humidity is only monitored and still found to be within specification with respect to temperature.
- 5.6. **SDI22-03** was initiated for four MadgeTech loggers in use past the calibration due date. This had no impact on the MOPS stability samples, as the next time point was pulled and tested and all lots met specification.

- 5.7. **SDI22-184** was initiated due to an out of specification low temperature readings Two loggers recorded OOS low temperatures with the lowest reading of 13.40°C due to the AC being turned on instead of the heat. This had no impact on the MOPS stability samples as the other five data loggers did not fall outside the specified temperature range of 15 – 30°C during the missing time.
- 5.8. **SDI23-07** was initiated because one of the Madge Tech data loggers fell from its bracket and stopped collecting data. This had no impact on the MOPS stability samples as the other six data loggers did not fall outside the specified temperature range of 15 – 30°C during the missing time frame.

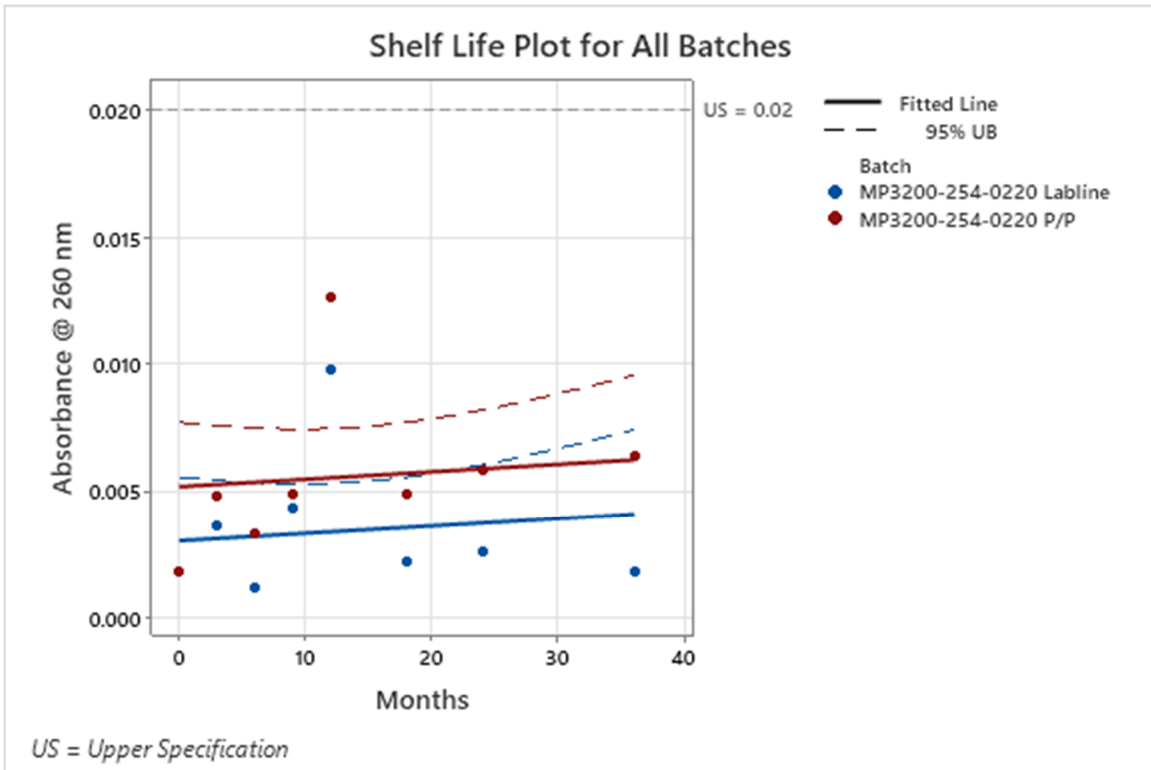
## 6. LOT EVALUATION:

**Table 2: MP3200-254-0220 P/P**

Analysis	Specification	T <sub>0</sub>	T <sub>3</sub>	T <sub>6</sub>	T <sub>9</sub>	T <sub>12</sub>	T <sub>18</sub>	T <sub>24</sub>	T <sub>36</sub>
Absorbance (0.1M)	0.02 a.u. max @ 260 nm	0.0018 a.u.	0.0048 a.u.	0.0033 a.u.	0.0049 a.u.	0.0126 a.u.	0.0049 a.u.	0.0058 a.u.	0.0064 a.u.
Appearance and Color	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals
Assay (Dried)	99.0% Min	99.06%	99.68%	99.61%	99.69%	100.18%	100.29%	100.41%	100.42%
Loss on Drying	1.0% Max	<0.0133 %	0.1120%	0.0333%	0.0531%	0.0598%	0.1130%	0.1100%	0.1699%
Karl Fischer	0.1% Max	0.06%	0.05%	0.04%	0.06%	0.02%	0.14%	0.12%	0.12%
Solutions Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test

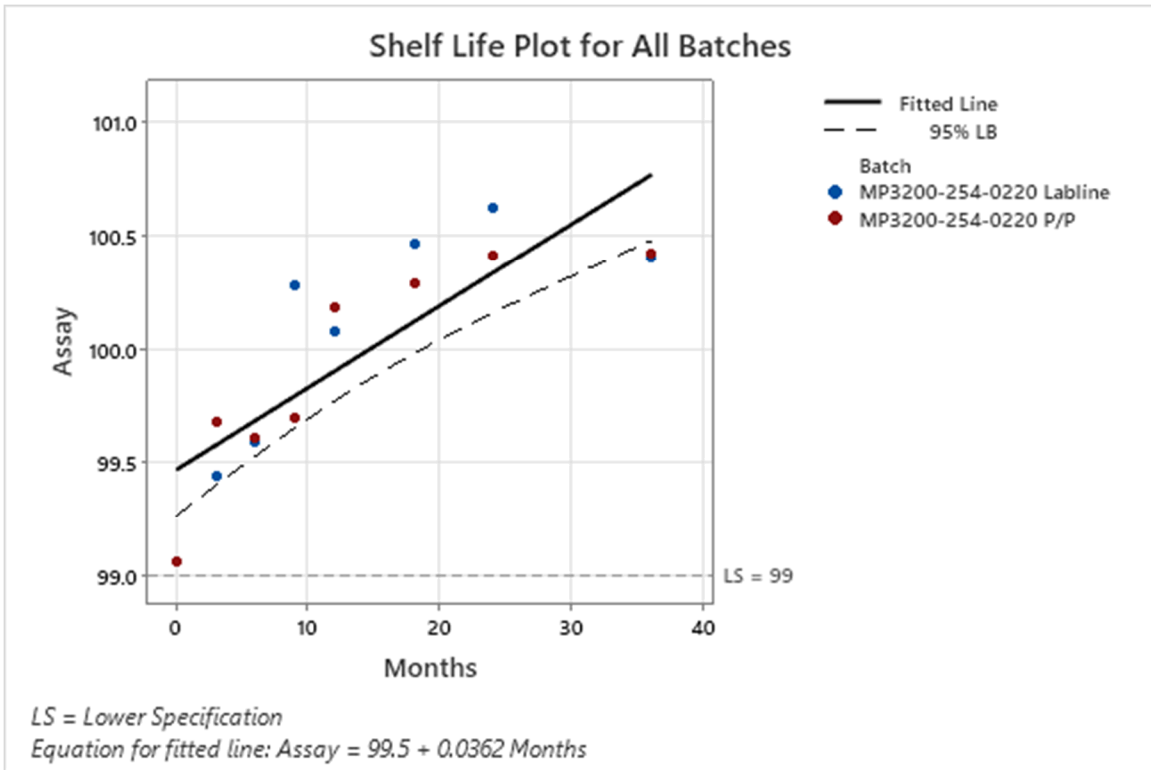
**Table 3: MP3200-254-0220 Labline**

Analysis	Specification	T <sub>0</sub>	T <sub>3</sub>	T <sub>6</sub>	T <sub>9</sub>	T <sub>12</sub>	T <sub>18</sub>	T <sub>24</sub>	T <sub>36</sub>
Absorbance (0.1M)	0.02 a.u. max @ 260 nm	0.0018 a.u.	0.0036 a.u.	0.0012 a.u.	0.0043 a.u.	0.0098 a.u.	0.0022 a.u.	0.0026 a.u.	0.0018 a.u.
Appearance and Color	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals	White / Crystals
Assay (Dried)	99.0% Min	99.06%	99.44%	99.59%	100.28%	100.07%	100.46%	100.62%	100.40%
Loss on Drying	1.0% Max	<0.0133 %	0.1318%	0.1195%	0.0266%	<0.0133 %	0.0652%	0.0195%	0.0657%
Karl Fischer	0.1% Max	0.06%	0.06%	0.03%	0.04%	0.03%	0.08%	0.08%	0.04%
Solutions Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test	Passes Test



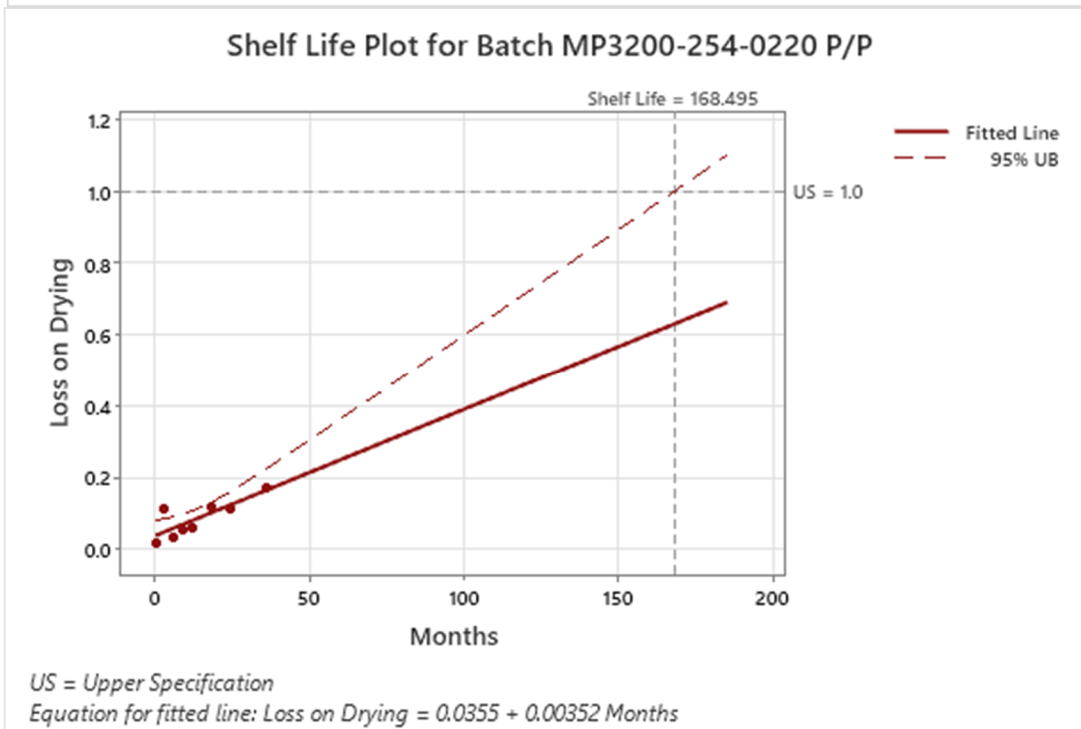
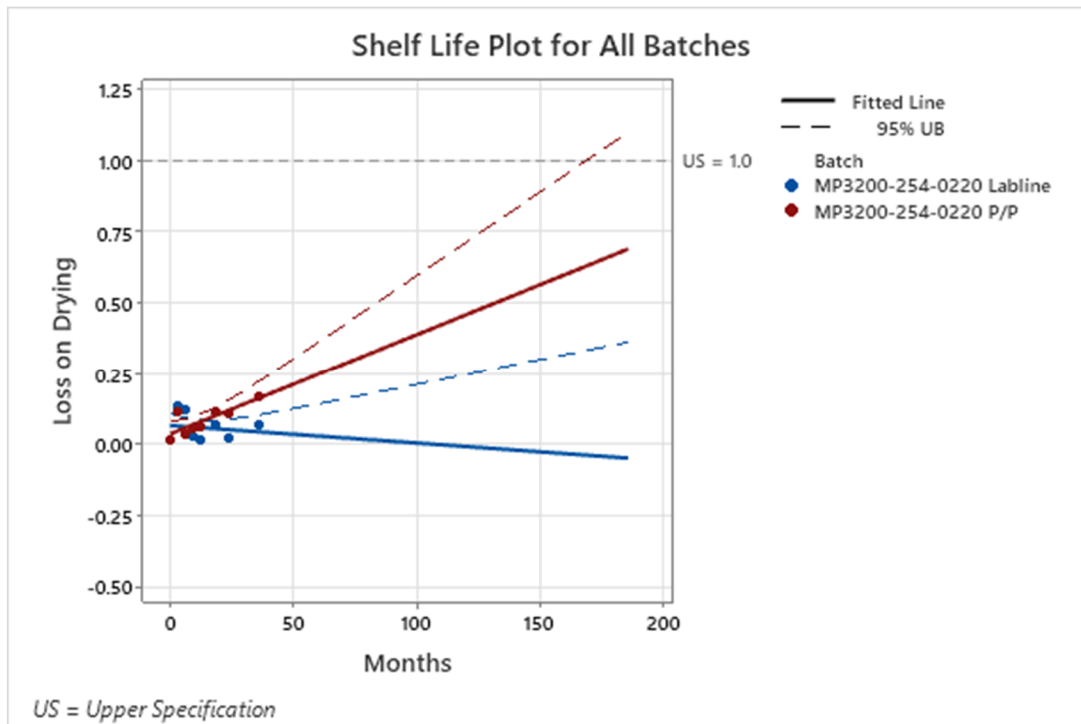
**GRAPH 1: ABSORBANCE @ 260 nm**

No Shelf-Life is able to be determined for Absorbance @ 260 nm, as the mean response slope is not significantly different from zero. There is no impact to the product or currently assigned expiration of this material.



**GRAPH 2: ASSAY (DRIED)**

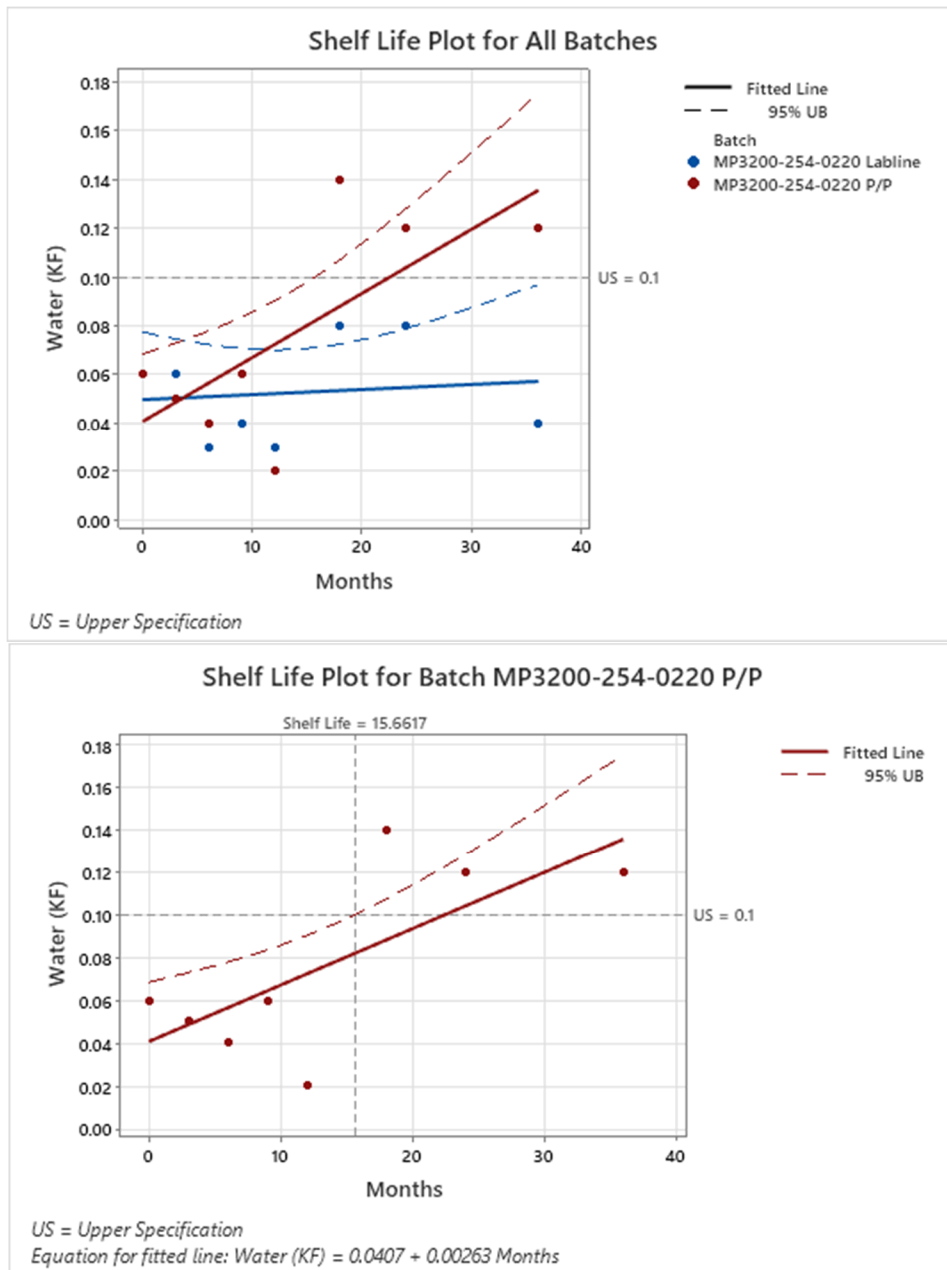
No Shelf-Life is able to be determined for Assay, as the mean response slope is not significantly different from zero. There is no impact to the product or currently assigned expiration of this material.



**GRAPH 3: LOSS ON DRYING**

The predicted Shelf-Life for Loss on Drying was determined to be 168.495 months. This is well beyond the 36-month stability study, therefore, there is no impact to the product or currently assigned expiration of this material.





**GRAPH 4: KARL FISCHER**

The predicted Shelf-Life for Karl Fischer was determined to be 15.662 months for the batch stored in P/P packaging and no Shelf-Life is able to be determined for Karl Fischer for the batch stored in the Labline packaging, as the mean response slope is not significantly different from zero. The shelf-life is defined as the time period in which you may be 95% confident that at least 50% of the response is within the required limits of specifications. There is no impact to the 36-month stability study as the material met the required specifications for both packaging configurations. The product will be released with a 24-month retest date assigned at the time of manufacturing and will be evaluated upon request for an extended retest date.

## **7. CONCLUSION:**

All data met the specification set forth in the Stability Testing Program for this lot MP3200-254-0220 when package in the Labline and P/P packaging. In accordance with ICH Q1E, the retest date may be proposed for up to  $2x$ , where  $x$  is the period covered by long-term stability data, but should be no more than 12 months beyond. The data obtained during this stability study indicates that MOPS Bio Excipient material packaged in Labline and P/P packaging is stable for 36 months. The KF obtained a shelf life of 15 months for P/P packaging but the material passed thus supporting a 24-month retest. The assigned retest date will remain at 24 months unless requested on an individual lot-by-lot basis.

## **8. STATEMENT OF COMMITMENT:**

- 8.1. BioSpectra is responsible for the following regarding Stability Data in this report:
  - 8.1.1. In the event that any stability analysis produces results found to be out of specification, the batch produced immediately before and after will be tested in full and analyzed in comparison with the batch in question.
  - 8.1.2. This will serve to provide information to effectively ensure that the root cause of the investigation has not impacted the batch manufactured before or after the batch in question.
  - 8.1.3. If a stability analysis is found to be out of specification, the batch will be withdrawn from the market through communication with the customer. Additionally, an investigation will be conducted to determine the possible withdrawal of the batches produced before and after the batch in question.
  - 8.1.4. In the event that any out of specification results are confirmed, all authorized users of the material will be notified.