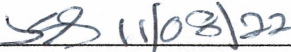
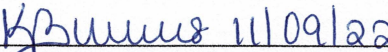
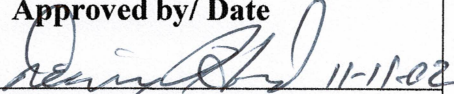
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Written by/ Date  11/08/22	Reviewed by/ Date  11/09/22	Approved by/ Date  11-11-22	
Title: Quality Control Director	Title: Quality Assurance Director	Title: VP of Quality & Regulatory Affairs	

## 1.0 Purpose

The purpose of this procedure is to outline the critical control points needed to meet required temperature and humidity ranges, and to ensure that the manufacturing and storage of materials and all cGMP operations are conducted within these guidelines.

## 2.0 Scope

This procedure applies to all stages of the manufacturing process, from receipt of raw materials to the shipping of finished product, as well as stability programs.

## 3.0 Responsibility

- 3.1 It is the responsibility of QC Management to maintain this procedure and train personnel.
- 3.2 It is the responsibility of QC Laboratory personnel to monitor the critical storage areas, completing evaluation and confirmation of conformance.
- 3.3 It is the responsibility of the Quality Managers, R&D, and the Head of QA to define the specific action to be taken when there is an excursion.
- 3.4 It is the responsibility of all production personnel to check the temperature and humidity indicators in their area, prior to performing cGMP operations, and to compare the conditions to the readouts.
- 3.5 It is the responsibility of QC to verify the data on all cGMP documentation.
- 3.6 It is the responsibility of QC to ensure that this procedure is being followed.

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## **4.0 Definitions**

- 4.1 **CCP** – Critical Control Point
- 4.2 **RH** – Relative Humidity
- 4.3 **Freezer** – A place in which the temperature is maintained thermostatically between -25°C and -10°C (-13°F and 14°F)
- 4.4 **Refrigerator** – A cold place in which the temperature is maintained thermostatically between 2°C and 8°C (36°F and 46°F)
- 4.5 **Controlled Room Temperature** – A temperature maintained thermostatically that brackets the usual and customary working environment of 20°C to 25°C (68°F to 77°F) that results in a mean kinetic temperature calculated to be not more than 25°C and that allows for minor fluctuations between 10°C and 30°C (59°F and 86°F) that are experienced in pharmacies, hospitals, and warehouses.
- 4.6 **QC** – Quality Control
- 4.7 **R&D** – Research and Development
- 4.8 **DC** – Document Control
- 4.9 **WIP** – Work in Progress
- 4.10 **BPR** – Batch Production Record
- 4.11 **cGMP** – Current Good Manufacturing Practices

## **5.0 References**

- 5.1 USP <659>, Packaging and Storage Requirements
- 5.2 C-201, SOP, Deviation and Investigation Procedure
- 5.3 D-715, SOP, Microbial Limit Testing using 3M Petrifilm Systems

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- 5.4 D-715.0, SOP, Microbial Limit Testing using Agar Plates
- 5.5 F-507, SOP, Warehouse Maintenance and Sanitation
- 5.6 D-821, SOP, DicksonOne Data Loggers
- 5.7 20-0049, Report, Temperature Mapping of Warehouse Areas

## **6.0 Procedure**

- 6.1 Temperature and humidity are monitored by two different methods.
  - 6.1.1 DicksonOne WIFI Data loggers are placed throughout all Ion Labs facilities where GMP environmental monitoring is required. These devices and associated Cloud Web Application allow real time monitoring of the temperature and relative humidity in any location as required. This allows for real time notification in the event of any temperature and/ or humidity excursion.
  - 6.1.2 Thermometer/Hygrometers alert personnel to the current conditions but do not store the results.
- 6.2 The strategy for monitoring environmental conditions includes placing data loggers in the locations where products and materials are stored, and also using the digital temperature and humidity indicators to manually check the areas where processes are performed.
  - 6.2.1 Production personnel are responsible for monitoring the temperature and humidity in the process areas and recording the data in the appropriate BPR.
- 6.3 Data Loggers
  - 6.3.1 The DicksonOne data loggers are placed in various locations throughout the building, including but not limited to:

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6.3.1.1 Locations identified in Report 20-0049, Temperature Mapping of Warehouse Area, as encompassing the most extremes for temperature in the warehouse.

6.3.1.2 Belcher warehouse locations as determined in Protocol PRTCL-22-0050.

6.3.1.3 Stability/ retain sample storage location(s).

6.3.1.4 Refrigerators used for the storage of raw materials and/ or laboratory supplies and standards.

6.3.1.5 Freezers used for the storage of laboratory supplies and standards.

6.3.1.6 Incubators used in the laboratory for microbial testing.

6.3.1.7 Other locations as needed or requested for monitoring.

6.3.2 Hygrometers are placed throughout all production areas and are for use as required in individual batch records.

#### 6.4 Specifications

6.4.1 All areas storing raw materials and/or product are required to be within 15°C – 30°C, and 20% RH – 75% RH.

6.4.2 Refrigerators are to maintain cool conditions of 2°C and 8°C.

6.4.3 Freezer specifications will be determined based on the needs of the material being stored and the freezer unit in use.

6.4.4 Production, packaging, laboratory, and other unlisted locations are to maintain a controlled room temperature of 10°C – 30°C with the RH under 75%. The exception being those locations in which humidity outside of these ranges is necessary for production purposes, i.e. any location using steam or where gummy dosage forms are in process.

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6.4.5 Incubation chambers for use with microbiological testing are maintained within temperature specifications described in D-715 and D-715.0.

6.5 Any excursion will be addressed according to the following guidelines.

6.5.1 DicksonOne WIFI data logger system is set up so as to provide immediate notification if an excursion occurs. Data for each device can be downloaded at any time and graphed for evaluation if needed. Reference SOP D-821, DicksonOne Data Loggers for additional details.

6.5.2 Minor temperature and humidity excursions for room temperature data loggers outside of the ranges (10°C – 30°C, 20% RH – 75% RH) but within the ranges (10°C – 35°C, 15% RH – 80% RH) may be tolerated for periods up to 24 hours provided the mean kinetic temperature does not exceed 30°C. When there is a minor excursion, a Deviation and Investigation procedure may be initiated at the discretion of QC Laboratory Management.

6.5.3 Minor temperature and humidity excursions for data loggers located in a refrigerator or cooler outside of the ranges (2°C – 8°C) but within the ranges (0°C – 10°C) may be tolerated for periods up to 24 hours provided the mean kinetic temperature does not exceed 8°C. When there is a minor excursion, a Deviation and Investigation procedure may be initiated at the discretion of QC Laboratory Management.

6.5.4 Minor temperature and humidity excursions for data loggers located in a freezer outside of the ranges (-25°C – -10°C) but within the ranges (-27°C – -8°C) may be tolerated for periods up to 24 hours provided the mean kinetic temperature does not exceed -10°C. When there is a minor excursion, a Deviation and Investigation procedure may be initiated at the discretion of QC Laboratory Management.

6.5.4.1 When an investigation is initiated an evaluation of the affected inventory (raw materials and/or products) will be performed to

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determine the worst case scenario and/or identify the material that has the highest probability of being affected by the excursion and testing may be performed to determine the impact of the excursion on the affected materials.

6.5.5 Excursions may be reported as a deviation (refer to SOP C-201 Deviation and Investigation Procedure).

#### 6.6 Verification and Calibration

6.6.1 The efficiency and accuracy of DicksonOne sensors will be calibrated annually, either internally against new sensors or sent out to Dickson for re-calibration.

6.6.2 Calibration is performed using NIST traceable standards as a 3 point calibration.

6.6.3 Alternatively, new sensors may be purchased and installed, removing the old, expiring sensors.

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## 7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	05/25/10	New	-	-
1	03/07/13	Updated SOP format and number.	-	-
2	08/14/13	Updated section 5.3 with new locations. Added QC responsibility.	13-584	R. Nguyen
3	08/01/14	Updated definition. Added additional monitoring locations. Created ID codes. Added HACCP limits. Added actions to be taken for nonconformance. Added Form F-505-F1.	14-0604	L. Titolo
4	01/26/15	Added new data loggers and monitoring locations. Added second warehouse. Added second retain room. Updated Monitoring Form. Gave QC responsibility for tracking warehouse and production. Created to forms for Laboratory and Warehouse/production. Defined minor excursion limits.	15-0071	B. Johns
5	06/11/15	Changed designation of data logger to WIP area. Added data logger to #2 laboratory refrigerator. Added sections 6.2.1 and 6.2.2. Reduced minor excursion from 48 hours to 24 hours. Clarified Investigation test parameters for an excursion. Added refrigeration and freezer humidity specifications as report only.	15-0412	D. Popp
6	02/08/16	Add new warehouse monitoring. Add new data loggers.	15-1147	R. Casabianca
7	02/24/17	Update SOP to reflect requirements of new facility: 8031 114 <sup>th</sup> Ave, Largo, FL 33773.	17-0203	B. Johns
8	12/13/17	Added verification and calibration steps. Added SensorPush Data Logger requirements.	17-1563	N. Zhang
9	01/02/19	Added data logger locations. Added procedure for temperature excursions. Revised forms.	19-0005	B. Drazer
10	02/22/21	Updated to be aligned with new data logger system. Removed forms F-505-F1 and F-505-F2.	CC-21-0078	J. Sassman
11	08/25/21	Removed references to HACCP. Added reference to USP <659>.	CC-21-0335	J. Sassman
12	11/07/22	Extended allowable temperature in production areas to 10°C. Added Belcher warehouse locations.	CC-22-0422	J. Sassman