3.2.P.3.3 Description of Manufacturing Process and Process Controls

This section contains the description of the Manufacturing Process and Controls for Clobetasol Propionate Foam, 0.05%.

1.0 Manufacturing Process Flowchart

The manufacturing process of Clobetasol Propionate Foam, 0.05% includes alcohol phase preparation, aqueous phase preparation, and transferring aqueous phase into alcohol phase. Figure 1 demonstrates the flow diagram for intended commercial compounding process.

The filling process of Clobetasol Propionate Foam, 0.05% includes concentrate filling, valve crimping, propellent charging, all unit weight checking, water batch leak checking, and actuator placement. Figure 2 demonstrates the flow diagram for intended commercial packaging process.

Figure 1. Flow Diagram of Clobetasol Propionate Foam Compounding Process (500 kg batch)

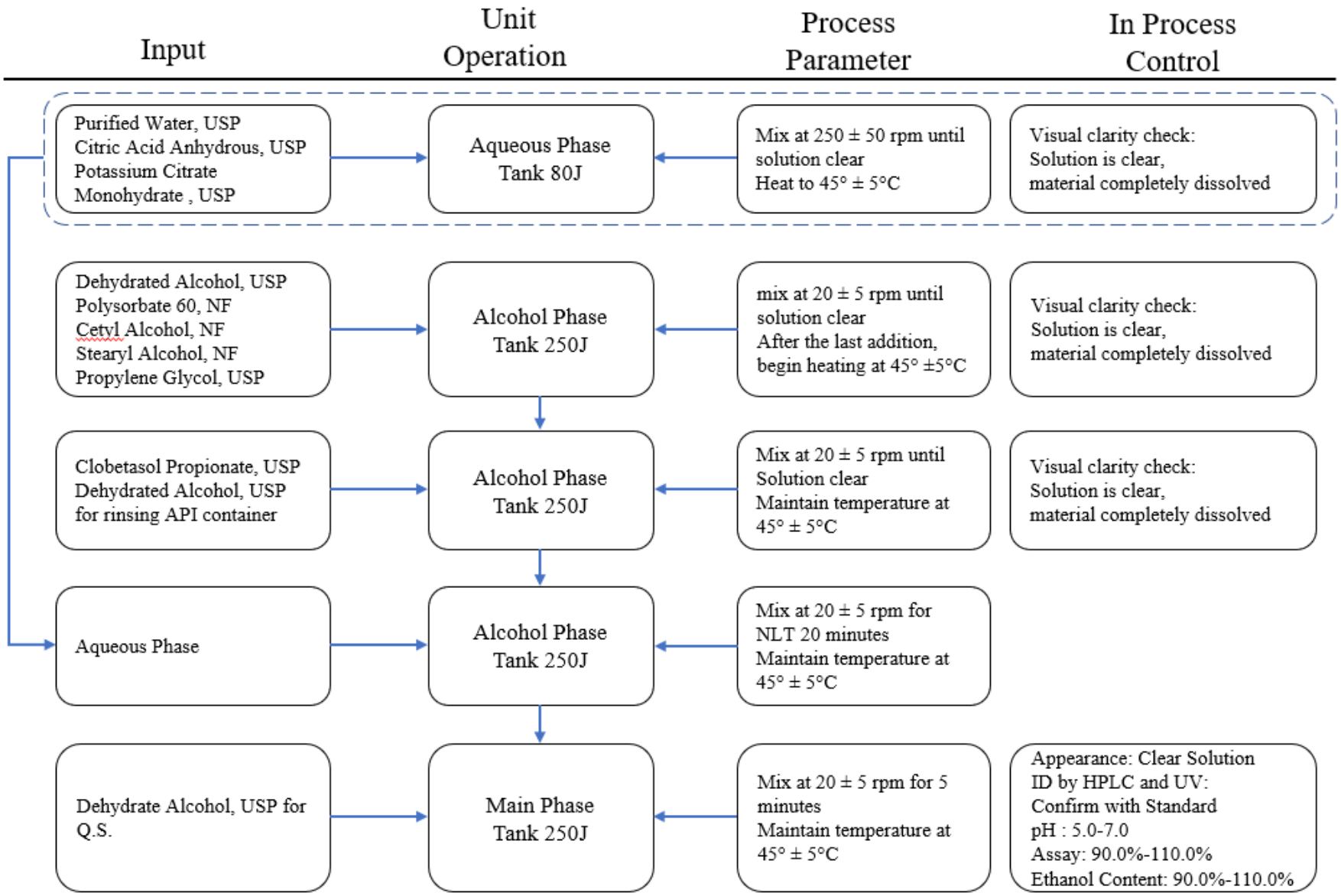
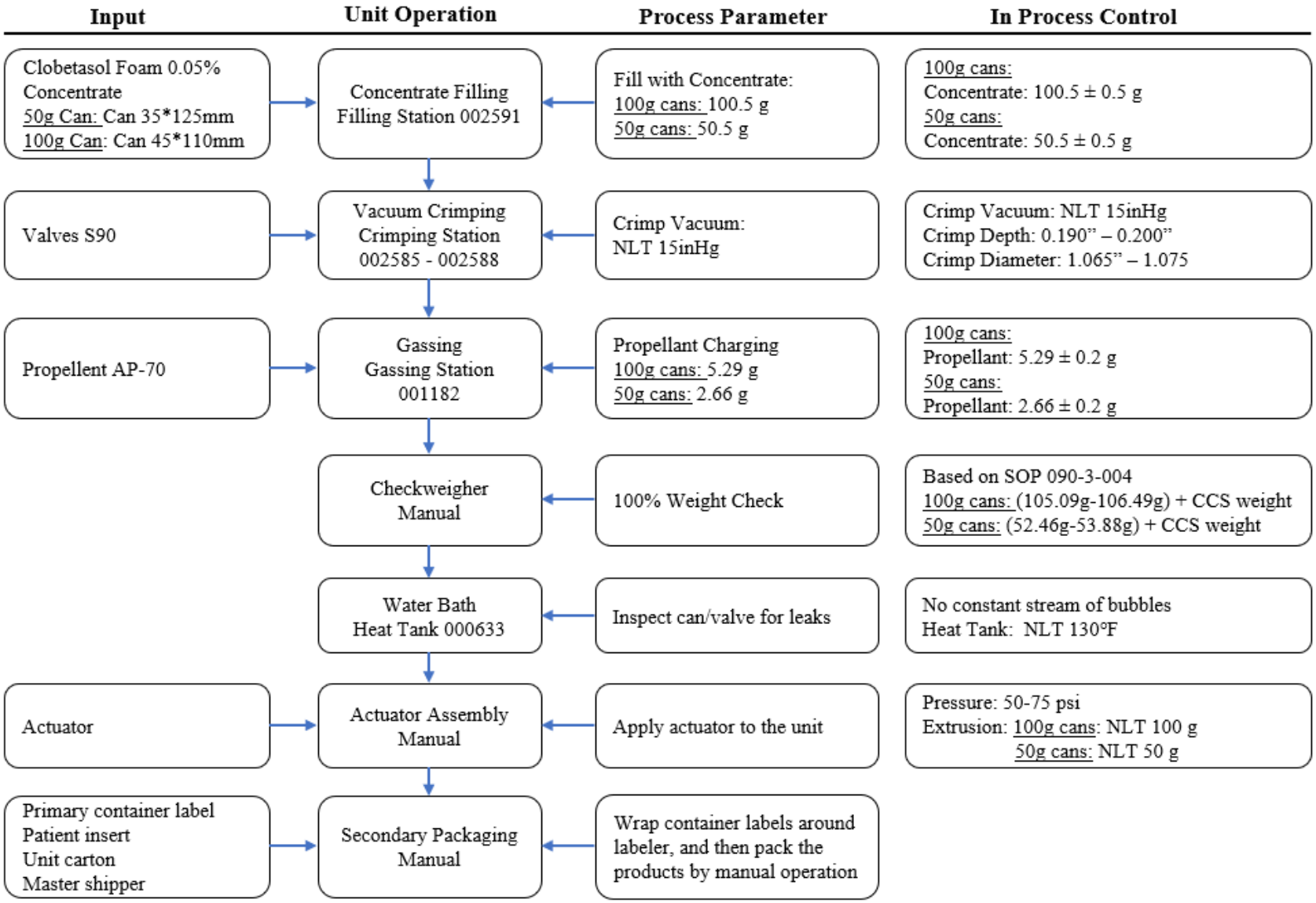


Figure 2. Flow Diagram of Clobetasol Propionate Foam Filling and Packaging Process (500 kg batch)



2.0 Manufacturing Process

The commercial manufacturing of Clobetasol Propionate Foam, 0.05% will be performed at the same place as registration batches. Pharmasol Corporation (Pharmasol) located in South Easton, MA will be the manufacturer of commercial Clobetasol Propionate Foam 0.05%.

The compounding manufacturing process consists of two phases: alcohol phase and aqueous phase. Dehydrate alcohol, polysorbate 60, cetyl alcohol, stearyl alcohol, propylene glycol and the drug substance would mix until clear to form the alcohol phase. Purified water, citric acid and potassium citrate would mix until clear to form the water phase. Due to the characteristic of the excipients, and to prevent formulation gelation, both phases need to be heated to around 45°C prior than combining. After combining two phases, the final bulk solution will be filled into aluminum cans, and vacuum crimp with aluminum valves. All units then pass by a checkweigher for 100% weight check. The units that pass weight check will proceed into a warm water bath to rule out leaking units. Finally, the actuator with cap will be caped onto the can.

In summary, the manufacturing of Clobetasol Propionate Foam, 0.05% includes: Alcohol phase mixing → Aqueous phase mixing → Combine alcohol phase and aqueous phase to form main phase → Solution Filling → Vacuum Crimping → Propellent Filling → Weight Check → Water bath leak check → Place actuator with cap on to the can

Table 1. Narrative Description of Clobetasol Propionate Foam Manufacture Process (500 kg batch)

Manufacturing	Narrative Description	
	Input	**Process Step**
Alcohol Phase Phase A	Dehydrated Alcohol, USP Polysorbate 60, NF Cetyl Alcohol, NF Stearyl Alcohol, NF Propylene Glycol, USP	Add ingredients, and then center propeller mix at 90 ± 5 rpm, and side scraper mix at 20 ± 10 rpm until clear solution After the last addition, begin heating at 45° ± 5°C
	Clobetasol Propionate, USP Dehydrated Alcohol, USP for rinsing	Center propeller mix at 90 ± 5 rpm, and side scraper mix at 20 ± 10 rpm until clear solution Maintain temperature at 45° ± 5°C
Aqueous Phase Phase B	Purified Water, USP Anhydrous Citric Acid, USP Potassium Citrate, USP	Add ingredients and mix at 250 ± 50 rpm After the first addition, heat to 45° ± 5°C
Main Phase	Transfer the Aqueous Phase (Phase A) into the Alcohol Phase (Phase B)	Center propeller mix at 90 ± 5 rpm, and side scraper mix at 20 ± 10 rpm for NLT 20 minutes Maintain temperature at 45° ± 5°C
	Collect material form the bottom of the tank and add to the top. Repeat two to three times	Maintain temperature at 45° ± 5°C Center propeller mix at 90 ± 5 rpm, and side scraper mix at 20 ± 10 rpm for additional 5 minutes
Bulk Solution homogeneity	Batch sampling	Collect samples from the top, middle and bottom of the tank

Table 2. Narrative Description of Clobetasol Propionate Foam Filling and Packaging Process (500 kg batch)

Packaging	Narrative Description	
	Input	**Process Step**
Primary Packaging	Fill and seal cans with concentrate and propellant	100g cans: Concentrate: 100.5 ± 0.5 g Propellant: 5.29 ± 0.2g Crimp Depth: 0.190" – 0.200" Crimp Diameter: 1.065" – 1.075" Crimp Vacuum: NLT 15 inHg Extrusion: NLT 100g Pressure: 50-75 psi 50g cans: Concentrate: 50.5 ± 0.5 g Propellant: 2.66 ± 0.2g Crimp Depth: 0.190" – 0.200" Crimp Diameter: 1.065" – 1.075" Crimp Vacuum: NLT 15 inHg Extrusion: NLT 50g Pressure: 50-75 psi
	Product Samples	Collect samples from the beginning, middle and end of the filled units

3.0 Master Batch Records

The proposed manufacturing and packaging batch records are included herein. The largest intended production run (commercial batch records) are no more than 10 times of the exhibit batch.

Master Formula (compounding) Batch Record

- Master Compounding Record for Clobetasol Propionate Foam, 0.05% (Doc # 8112010E-250J)

Master Packaging & Labeling Batch Record

- Master Filling & Packaging Record for Clobetasol Propionate Foam, 0.05% 50g (Doc # 8012010)
- Master Filling & Packaging Record for Clobetasol Propionate Foam, 0.05% 100g (Doc # 8012020)

4.0 Sterile Product

Clobetasol Propionate Foam, 0.05% is not a sterile product.

5.0 Reprocessing Statement

Aucta Pharmaceuticals, Inc. (Aucta) hereby states that there will be no reprocessing or rework of the drug product and any process intermediate. If in the post-approval production of this product, a reprocessing procedure is desired, the procedure will be in compliance with *21 CFR 211.115.* The procedure will first be submitted to the ANDA as a supplement in accord with Section 506A of the FD&C Act and the Guidance for Industry: Changes to an Approved NDA or ANDA. The signed reprocessing statements are provided.

- Pharmasol Reprocessing Statement (Drug Product Manufacturer)
- Aucta Reprocessing Statement (Applicant)