PRE-MARKET APPLICATION

CFS™ FOR TREATMENT OF KNEE-LIGAMENT INJURIES

PLASTAFIL, INC.

VOLUME 2

VOLUME 2

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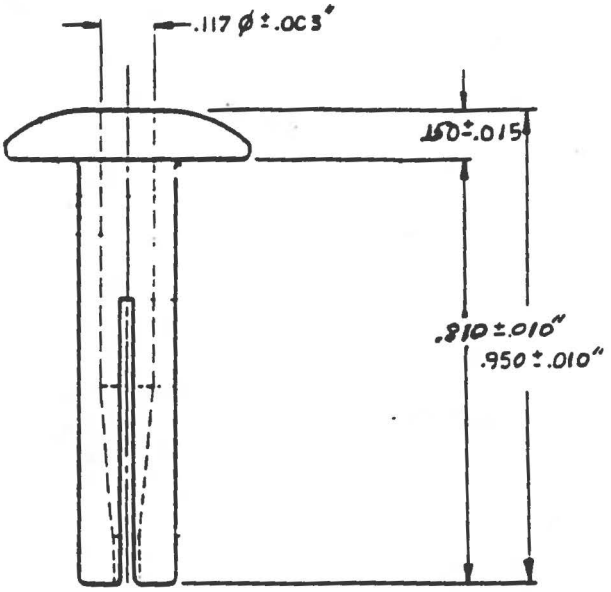
PROTOTYPE OPERATIONAL QUALIFICATION PROCEDURE

1. Operational Qualification of a Mettler AE163 Analytical Balance

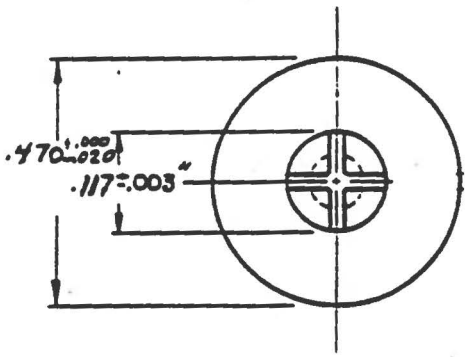
3. ENVIRONMENTAL ASSESSMENT

PICTORIAL DESCRIPTION OF THE DEVICE AND ACCESSORY ITEMS

Bollard



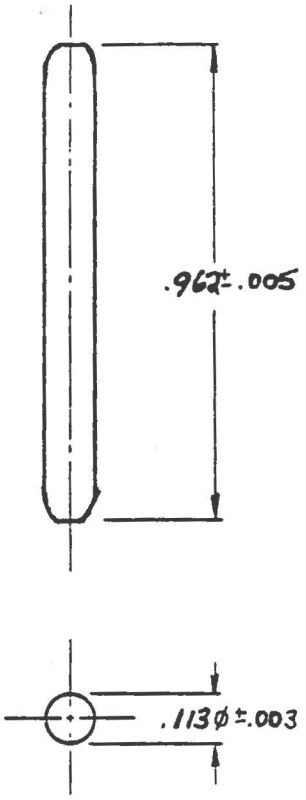
NOTE:
1. BREAK ALL SHARP CORNERS & EDGES .015 ±.005 R



(Bollard) Pin

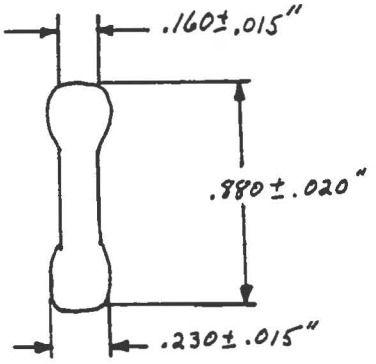
NOTE:

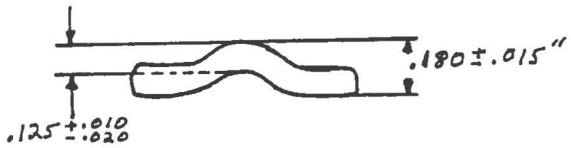
1. BREAK ALL SHARP CORNERS & EDGES .015 ±.005 R



Carbon-Fiber Implant

Toggle





PURCHASED COMPONENT SPECIFICATIONS

Item: Carbon Fiber Tow - 10,000 Filaments (nominal) Part No. 0102

Date of Issue: _____ Supersedes NEW

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Black tow, essentially free of foreign matter and broken strands tightly wound on a clean core and each core wrapped in sealed film.

B. Sizing: Free of Sizing
C. Tensile strength, Psi on 1" length (calculated): $\geq$ 450,000
D. Tensile modulus, Psi (calculated): $34 \pm 2 \times 10^6$
E. Density, gm/cc^3 (calculated): 1.80 ± 0.14
F. Carbon content: not less than 95%

II. Container/Delivery Criteria

A. Shipments of wound cores shall be in an inner plastic bag packaged tightly in corrugated containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initiallly shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to :

(See Reverse For Sampling and Release Criteria)

IV. Sampling and Inspection

A. Carefully examine each wound core as per IA. Take approximately 1 X 4 foot length for retention.

B. Review certification
   a. The lot must meet all criteria listed in IB.

C. Release the lot if all criteria in I have been met.

V. Safety Precautions

A. Wear clean gloves when handling fibers.

B. Consult MSDS.

VI. Storage Requirements

A. Store tightly closed at room temperature.

VII. Approved Vendor(s)

Hercules

PURCHASED COMPONENT SPECIFICATIONS

Item: Gelatin, Pork Skin, 300 Bloom, 20 Mesh Part No. 0101

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Light tan granules, essentially free of foreign matter.
B. Bloom: NLT 250
C. pH (10% @ 55°C): 5.4 - 6.5
D. Water (18h, 105°C): 10-13%
E. Ash (USP): Less than 2%
F. Heavy Metals (USP): 50 ppm max.
G. Arsenic (USP): 1 ppm max.
H. Total Microbial Count (USP): Less than 500/g
I. Pyrogen (USP @ 10 mg/Kg): Passes
J. Caliform, E. Choli, Sulfitereduced Chlostritium: Negative
K. Salmonella: Negative

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling/Inspection/Release

A. Visually examine contents of 2 containers at random.

B. Sample aseptically into a sterile container taking approximately 5 gram from each of 2 random containers and from a composite. Send sample to contract laboratory for total microbial count.

C. Release lot if A is satisfactory, certification is received for B-K and total microbial count is less than 500 organisms/gram.

V. Safety Precautions

A. No special precautions.

VI. Storage Conditions

A. Store tightly closed in a cool dry place.

B. Retest for IV. B. six months from date of release.

VII. Approved Supplier(s)

Deutsche Gelatine - Fabriken Stoess & Co. GMGH

PURCHASED COMPONENT SPECIFICATIONS

Item: Sterile Water for Irrigation Part No. 0100

Date of Issue: _____ Supersedes _____

Approvals:

_____ _____

EMPIRICAL FORMULA: H_2O

I. Analytical Criteria

A. Description: Clear colorless liquid essentially free of foreign matter.
B. Endotoxin (USP): Not more than 0.25EU/ml
C. Sterility (USP): Passes test
D. Particulate matter (USP): Passes test
E. Ammonia (USP): Passes test
F. Chloride, Sulfate, Calcium, Carbon Dioxide (USP): Passes test
G. Oxidizable Substances, Total Solids (USP): Passes test
H. pH (USP): Between 5.0 and 7.0
I. Heavy Metals (USP): Passes test

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling/Inspection/Release

A. Inspect lot for criterion IA.
B. Check certification for compliance to criteria IB-I.
C. Release lot if all criteria IA-I are satisfied.

V. Safety Precautions

A. Use care in handling glass containers and when removing closures.

VI. Storage Conditions/Stability

A. Store in a cool place.
B. Do not use beyond manufacturers' expiration date.

VII. Approved Supplier(s)

PURCHASED COMPONENT SPECIFICATIONS

Item: Glycerin, USP Part No. 0107

Date of Issue: _____ Supersedes _____

Approvals:

_____ _____

EMPIRACAL FORMULA: $C_3H_8O_3$

I. Analytical Criteria

A. Description: Clear colorless liquid essentially free of foreign matter.
B. Identification (USP): Passes test
C. Specific Gravity (USP): Passes test
D. Color, Residue on Ignition, Chloride (USP): Passes tests
E. Sulfate, Chlorinated Compounds (USP): Passes tests
F. Arsenic (USP Method I): Not more than 1.5 ppm
G. Heavy Metals (USP): Not more than 5 ppm
H. Fatty Acids and Esters (USP): Passes test
I. Assay (USP): Not less than 95.0% nor more than 101.0%

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

Plastafil

C. Lots rejected initially shall not be resubmitted without specific written approval from

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling/Inspection/Release

A. Inspect lot for criterion IA.
B. Sample one container at random and test for IB.
C. Check certification for criteria IC-I.
D. Release lot if IA-I are satisfied.

V. Safety Precautions

A. Use care in handling glass containers and when removing closures.

VI. Storage Conditions/Stability

A. Store in a cool place.
B. Inspect for criterion IA if to be used after six months from date of receipt.

VII. Approved Supplier(s)

PURCHASED COMPONENT SPECIFICATIONS

Item: Araldite[R] Resin w/Hardner Part No. 0104

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

		Resin	Hardner
A.	Description:	Creamy, viscous liquid	Amber liquid
B.	Viscosity @ 25°C:	50,00 cps ± 10%	35,000 cps ± 10%
C.	Specific Gravity @ 21°C:	1.13 - 1.21	0.89 - 0.95
D.	Flash Point:	210°C	110°C

E. When mixed at 1/1 Ratio by Volume:
Viscosity @ 25°C: 45,000 CPS ± 10%
Potlife @ 25°C: N.L.T. 2 hours

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

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(See Other Side)

IV. Sample/Inspection/Release

A. Inspect for IA.
B. Check Certification for IB-E
C. Release if Criteria IA-E are met.

V. Safety Precautions

A. Avoid contact with eyes, skin or clothing.
B. Consult MSDS.

VI. Storage Requirements

A. Store at room temperature away from heat or sunlight.

VII. Approved Vendor(s)

Ciba - Geigy

Resin, Item AW-106
Hardner, Item HV-953

PURCHASED COMPONENT SPECIFICATIONS

Item: Shrink Sleeve, Yellow, Unprinted Part No. 0105

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Yellow tubing on spools.
B. Appearance: Uniform tubing essentially free of foreign matter.
C. Internal Diameter (ID): 1/8" (3.2 mm) nominal.
D. Meets Mil 46846 Type 5 specifications (certification):
   1. Tensile Strength NLT 4500 psi
   2. Ultimate elongation: 400% nominal
   3. Longitudinal change: Less than 10%
   4. Heat shock: No dripping, cracking or flowing
   5. Low temperature flexibility: No cracking

II. Container/Delivery Criteria

A. Shipments shall be on spools with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

IV. Sampling/Inspection/Release

A. Visually examine shipment for A & B.

B. Take two spools at random and check ID (range 2.9 - 3.5 mm)

C. Take a 5" length from one roll and check for proper shrinkage using the manufacturing heater to be used to shrink the tubing. Shrinkage is satisfactory if tubing shrinks uniformly to not less than 60% of starting ID.

D. Accept lot if all the above inspections are satisfactory and certification to Mil 45846 Type 5 is received.

V. Safety Precautions

A. No special precautions.

VI. Storage Conditions

A. Store at room temperature away from a heat source or sunlight.

VII. Approved Supplier(s)

Raychem Corp., Item RT-876, 1/8" ID

PURCHASED COMPONENT SPECIFICATIONS

Item: Chrome Alloy Stainless Steel Wire, Type 304 Part No. 0106

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Smooth, bright, uniform diameter wire, 30x14"/pkg.
B. Diameter: 0;40 mm nominal (Range 0.30-0.50)
C. Appearance: Wire shall be essentially free of foreign matter.

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

Rev. 6/2/88

(See Other Side)

IV. Sampling/Inspection/Release

A. Visually examine shipment for A & C.

B. Take 2 packages at random and measure 1 wire from each for B.

C. Accept lot if A, B & C requirements are met.

V. Safety Precautions

A. Exercise care to prevent puncture wounds when handling wire.

VI. Storage Conditions

A. Store at room temperature.

VII. Approved Supplier(s)

Rocky Mountain Orthodontics, Item E9

PURCHASED COMPONENT SPECIFICATIONS

Item: N-Methyl-2-Pyrolidone Part No. 0103

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

Empirical Formula: C_5H_9NO

I. Analytical Criteria

A. Description: Colorless liquid, essentially free of foreign matter
B. . Color (APHA): 50 maximum
C. . Flash Point (ASTM D93-73): 91°C
D. . Density @ 25°C: 1.026 - 1.030 g/ml
E. . Assay (GC): not less than 99.8%

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to :

(See reverse side for sampling and release criteria

IV. Sampling and Inspection

A. Sample the square not of the containers which made up the reclined end and check for appearance.

B. Review Certification

1. The lot must meet all criteria listed in IB-IE.

C. Release the lot if all criteria in I. have been met.

V. Safety Precautions

A. Wear suitable rubber or plastic gloves when handling material. Handle only in a hood or where there is adequate ventilation.

B. Wear eye protection.

C. Consult MSDS .

VI. Storage Requirements

A. Store tightly closed at room temperature.

VII. Approved Vendor(s)

BASF
Ashland

PURCHASED COMPONENT SPECIFICATIONS

Item: Graphite Powder Part No. 0109

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

EMPIRICAL FORMULA: C

I. Analytical Criteria

A. Description: Fine black powder.
B. Graphite: Not less than 99.9%
C. Total Ash Content: Less than or equal to 2 ppm

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

IV. Sampling/Inspection/Release

A. Visually examine contents of container.
B. Review certification from supplier for B & C.
C. Release lot if A, B, & C are met.

V. Safety Precautions

A. No special precaution.

VI. Storage Conditions

A. Store at room temperature.

VII. Approved Supplier(s)

Le Carbone - Lorraine, Item 9901, Purity 8

PURCHASED COMPONENT SPECIFICATIONS

Item: Udel® Polysulfone (Medical Grade) Part No. C//0

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Transparent, amber colored pellets, essentially free of foreign matter and residual DMSO.
B. .Melt Flow @ 650°C, 44 psi, g/10 minutes (ASTMD1238): 6.5 ± 5%
C. .Density, g/cm^3 (ASTMD1505): 1.24 ± .5%
D. .Water Absorption % in 24 hours. (ASTM 570): 0.3 ± 5%
E. .Tensile Strength @ Yield, psi (ASTM D638): 10,200 ± 10%
F. .Tensile Modulus, psi (ASTM D638): 360,000 ± 10%
G. .Tensile Elongation @ Break, % (ASTM D638): 50-100 ± 10%
H. .Flexural Strength, psi (ASTM D790): 15,400 ± 10%
I. .Flexural Modulus, psi (ASTM D790): 390,000 ± 10%
J. .Heat Deflection Temperature @ 264 psi (ASTM D643): 345°F ± 15°F

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastifil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to :

(See Reverse for Sampling and Release Criteria)

IV. Sampling and Inspection

a. Carefully open and examine each container as per I.a.. Take approximately 2 oz. sample for retention.

b. Review Certification.

1. Certification must indicate that the lot is medical grade (P-1700).

2. The lot must meet all criteria listed.

c. Release the lot if all criteria in I. have been met.

V. Safety Precaution

a. Consult MSDS.

VI. Storage Requirements

a. Store tightly closed at room temperature.

VII. Suppliers

a. Amoco, Cat. No. P-1700

PURCHASED COMPONENT SPECIFICATIONS

Item: Triton X100 Part No. 0108

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Clear, whtie to off-white liquid, essentially free of foreign matter.
B. Specific Gravity @ 25°C: 1.060 - 1.070
C. Viscosity @ 25°C (Brookfield): 240 CPS ± 20%
D. Color (APHA): 100 max.
E. pH (5% solution): 6.9 - 7.1

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling and Inspection

A. Check one sample for appearance of contents.
B. Review certification.

1. Lot must meet criteria IB-E.

C. Release lot if all criteria in I have been met.

V. Safety Precautions

A. Avoid contact with skin or eyes.
B. Consult MSDS.

VI. Storage Requirements

A. Store tightly closed at room temperature.

VII. Approved Vendor(s)

Rhom & Haas

PURCHASED COMPONENT SPECIFICATIONS

Item: Paper/Foil Pouch Part No. 0112

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: White pouches composed of laminated paper 25#, 10# polyethyline, 0.0007 aluminum foil, 25# polyethyline, free of discoloration, holes or discontinuities.
B. Seals: These pouches shall be preformed and sealed on 3 sides.
C. Seal Integrity: Samples at random shall be sealed using the heat sealer. All samples shall pass this test (PLT-101).
D. Dimensions: Meets print requirements.
E. Identity: Positive (Visual examination indicates a laminate of paper film, foil and film).
F. Classification of Defects: Meets PLT-100.

II. Container/Delivery Criteria

A. Shipments shall be in suitable containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling and Inspection

A. Examine random samples per carton for IA, F.
B. Take five samples for B, C, D & E, using the same samples for all tests.
C. Release lot if all criteria IA-F are met.

V. Safety Precautions

A. No special precautions.

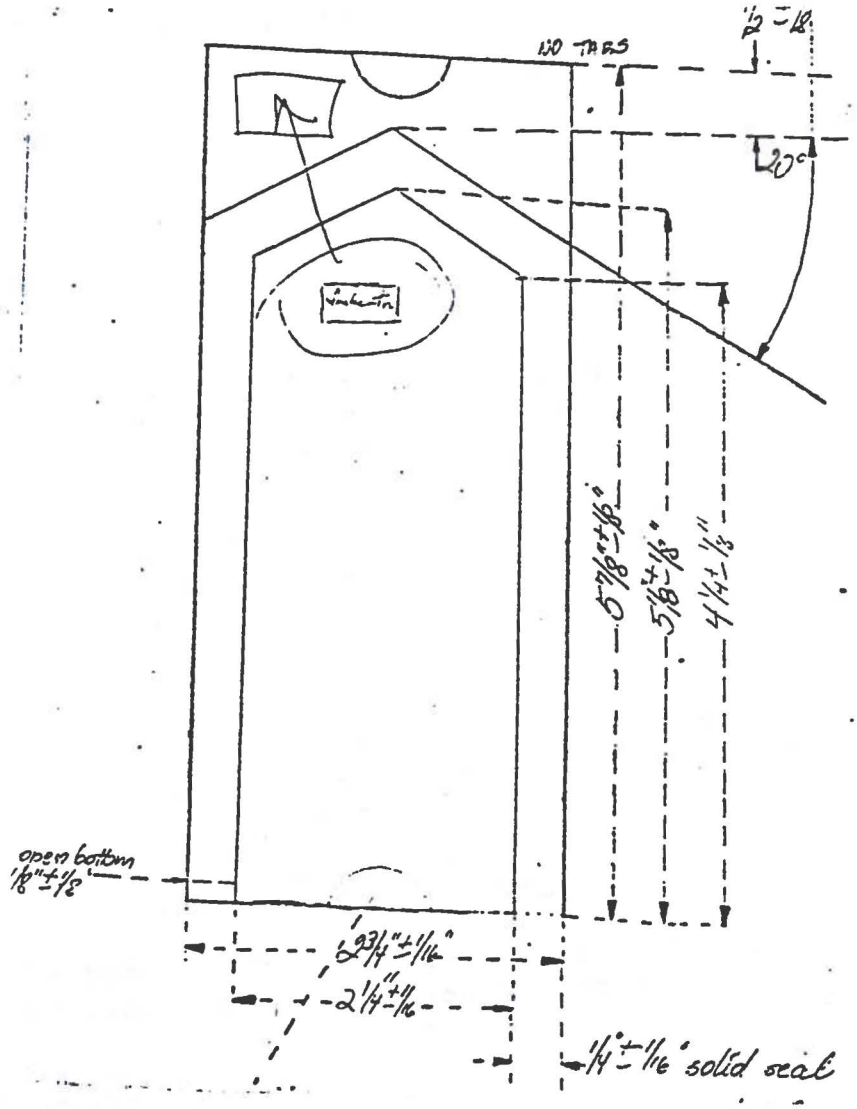
VI. Storage Requirements

A. Store closed at room temperature.

VII. Approved Vendor(s)

DRG

VIII. Print



PURCHASED COMPONENT SPECIFICATIONS

Item: Paper/Film Pouch Part No. 0113

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Analytical Criteria

A. Description: Paper sealed to PET/PE film, free of discoloration, holes and discontinuities.
B. Seals: These pouches shall be preformed and sealed on three sides.
C. Seal Integrity: Samples at random shall be sealed with the heat sealer. All shall pass the test (PLT-101).
D. Dimensions: Meets print requirements.
E. Identity: Positive (Visual examination indicates a pouch formed from film and paper.)
F. Classification of Defects: Meets PLT-100.

II. Container/Delivery Criteria

A. Shipments shall be in containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

(See Other Side)

IV. Sampling and Inspection

A. Examine random samples per carton for IA, F.
B. Take five samples for B, C, D & E, using the same samples for all tests.
C. Release lot if all criteria IA-F are met.

V. Safety Precautions

A. No special precautions.

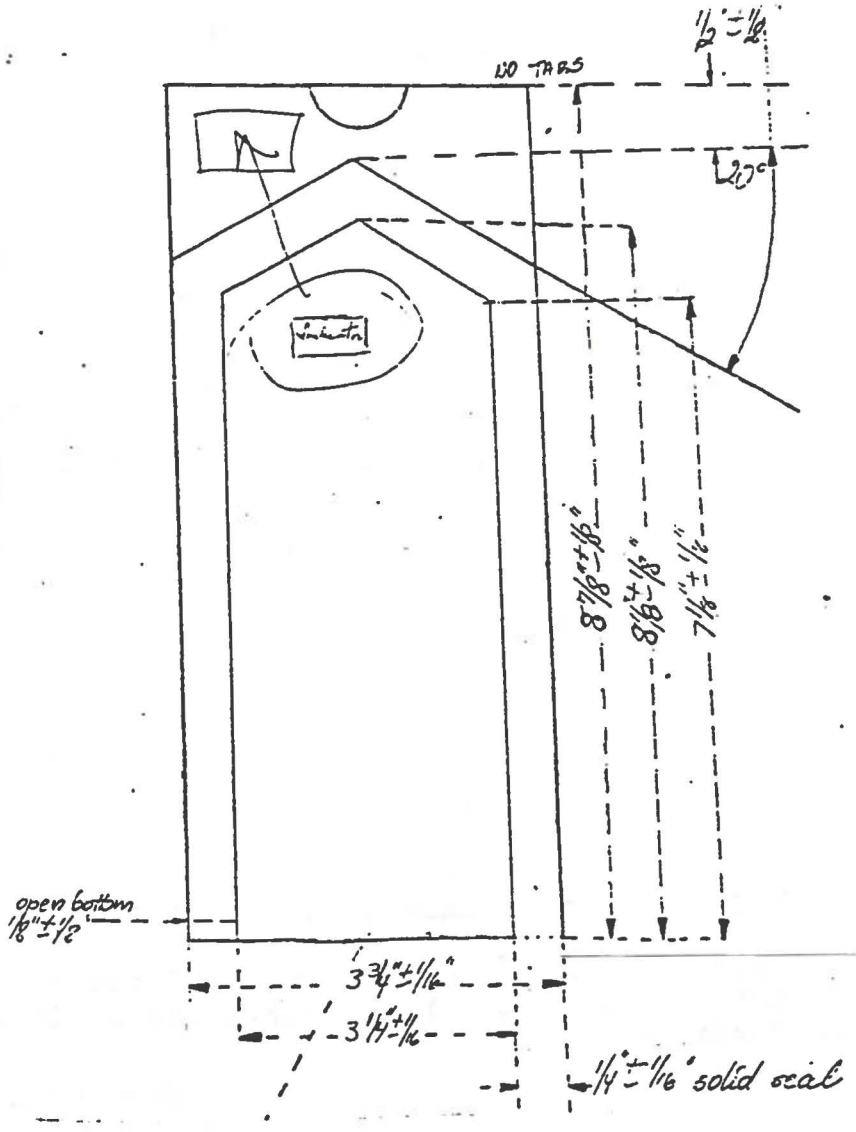
VI. Storage Requirements

A. Store closed at room temperature.

VII. Approved Vendor(s)

DRG

VIII. Print



PURCHASED COMPONENT SPECIFICATIONS

Item: Radiation Tell-Tale Label Dots Part No. 2000

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. Physical Criteria

A. Description: Round yellow dot 1/2" in diameter on backing paper. (The color changes to bright red after sterilization.)

B. Composition: Radiation sensitive Detex™ backed with permanent adhesive.

II. Container/Delivery Criteria

A. Shipments shall be 1000 per roll, with one manufacturer's lot preferred packaged in cardboard dispenser box.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from Plastafil.

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to Plastafil.

IV. Sampling

Check three random samples per case for dimensions, satisfactory adhesion to implant overpouch and for color.

V. Approved Suppliers

Avery Labels

PROPERTIES OF THE DEVICE RELEVANT TO THE
TREATMENT OR MITIGATION OF THE DISEASE OR CONDITION

FACILITIES, METHODS, CONTROLS USED IN THE MANUFACTURING,
PROCESSING, PACKING, STORAGE, ETC.

Building and Facilities

The new Plastafil facilities will occupy an area of approximately 2,500 square feet and will be within a larger building. This new facility will be located in an area zoned for light industry. No heavy manufacturing will take place within the overall building. Manufacturing will occupy a separate area within this facility and additional areas will be devoted to offices; quality assurance; shipping, receiving and storage; rest rooms; and other support functions.

Access to the Plastafil facility will be through the main entrance or through the shipping and receiving area.

This building will be of concrete block construction on a poured slab. The facility will be air conditioned. Within this building, the Plastafil facility will be completely partitioned from the rest of the building. Lighting fixtures in the manufacturing facility are fluorescent and are recessed for safety and cleaning purposes. Water for general use is supplied from the local municipal water source. All areas have adequate ventilation and special exhaust and air handling systems will be installed where necessary. Electrical service will be adequate for all current and future needs. The building will be maintained in a good state of repair by Plastafil staff and the services of several contractors.

The drainage disposal system will be connected to the local municipal sewerage system. Solid waste will be disposed of in accordance with EPA regulations using the services of a licensed contractor. The facility will be maintained in a clean and sanitary condition by Plastafil personnel in conjunction with the services of a professional cleaning service company.

All water for process use and for final rinsing of manufacturing equipment will be distilled water obtained from a qualified supplier (Water for Irrigation, part no. 0100).

A proposed floor plan is included in Exhibit I. This will show the proposed location of the various areas and will also show air flow, the flow of raw materials, product processing and finished product handling and shipping.

Exhibit II provides a listing of those major activities which will occur in each area and area construction details.

EXHIBIT I PLANNED FACILITY

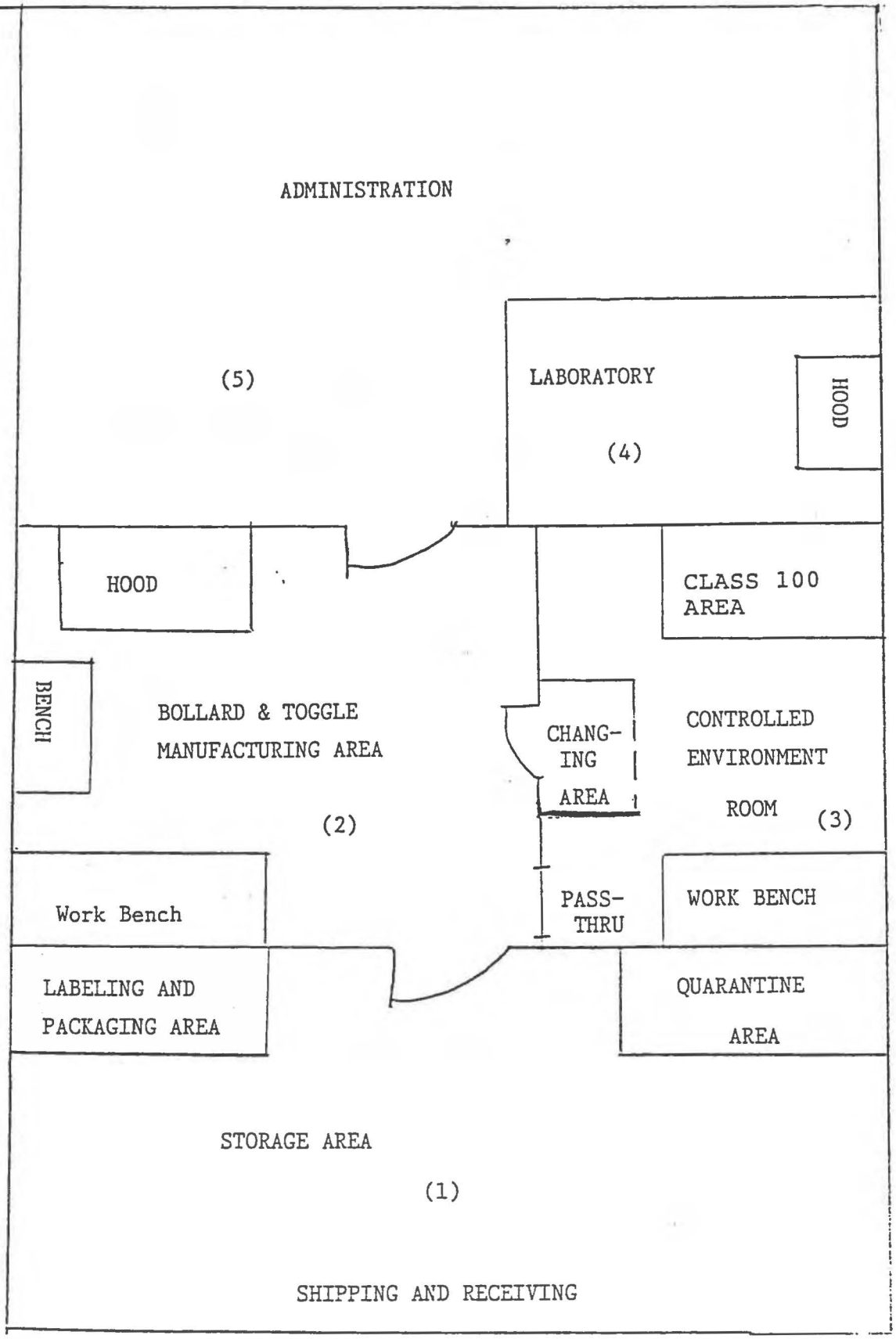


EXHIBIT I PLANNED FACILITY

a. Air Flow

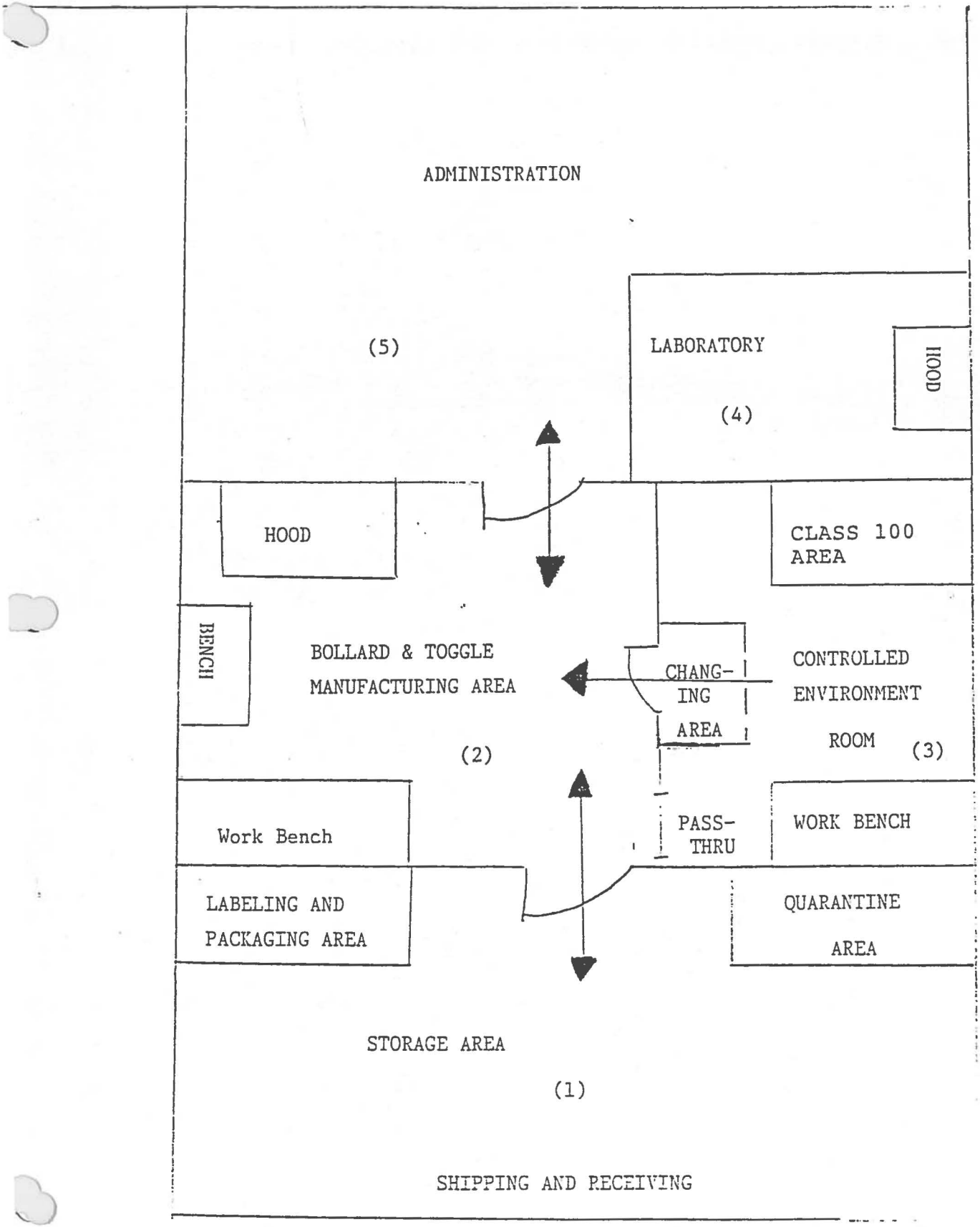


EXHIBIT I PLANNED FACILITY

b. Product Processing

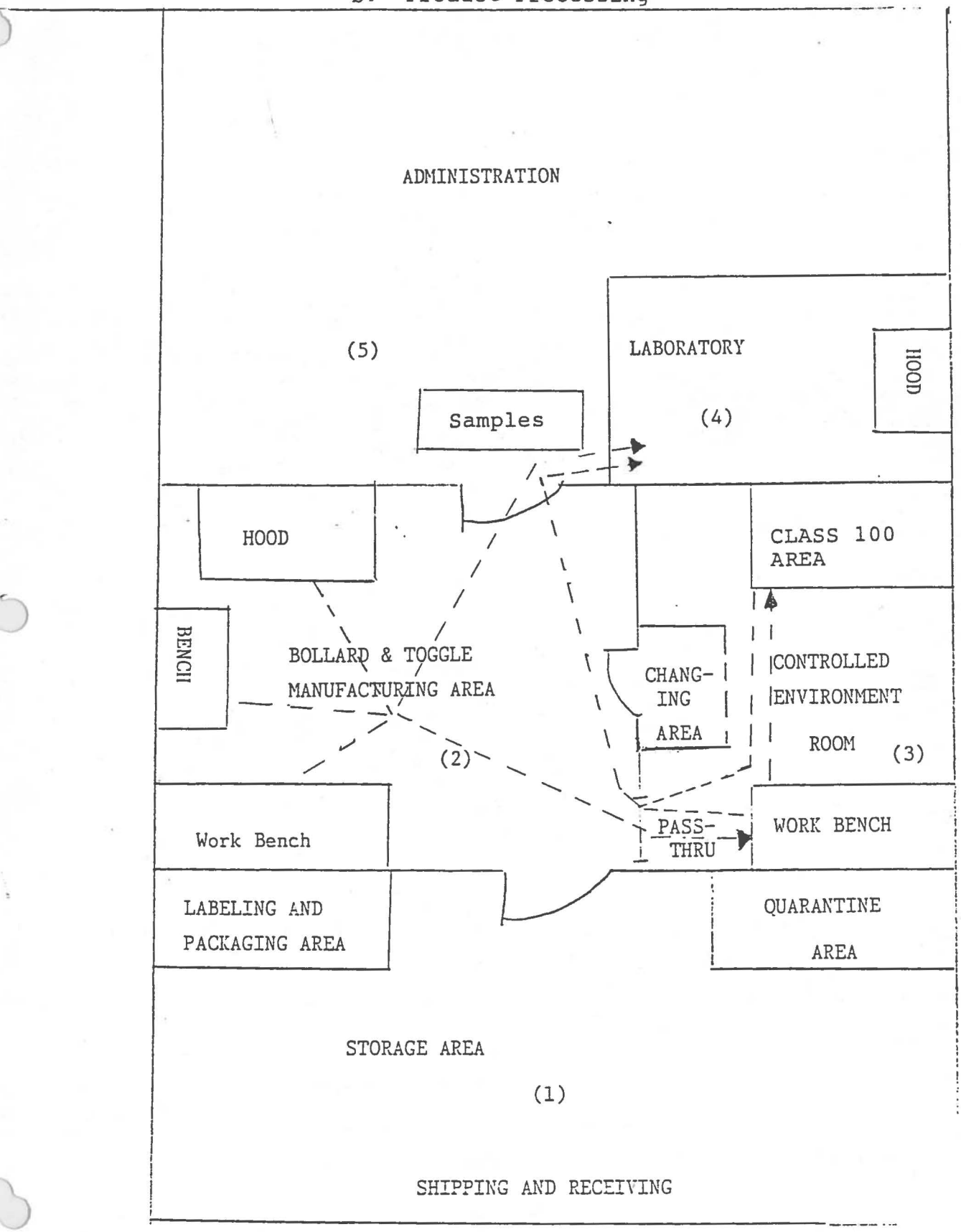


EXHIBIT I PLANNED FACILITY

c. Raw Materials Flow

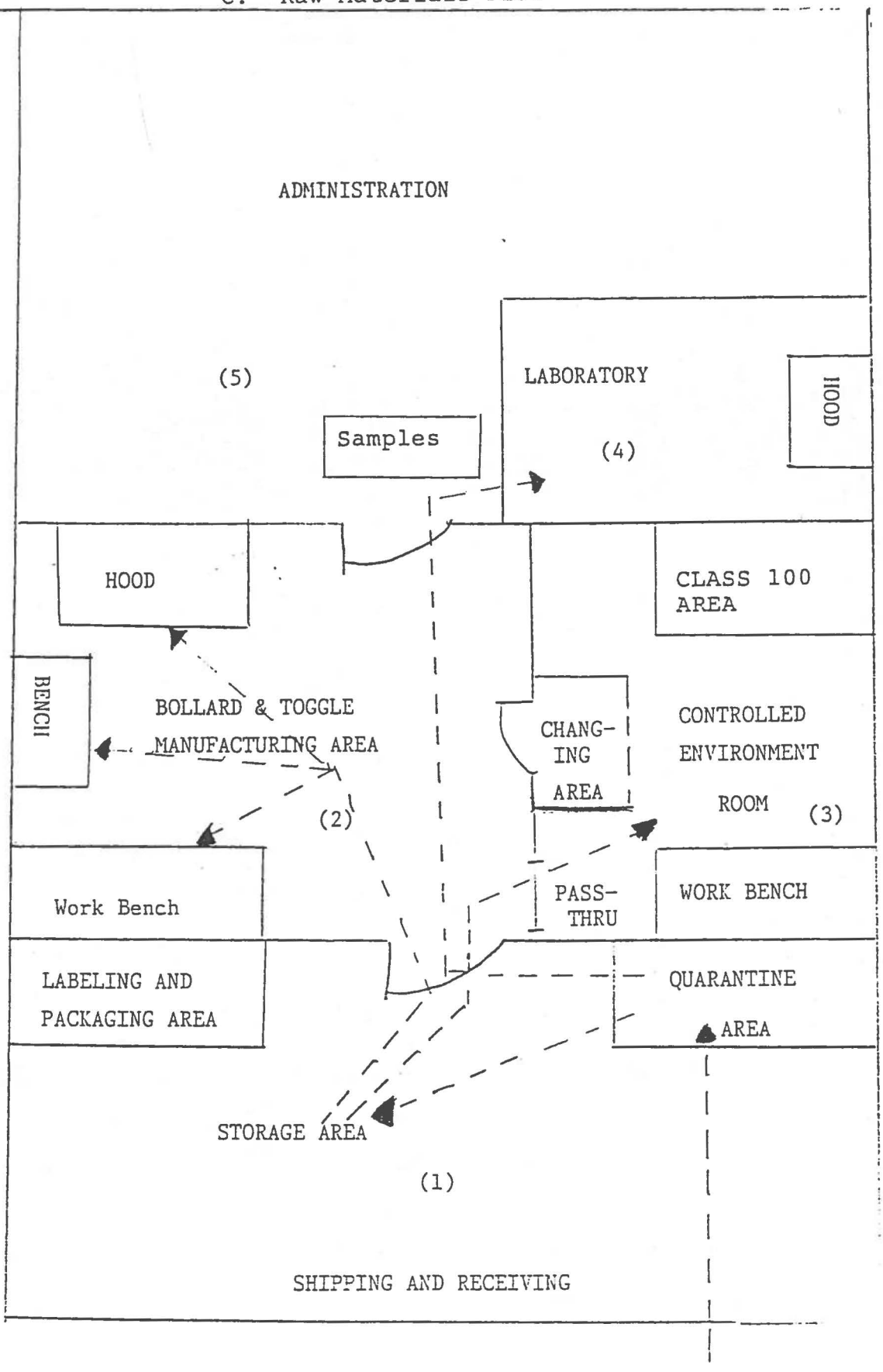


EXHIBIT I PLANNED FACILITY

d. Finished Product Flow

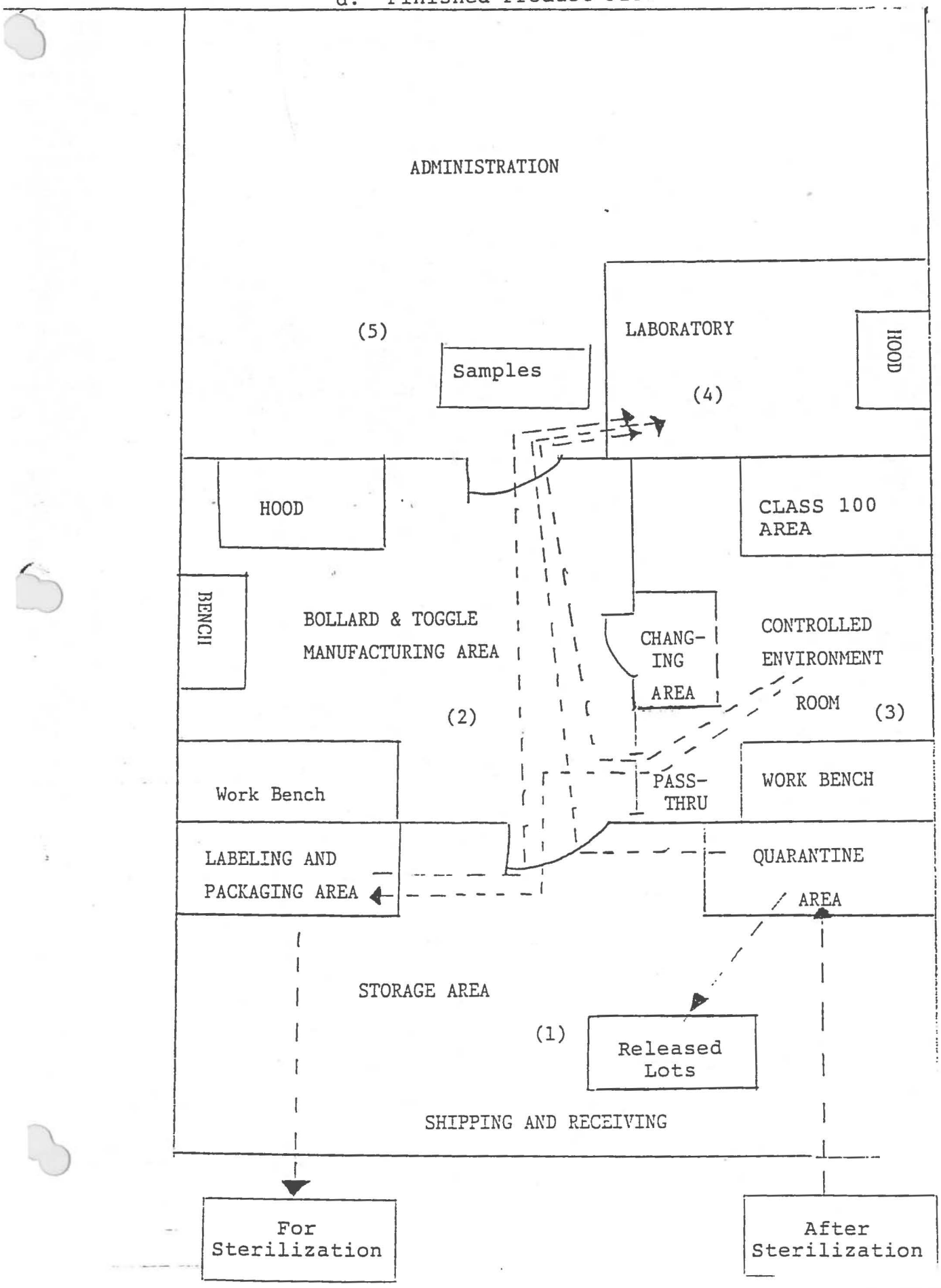


EXHIBIT IIa

A description of the construction of the new Plastafil facilities are as follows (See Exhibit I for areas 1-5 described below):

1. Normal industrial construction. Poured concrete floor will be sealed to prevent flaking. This area will be supplied with air conditioning for protection of product and employee comfort. Doors will be maintained closed at all times except when required for ingress/egress. Adequate light will be provided for inspection.
2. This area will have a sealed, poured concrete floor. Walls will be sealed and painted plasterboard. Ceiling will be acoustic tile. Filtered conditioned air will be supplied for product protection and employee comfort. This area will contain an exhaust hood and exhausts for the high temperature cleaning oven. Adequate lighting will be supplied.
3. This area will have a sealed poured concrete floor. Walls will be sealed and painted. Walls will be sealed to the floor with silicone. Ceiling tiles will be coated and sealed with silicone. All lights will be recessed and sealed. This room will be supplied with air conditioned air filtered through a HEPA filter. Personnel will enter into this room through a change area where they will don special gowns and hair covers. Materials will enter and leave this room through a special pass-through. This room will have a class 100 vertical laminar flow area for formation of the gelatin coated implant. This laminar flow area will have an air exchange of 90 cubic feet/min. $\pm$ 20 cubic feet.

   This room will be at positive air pressure to the surrounding rooms. Air temperatures will be maintained between 65°F and 80°F for product protection and comfort of employees wearing special gowns.

4. This room will have sealed concrete floor with walls constructed of painted plasterboard. Ceiling will be of standard acoustic tiles with adequate lighting. This room will have an exhaust hood. This room will be air conditioned for product protection and employee comfort.

5. This area will be of standard office construction with painted plasterboard walls and acoustic tile ceiling. Adequate lighting and air conditioning will be supplied. Rest rooms will have air exhausts.

EXHIBIT IIb

B. The description of the various operations which will be performed within the new facility are as follows (See Exhibit I for areas 1-5 described below):

1. Receiving of incoming components and sterilized packages.

   Sampling of incoming components.

   Quarantine of unreleased components, packaged product awaiting release and unsatisfactory components or product awaiting disposition.

   Storage of released components.

   Labeling and packaging of completed components.

   Shipping of packaged product to outside contractor for sterilization

   Shipping of packaged released products to customers.

2. Manufacture of Bollard.

   Manufacture of Toggle.

   Heat cleaning of graphite filaments.

   Wind graphite after heat cleaning.

   Weigh, mix and dissolve polysulfone powder.

   Coat carbon fibers with resin mix.

   Prepare blanks for Bollards, pins and toggles.

   Preclean Bollards, pins and toggles.

   Sampling of Bollards, pins and toggles.

3. Weigh, mix and dissolve gelatin.

   Coat and inspect graphite filaments.

   Wind coated filaments and dry on a carousel frame.

   Cut to size, twist and attach a shrink sleeve.

   Clean tip ends to remove gelatin.

   Attach probe wire using epoxy cement to implant tips.

   Heat shrink sleeve.

Ultrasonically clean Bollards, pins and toggles.

Visually inspect implants, Bollards, pins and toggles.

Sample for quality assurance testing.

Package one implant, one Bollard and pin and one toggle in an aluminum/film pouch and heat seal.

Overpackage sealed aluminum/film pouch into a film/paper overpackage and heat seal.

Sampling of inprocess implants, cleaned Bollards, pins and toggles, sealed pouches and overpacks and finished units.

4. Components, labeling and packaging supplies are inspected or tested, as appropriate.

Inprocess tests for Bollards, pins and toggles.

Inprocess tests for coated graphite fibers.

Product tests for coated implants.

Pouch and overpack seal testing.

Finished products inspection/testing.

Environmental monitoring testing.

Stability samples storage and inspection/testing

In-house calibration.

Final release of packaged, sterilized products.

5. General office area.

Records: batch history records, receiving records, testing/inspection results, SOP's, personnel records, training records, orders, shipping records, etc.

Payroll and other accounting records.

Rest rooms.

Methods: Standard Production Formulations

Date Issued	STANDARD PRODUCT FORMULATION		Page 1 of 5
Theoretical Yield	Product Name Carbon Fiber Implant	Product No. 5000	Batch No.
		Date Started	Date Completed

First Effective Batch	Standard Batch Size 100	This Batch Size	Actual Quantity Produced
Product Description Black fiber strand with lead wire and sleeve at one end.		Standard Batch Factor	Gain or Loss

Component Code Or Grade	Components	Unit of Measure	Standard Quantity	Quantity For This Order
0102	Carbon Fiber Tow, 10,000	1x60"	500'	
0101	Gelatin	GMS	10	
0100	Water for Irrigation	ML	150	
0107	Glycerin	ML	100	
0100	Water for Irrigation	ML	Ad Lib.	
0104	Araldite Epoxy Resin & Hardner	Packs	1 ea.	
0105	Polyolefin Shrink Sleeve	4½"	100	
0106	Lead Wire	6"	100	
	SPECIAL CONDITIONS			
	1. Perform all operations for coating through final assembly			
	in controlled environment area in the laminar flow hood.			
	2. Wear clean lab coat, gloves and approved hair covering.			
	3. See attached equipment list.			
	Air pressure differential test (positive) (unsatisfactory)			
	By Date			
	COMPLETE LOT WITHIN 48 HRS. AFTER STARTING.			

Approvals	Manufacturing	Date	Qual. Assur.	Date

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 2 of 5	
	Product Name Carbon Fiber Implant	Product No. 5000	Batch No.

		Operator	Date	Checker
1.	Wind sufficient carbon fiber tow on the carbon spool and place into the special carbon-lined oven, close tightly and set to maintain 350°C - 380°C. Quantity of Carbon Fiber _____ Receiving Number _____	*	**	
2.	When oven temperature reaches specified range, begin timing. After 20 minutes at temperature, turn off and allow to cool to ambient temperature with the door tightly closed. Time Start_____ Time Stop_____ Time Removed_____	*	**	
3.	Prepare gelatin coating mix. Add _____g of gelatin, Rec. No._____ to _____ml water for irrigation, Rec. No. _____. Heat to 80°C ± 5°C on a hot plate and completely dissolve. Stir as needed with a clean stirring rod. Add _____ml of glycerin, Rec. No. _____. Stir to form a complete solution. Cool to 50°C ± 10°C to use for coating.	*	**	*
4.	(Perform these and subsequent operations in the laminar flow hood.) Pour coating mix into the coating pan. Place end of tow into the pan and place a stainless steel rod across the tow to keep it submerged in the mix. With clean tweezers slowly draw the tow through the mix and between two sterile cellulose sponges to wipe off excess mix. Repeat the procedure, using fresh mix and unused cellulose sponges. Wind on a carousel frame. Change sponges every 2-3 frames.	*	**	

* Indicates person performing function
** Enter date operation completed

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 3 of 5	
	Product Name: Carbon Fiber Implant	Product No.: 5000	Batch No.:

		Operator	Date	Checker
5.	Allow the coated tow to dry for about one hour in the laminar flow hood. Cut each tow in 60" lengths.	*	**	
6.	Take five samples from the beginning of the coating operation, the middle and the end. These are to be checked for coating content and for uniformity by Quality Assurance. Provide five lengths of uncoated tow to be used as tare. Average Wt of Coating, Begin._____ Average Wt of Coating, Mid._____ Average Wt of Coating, End_____ QA Approval to Continue By_____	*	**	*
7.	Take a cut length and bring the two ends together. Holding the loop end, make four twists and bring this end together with the cut ends. Place a wire loop around the bow ends and using this loop gently pull through a shrink sleeve leaving about (1") 25mm of the ends protruding. No. of Sleeves Used_____ Receiving No._____	*	*	
8.	Dip the exposed ends in water for irrigation, Rec. No._____, which has been heated to 80°C ± 10°C and wash to remove the gelatin. Place on a rack and allow to dry in the laminar flow hood.	*	**	
9.	When all units have been washed and dried, mix the 2 pack Araldite epoxy and place in a suitable container. Note this mix is only good for 1 hour before it completely sets up. _____ packs Resin, Rec. No. _____ _____ packs Hardner, Rec. No._____			

* Indicates person performing function
** Enter date operation completed

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Carbon Fiber Implant	Page 4 of 5 Product No. 5000	Batch No.

	Operator	Date	Checker
10. Take a 6" length of 0.4mm wire and form a hook at one end and a closed loop at the other end (see sample). Dip the hook end into the epoxy resin and push the coated end into the carbon fibers at the end of the sleeve. Twist the hook around the fibers to form a mechanical joint and pull the sleeve up to the closed loop end. _____ lengths of wire, Rec. No._____ _____ Used	*	**	
11. Apply heat from a hot air gun to the sleeve end to shrink the sleeve and set the epoxy resin. The end point is reached when the sleeve has shrunk to form a tight fit to the end of the fibers and the wire leader.	*	**	
12. Inspect each unit for satisfactory appearance. Record the total number of units made, number of rejects and number of satisfactory units for packaging. Total number made(1) _____ Number of rejects_____ Total satisfactory units for Pkg._____	*	**	
13. Proceed to package units per packaging order. Take 3 samples (one from beginning, middle and end of lot) for testing. Complete packaging same day as it is started.	*	**	
(1) Satisfactory yield is -10% + 2% of Batch Size Calculations:			
Record Reviewed by Supervisor_____		Date_____	

* Indicates person performing function
** Date Operation Completed

Date Issued		Page
	STANDARD OPERATING INSTRUCTIONS	5 of 5
	Product Name	Product No. / Batch No.
	Carbon Fiber Implant	5000

	Operator	Date	Checker

Equipment List

1. Controlled environment area
2. Laminar Flow Hood
3. Carbon-lined oven
4. Carbon spools
5. Clean, depyrogenated beakers
6. Clean, depyrogenated stirring rods
7. Calibrated thermometers
8. Clean, depyrogenated stainless steel rod
9. Clean, depyrogenated dipping pan
10. Clean, depyrogenated tweezers
11. Clean, depyrogenated carousel frames
12. Calibrated balance capable of reading to 1 mg.
13. Clean, depyrogenated drying racks
14. Epoxy mixing container
15. A cutting device
16. A hot air gun
17. Needle nose pliers
18. 12" length of 0.5mm stainless steel wire
19. Temperature controlled hot plate
20. Sterile cellulose sponges
21. Sponge holding device

*** Indicates person performing function**
**** Enter date operation completed**

Date Issued	STANDARD PRODUCTION FORMULATION	Page 1 of 4

Theoretical Yield	Product Name	Product No.	Batch No.
	Coated Carbon Fiber	4000	
Weight	Bundles for Molding	Date Started	Date Completed

First Effective Batch	Standard Batch Size	This Batch Size	Actual Quantity Produced

Product Description	Standard Batch Factor	Gain or Loss
Black coated fiber bundles		

Component Code Or Grade	Components	Unit of Measure	Standard Quantity	Quantity For This Order
0102	Carbon Fiber Tow	GM	150	
0110	Polysulfone Powder	GM	100	
0103	N-Methyl-2-Pyrolidone	ml	150	
0109	Graphite	GM	0.25	
	Special Precautions			
	1. Perform operations in the manufacturing area.			
	2. Perform coating, drying in a chemical exhausting hood.			
	3. Wear safety glasses or goggles.			
	4. Wear gloves when handling resin, solvent or coated tows.			
	Note: Each lot should be completed within 5 days of initiation. Coated bundles must be used for molding within 30 days of mfg.			

Plant Mgr.	Date	Research Mgr.	Date	Qual. Assur. Mgr.	Date

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Coated Carbon Fiber for Molding	Page 2 of 4 Product No. 4000	Batch No.

	Operator	Date	Checker
1. Weigh the polysulfone and graphite powder into a suitable dissolving vessel, add the N-Methyl-2-Pyrolidone and mix at high speed for 4 hours ± 15 minutes. Polysulfone, Rec. No._____ Graphite Powder, Rec. No._____ N-M-P, Rec. No._____ Time Start_____Time Finish_____	*	**	*
2. Cover dissolved polysulfone resin and allow to stand for 4 hours ± 15 minutes. Time Start_____Time Finish_____	*	**	
3. Heat clean carbon fiber tow in the oven by winding the required amount of tow onto a carbon spool and heat at 350°C - 380°C for 20 minutes. Carbon Fiber Tow, Rec. No._____	*	**	
4. Remove cleaned fiber tow and cut into 14" lengths. Group into even number of bundles on separate frames. Take 3 lengths and drape over a leader. Take 4 lengths and drape over a leader. These lengths should form equal lengths over these leaders. _____ 3 length bundles _____ 4 length bundles	*	**	
5. Pull each bundle through the resin solution by grasping the wire leader with forceps and then through the spring device to remove excess resin. Place the bundle on a glass plate and work in additional resin with a rod to assure that the fibers are completely wet. Pull bundle through the spring to remove excess resin and hang to dry in the hood on a frame.	*	**	

* Indicates person performing function
** Date Operation Completed

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Coated Carbon Fibers for Molding	Page 3 of 4 Product No. 400D	Batch No.

	Operator	Date	Checker
6. Place bundles, separate by bundle make-up, into the vertical drying oven. Set at 105°C ± 5°C for at least one hour. Then set for 180°C ±10°C for at least 3 hours. (Perform these drying steps in the hood). Time Start_____ Time Finish_____	*	**	
7. Take all of the bundles made up of 4 lengths of tows, cut at the wire leader and divide in two vertically. Place into a bin labeled "40K". Inspect. No. of 40K Lengths_____	*	**	
8. Take three fourths of the bundles made up of three lengths. Cut at the wire leader but do not divide. Place these into a bin labeled "60K". Inspect. No. of 60K Lengths_____	*	**	
9. Take the remaining bundles made up of these lengths cut at the wire leader and divide in two vertically. Place in bin labeled "30K". Inspect. No. of 30K Lengths_____	*	**	
10. Cover each bin, label with product lot number and count and date beyond which these should not be used. These will be used to mold Bollards, pins and toggles.	*	**	
No. of 30K lengths_____ No. of 40K lengths_____ No. of 60K lengths_____ No. of defects_____ Received By_____	Date		

* Indicates person performing function
** Date Operation Completed

Equipment List, Product 4000

1. Chemical exhausting hood
2. Carbon lined oven capable of maintaining 350°C-380°C
3. Carbon spool
4. Stainless steel bow
5. Stainless steel wire leaders
6. Forceps
7. Stainless steel resin pan with hold down device for fiber coating
8. Stainless steel spring wih 3.2mm ID
9. Glass plates
10. Stainless steel mixing rod
11. Stainless steel drying frame
12. Glass tube vertical drier with heater and thermometer
13. Stainless steel or glass resin dissolving vessel
14. Suitable high speed mixer
15. Suitable balance
16. Cutting device
17. 3 bins to hold cut bundles

Date Issued	STANDARD PRODUCTION FORMULATION	Page 1 of 5

Theoretical Yield	Product Name	Product No.	Batch No.
	Bollard	4001	-
Weight		Date Started	Date Completed

First Effective Batch	Standard Batch Size	This Batch Size	Actual Quantity Produced
	100		
Product Description: Black expandable rivet-like device		Standard Batch Factor	Gain or Loss

Component Code Or Grade	Components	Unit of Measure	Standard Quantity	Quantity For This Order
4000	Coated Fiber Bundle	60K	40	
4000	Coated Fiber Bundle	40K	40	
0110	Polysulfone Powder	GM	50	
0109	Powdered Graphite	GM	2	
	Polysulfone Sol. From Item 4000		AD.LIB	
	SPECIAL PRECAUTIONS			
	1. Perform operations in the manufacturing area.			
	2. Wear safety glasses or goggles.			
	3. Wear approved mask when grinding or polishing units.			
	4. Wear gloves when handling resin or coated bundles.			
	5. Wear sterile gloves when handling dried units.			
	Note: Each lot should be completed within			
	5 days of initiation of the lot.			

Plant Mgr.	Date	Research Mgr.	Date	Qual. Assur. Mgr.	Date

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 2 of 5	
	Product Name Bollard	Product No. 4001	Batch No.

		Operator	Date	Checker
1.	Take the required number of 60K and 40K bundles and place the bins next to the mold. No. of 60K bundles _____ No. of 40K bundles _____	*	**	
2.	Take suitable amount of Polysulfone and grind in grinder to a fine powder.	*	**	
3.	Weigh Polysulfone and Graphite powders into a suitable container and mix well to form a uniform appearance. Polysulfone, Rec. No. _____ Graphite Powder, Rec. No. _____	*	**	*
4.	Heat oven to 285°C ± 20°C.	*	**	
5.	Select one bundle of 60K fibers and place in the open mold. To a 40K bundle paint one side with the Polysulfone solution and place the painted side against the 60K bundle in the mold. Place the open mold and top half into the oven for 10-12 minutes. Remove the two halves, place the upper "male" portion onto the lower portion of the mold and press for 8-10 minutes. Water cool. Open the mold and cut into 29 mm lengths. Polysulfone Solution Lot _____	*	**	
6.	Discard unsatisfactory appearing units into a reject box for later counting. Place satisfactory units into a labeled container for further processing. No. of good units _____ No. of rejects _____	*	**	

* Indicates person performing function
* Date Operation Completed

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Bollard	Page 3 of 5 Product No. 4001	Batch No.

		Operator	Date	Checker
7.	Take two satisfactory half rounds. Paint the flat side of one with the Polysulfone solution, Lot _____, and press together manually. Insert these into the holes in the Bollard mold. Tap firmly into the mold with the set punch. Insert shaping punch into the hole between the half rounds. Add mixture of Polysulfone and Graphite powder around the upper portion of the rounds and tap the punch firmly to splay the ends. Add additional mixture of Polysulfone and Graphite to fill up the head portion of the cavity. Pack tightly to assure there is sufficient powder to properly form head.	*	**	
8.	Place both upper and lower portions of the mold into the oven to heat up for about 5 minutes. Put the two halves of the mold together and press to partially close. Return the mold to the oven for 5 minutes, take out and press to partially close. Repeat for two more times at the end of which press tightly to completely close the mold. Return to the oven and heat for 10 minutes. Remove, place in the press tightly closed for 5 minutes. Add water cooling.	*	**	
9.	Remove from mold and inspect for satisfactory appearance. Set unsatisfactory units aside and place good units in the container for further processing.	*	**	
10.	Take good units and cut slots into the shank end per blue-print.			
11.	Lightly grind the unit to finish followed by light sanding to smooth out mold lines and flashing.	*	**	

* Indicates person performing function
** Date Operation Completed

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Bollard	Page 4 of 5 Product No. 4001		Batch No.
		Operator	Date	Checker
12.	Inspect units for appearance and dimensions in accordance with the item specifications. Set aside unsatisfactory units and place good units into a container for further processing.	*	**	
13.	Place good units into an ultrasonic cleaner containing a solution of hot tap water with 3 drops of Triton X 100 wetting agent, turn on the unit and clean for 10 minutes.	*	**	
14.	Remove units, place on a drainer and rinse thoroughly with hot tap water and allow to drain.	*	**	
15.	Place drained units into a second ultrasonic cleaner containing water for irrigation, turn on and clean for 10 minutes. Repeat with fresh WFI.	*	**	
16.	Remove cleaned units and place in second clean drainer to drain. Discard water from ultrasonic cleaner.	*	**	
17.	Place drained units on a tray and place tray into oven for 1 hour at 105°C ± 5°C.	*	**	
18.	Remove units from oven. Put on sterile gloves and take samples for testing. Inspect and count units. Place satisfactory units into a sterile pouch labeled with product and lot number and count. Seal pouch. No. of units made_____ No. of good units_____ No. of rejects_____ No. of samples_____ Yield_____ An acceptable yield is planned lot size ± 10%.			
Record checked by_____		Date_____		

* Indicates person performing function
** Date Operation Completed

EQUIPMENT LIST, BOLLARD

1. Mold for half rounds and mold for complete units.
2. Oven designed for heating molds.
3. Press with water cooled plattens.
4. Dremel Grinder or equivalent.
5. Wet and dry polishing papers.
6. 2 small ultrasonic cleaning baths.
7. Calibrated micrometer or caliper capable of reading accurately to 0.001".
8. Oven for drying cleaned units.
9. Sterile pouches for storing cleaned units.
10. Brush, 1/4"
11. Container to mix polysulfone and graphite.
12. Rod to mix powders.
13. Measuring device graduated in mm.
14. Cutting device to cut slots into the shank end of the Bollard.
15. Insulated gloves for handling hot molds.
16. Timing device.
17. Appearance models.
18. 2 clean stainless steel drainers.
19. Clean drying tray.
20. Sterile gloves.
21. Cutting device for cutting fiber bundles.
22. Punches (1 set punch and 1 shaping)
23. Hammer
24. Grinder

Date Issued	STANDARD PRODUCTION FORMULATION	Page 1 of 4

Theoretical Yield	Product Name	Product No.	Batch No.
	Pins	4002	
Weight		Date Started	Date Completed

First Effective Batch	Standard Batch Size	This Batch Size	Actual Quantity Produced
	100		
Product Description: Black pins		Standard Batch Factor	Gain or Loss

Component Code Or Grade	Components	Unit of Measure	Standard Quantity	Quantity For This Order
4000	Coated Fiber Bundles	60K	15	
4000	Coated Fiber Bundles	40K	15	
0110	Polysulfone Powder	GM	10	
0109	Powdered Graphite	GM	0.4	
	Polysulfone Sol. From Item 4000		AD. 1K	
	SPECIAL PRECAUTIONS			
	1. Perform operations in the manufacturing area.			
	2. Wear safety glasses or goggles.			
	3. Wear approved mask when grinding or polishing units.			
	4. Wear gloves when handling resin or coated bundles.			
	5. Wear sterile gloves when handling dried units.			
	Note: Each lot should be completed within			
	5 days of initiation of the lot.			

Plant Mgr.	Date	Research Mgr.	Date	Qual. Assur. Mgr.	Date

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 2 of 4	
	Product Name: Pin	Product No.: 4002	Batch No.

		Operator	Date	Checker
1.	Take the required number of 60K and 30K bundles and place the bins next to the mold. No. of 60K bundles_____ No. of 40K bundles_____	*	**	
2.	Weigh Polysulfone and Graphite powders into a suitable container and mix well to form a uniform appearance. Polysulfone, Rec. No._____ Graphite Powder, Rec. No._____	*	**	*
3.	Heat oven to 285°C ± 20°C.	*	**	
4.	Select one bundle of 60K fibers and one of 30K and cut each in half. Place the 60K bundle into the mold. Paint one side of the 30K bundle with the Polysulfone solution and place the coated side down on top of the 60K bundle in the mold. Place both halves of the mold in the oven for 8-10 minutes. Remove mold, put the two halves together and hold in press or 5 minutes. Water cool and remove the lengths. Polysulfone Solution, Lot_____	*	**	
5.	Cut into 1" (25.4mm) lengths and lightly grind the unit to finish followed by light sanding to smooth out mold lines and flashing.	*	**	
6.	Inspect units for appearance and dimensions in accordance with the item specifications. Set aside unsatisfactory units and place good units into a container for further processing.	*	**	

* Indicates person performing function
** Date Operation Completed

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 3 of 4	
	Product Name: Pin	Product No.: 4002	Batch No.

	Operator	Date	Checker
7. Place good units into an ultrasonic cleaner containing a solution of hot tap water with 3 drops of Triton X100 wetting agent, turn on the unit and clean for 10 minutes.	*	**	
8. Remove units, place on a drainer and rinse thoroughly with hot tap water and allow to drain.	*	**	
9. Place drained units into a second ultrasonic cleaner containing water for irrigation, turn on and clean for 10 minutes. Repeat with fresh WFI.	*	**	
10. Remove cleaned units and place in second clean drainer to drain. Discard water from ultrasonic cleaner.	*	**	
11. Place drained units on a tray and place tray into oven for 1 hour at 105°C ± 5°C.	*	**	
12. Remove units from oven. Put on sterile gloves and take samples for testing. Inspect and count units. Place satisfactory units into a sterile pouch labeled with product and lot number and count. Seal pouch. No. of units made_____ No. of good units_____ No. of rejects_____ No. of samples_____ Yield_____ An acceptable yield is planned lot size ± 10%			
Record checked by_____		Date_____	

* Indicates person performing function
** Date Operation Completed

EQUIPMENT LIST, PIN

1. Mold
2. Oven designed for heating mold
3. Press with water cooled plattens
4. Dremel Grinder or equivalent
5. Wet and dry polishing papers
6. 2 small ultrasonic cleaning baths
7. Calibrated micrometer or caliper capable of reading accurately to 0.001"
8. Oven for drying cleaned units
9. Sterile pouches for storing cleaned units
10. Brush, 1/4"
11. Container to mix polysulfone and graphite
12. Rod to mix powders
13. Measuring device graduated in mm
14. Insulated gloves for handling lot mold
15. Timing device
16. Appearance models
17. 2 clean stainless steel drainers
18. Clean drying tray
19. Sterile gloves
20. Cutting device for cutting molded lengths
21. Grinder

Date Issued	STANDARD PRODUCTION FORMULATION	Page 1 of 5

Theoretical Yield	Product Name	Product No.	Batch No.
	Toggle	5001	
Weight		Date Started	Date Completed

First Effective Batch	Standard Batch Size	This Batch Size	Actual Quantity Produced
	100		
Product Description	Black barbell shaped device.	Standard Batch Factor	Gain or Loss

Component Code Or Grade	Components	Unit of Measure	Standard Quantity	Quantity For This Order
4000	Coated Fiber Bundles	60K	15	
4000	Coated Fiber Bundles	30K	15	
0110	Polysulfone Powder	GM	10	
0109	Powdered Graphite	GM	0.4	
	Polysulfone Sol. From Item 4000		AL. 416.	
	SPECIAL PRECAUTIONS			
	1. Perform operations in the manufacturing area.			
	2. Wear safety glasses or goggles.			
	3. Wear approved mask when grinding or polishing units.			
	4. Wear gloves when handling resin or coated bundles.			
	5. Wear sterile gloves when handling dried units.			
	Note: Each lot should be completed within			
	5 days of initiation of the lot			

Plant Mgr.	Date	Research Mgr.	Date	Qual. Assur. Mgr.	Date

Date Issued	STANDARD OPERATING INSTRUCTIONS Product Name Toggle	Page 2 of 5 Product No. 5001		Batch No.
		Operator	Date	Checker
1.	Take the required number of 60K and 30K bundles and place the bins next to the mold. No. of 60K bundles_____ No. of 30K bundles_____	*	**	
2.	Take suitable amount of Polysulfone and grind in grinder to a fine powder.	*	**	
3.	Weigh Polysulfone and Graphite powders into a suitable container and mix well to form a uniform appearance. Polysulfone, Rec. No._____ Graphite Powder, Rec. No._____	*	**	*
4.	Heat oven to 285°C ± 20°C.	*	**	
5.	Select one bundle of 60K fibers and one of 30K. Place side by side and cut into 29 mm lengths. Place a cut portion of the 30K bundle into the mold, paint one side of the cut portion of the 60K bundle with the Polysulfone solution and place the painted side down onto the 30K portion in the mold. Add sufficient mixture of Polysulfone and Graphite powder to fill the cavity. Place both halves of the mold into the oven for 8-10 minutes. Remove mold. Put the two halves of the mold together and hold in press for 5 minutes. Water cool and remove toggles. Polysulfone Solution, Lot_____	*	**	
6.	Discard unsatisfactory appearing units into a reject box for later counting. Place satisfactory units into a labeled container for further processing. No. of good units_____ No. of rejects_____	*	**	

* Indicates person performing function
** Date Operation Completed

		Operator	Date	Checker
7.	Lightly grind the unit to finish followed by light sanding to smooth out mold lines and flashing.	*	**	
8.	Inspect units for appearance and dimensions in accordance with the item specifications. Set aside unsatisfactory units and place good units into a container for further processing.	*	**	
9.	Place good units into an ultrasonic cleaner containing a solution of hot tap water with 3 drops of Triton X100 wetting agent, turn on the unit and clean for 10 minutes.	*	**	
10.	Remove units, place on a drainer and rinse thoroughly with hot tap water and allow to drain.	*	**	
11.	Place drained units into a second ultrasonic cleaner containing water for irrigation, turn on and clean for 10 minutes. Repeat with fresh WFI.	*	**	
12.	Remove cleaned units and place in second clean drainer to drain. Discard water from ultrasonic cleaner.	*	**	
13.	Place drained units on a tray and place tray into oven for 1 hour at 105°C ± 5°C.	*	**	

* Indicates person performing function
** Date Operation Completed

Date Issued	STANDARD OPERATING INSTRUCTIONS	Page 4 of 5	
	Product Name: Toggle	Product No.: 5001	Batch No.

	Operator	Date	Checker
14. Remove units from oven. Put on sterile gloves and take samples for testing. Inspect and count units. Place satisfactory units into a sterile pouch labeled with product and lot number and count. Seal pouch.			
No. of units made _____			
No. of good units _____			
No. of rejects _____			
No. of samples _____			
Yield _____			
An acceptable yield is planned lot size ± 10%			
Record checked by _____ Date _____			

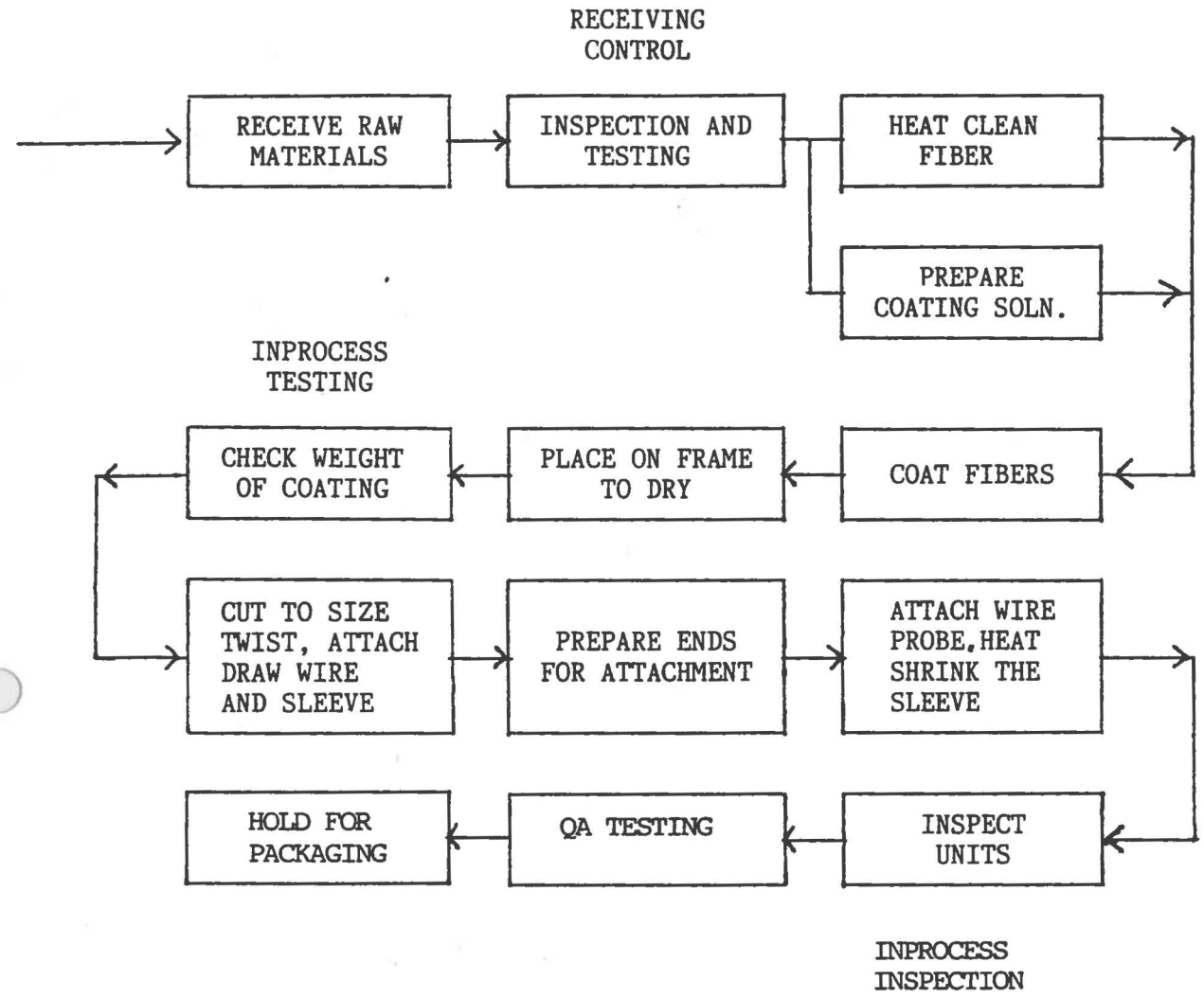
* Indicates person performing function
* Date Operation Completed

EQUIPMENT LIST, TOGGLE

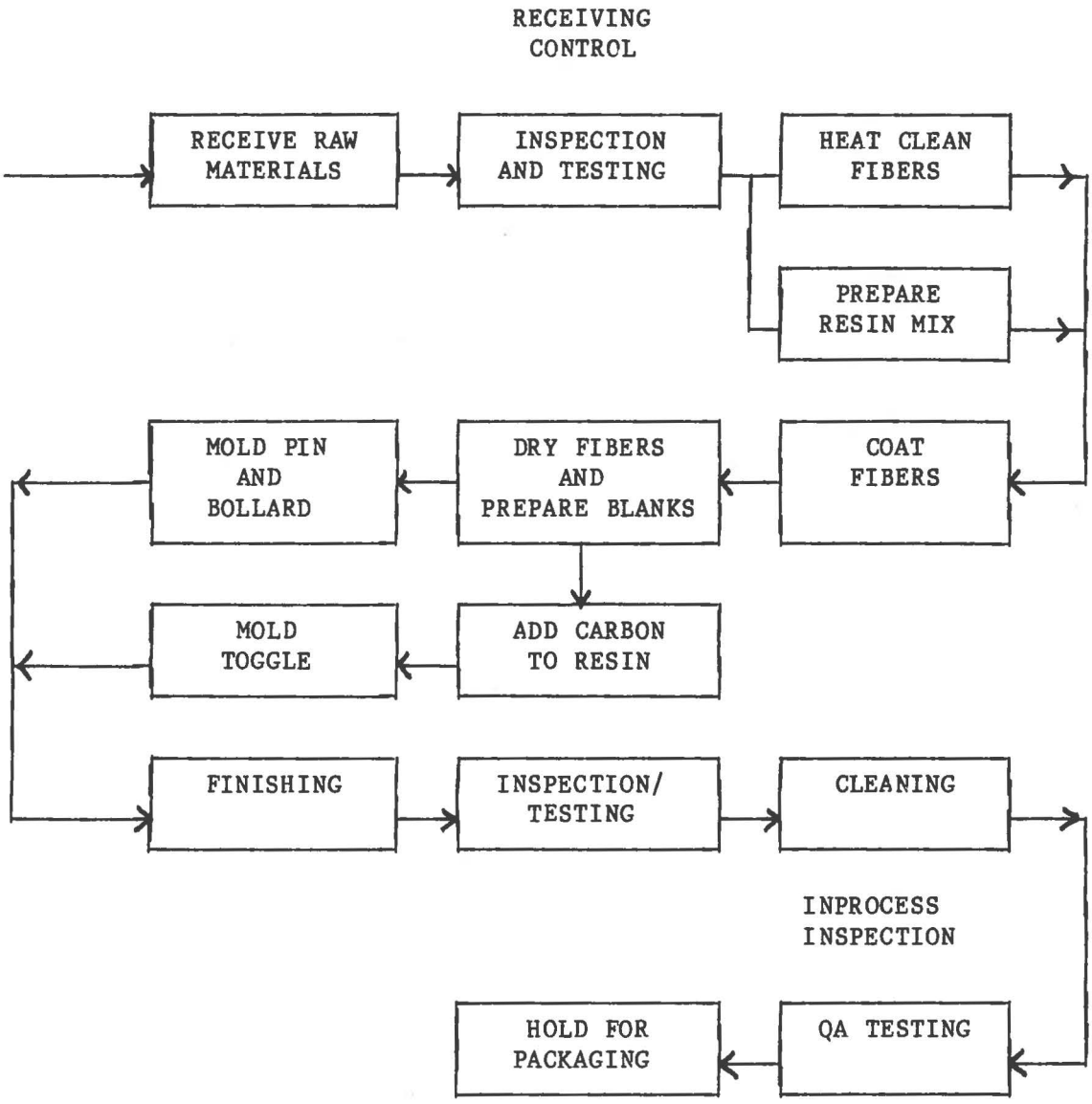
1. Mold
2. Oven designed for heating molds
3. Press with water cooled plattens
4. Dremel Grinder or equivalent
5. Wet and dry polishing papers
6. 2 small ultrasonic cleaning baths
7. Calibrated micrometer or caliper capable of reading accurately to 0.001"
8. Oven for drying cleaned units
9. Sterile pouches or storing cleaned units
10. Brush, 1/4"
11. Container to mix polysulfone and graphite
12. Rod to mix powders
13. Measuring device graduated in mm
14. Insulated gloves for handling hot mold
15. Timing device
16. Appearance models
17. 2 clean stainless steel drainers
18. Clean drying tray
19. Sterile gloves
20. Cutting device for cutting fiber bundles
21. Grinder

Manufacturing Schema

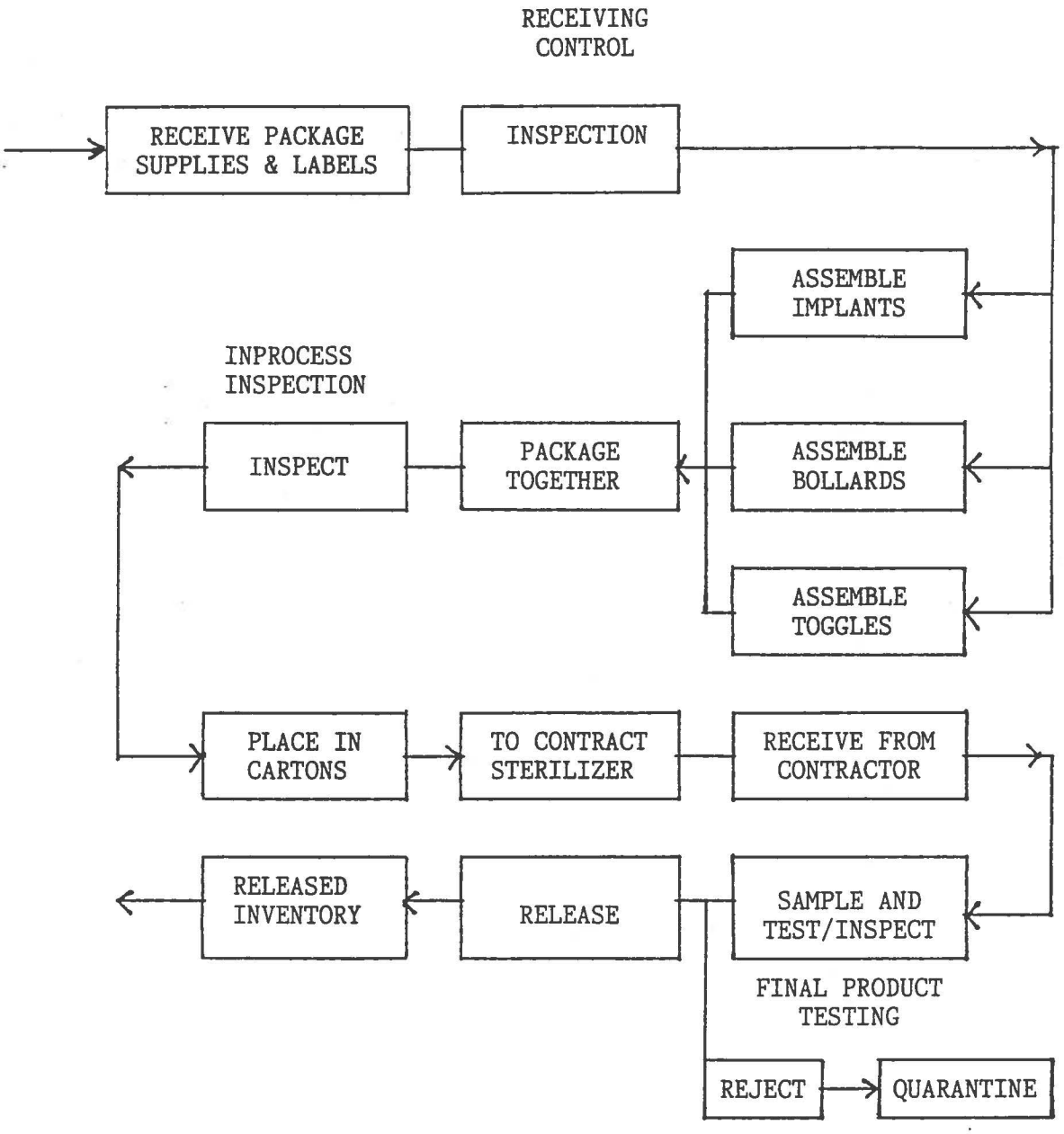
MANUFACTURING SCHEMA - CARBON FIBER IMPLANT



MANUFACTURING SCHEMA - BOLLARD AND TOGGLES



PACKAGING AND RELEASE SCHEMA



PRODUCT SPECIFICATIONS

Item: Coated Fiber Implant Part No. 5000

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. CRITERIA

A. Description: A double loop of coated black fibers with a yellow sleeve and wire loop at one end.

B. Dimensions: Shall conform to dimensions A & B on the print.

C. Leader Attachment Strength: Five samples at random held at the loop end shall remain intact when a five pound weight is suspended by the leader end of each for at least 10 seconds.

D. Visual Examination:

1. The implant shall have the sleeve and leader properly attached.
2. No foreign matter present on the coated fibers.
3. Not more than an estimated 5% of fibers shall be uncoated.
4. Not more than an estimated 5% of the fibers shall be broken or frayed.

E. Cytotoxicity (Agar Overlay): A 3" sample of heat-cleaned fibers used for this lot shall be tested for cytotoxicity by a contract laboratory. The sample shall pass this test.

F. Fiber Coating Uniformity:

1. Samples taken in-process after coating shall be uniform throughout the lot. No set of samples (B, M, E) shall have a coating which varies by more than 5% from the average.

II. Sample/Inspection/Release:

A. Perform inspection in the Controlled Environment Area. Wear sterile gloves. Inspect the number of samples equal to the square root plus 1 of the lot size for IB.

B. Take five samples at random for IC.

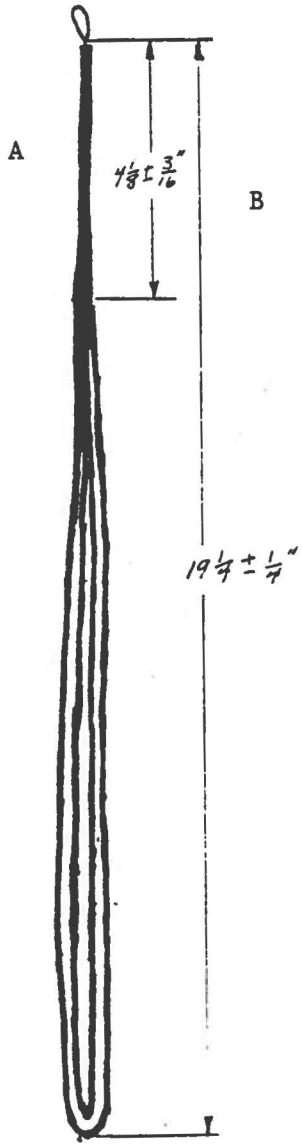
C. Inspect 100% for IA & D.

D. Release the lot if criteria IA-F are met. (All defectives found during the 100% inspection must be removed from the lot and the balance released for packaging or sterilization)

III. Storage Requirements

A. Store in sealed sterile pouches at room temperature until packaging.

IV. Print Dimensions



Carbon Fiber
Implant Print

PRODUCT SPECIFICATIONS

Item: Bollard Part No. 4001

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. CRITERIA

A. Description: Black rivet shaped device.

B. Dimensions: Shall conform to dimensions A, B & C listed on Bollard Print (page 2).

C. Mechanical Strength: Samples taken at random shall meet the following test. All must pass test.

1. Head Shear - not less than 1000 newtons.
2. Body Shear - not less than 1000 newtons.

Note A: This test is conducted by a contract laboratory using an Instron testing machine.

Note B: These tests are conducted with the pin set into the Bollard sufficiently to splay the ends.

D. Visual Examination:

1. No cracks or voids present.
2. Surfaces must be essentially smooth.
3. The end of the Bollard shall be uniform with no section shorter than the others.
4. No foreign matter or contamination shall be visually apparent.

E. Cytotoxicity (Agar Overlay):

1. Submit one sample in a sterile pouch per lot for testing for cytotoxicity to a contract laboratory. The sample shall pass this test.

II. Sample/Inspection/Release

A. Perform inspection in the Controlled Environment Area. Wear sterile gloves. Inspect the number of samples equal to the square root plus 1 of the lot size for IB.

B. Test five samples at random for IC and one for IE.

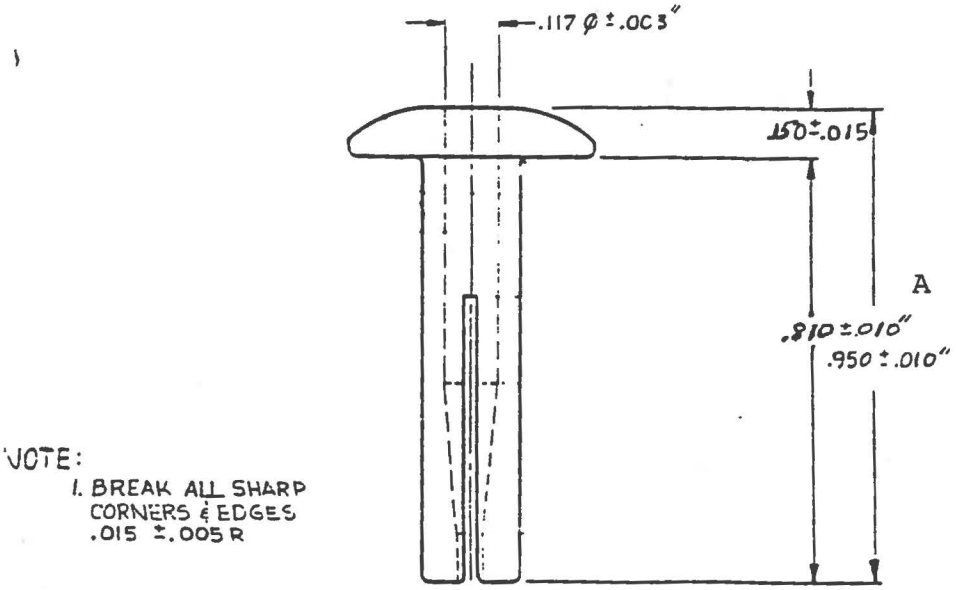
C. Inspect 100% for IA & D.

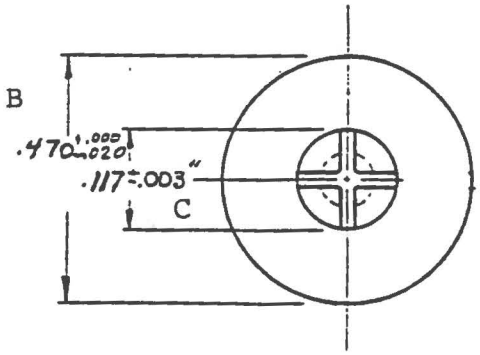
D. Release the lot if criteria IA-E are met. (All defectives found during the 100% inspection must be removed from the lot and the balance released for packaging or sterilization)

III. Storage Requirements

A. Store in sealed sterile pouches at room temperature until packaging.

IV. Print Dimensions





Bollard Print

3/1/89

PRODUCT SPECIFICATIONS

Item: Pin Part No. 4002

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. CRITERIA

A. Description: Black pin.

B. Dimensions: Shall conform to dimensions A & B listed on Pin Print (page 2).

C. Mechanical Strength: Samples taken at random shall meet the following test. All must pass test.

1. Pin Shear - not less than 200 newtons.

Note: This test is conducted by a contract laboratory using an Instron testing machine.

D. Visual Examination:

1. No cracks or voids present.
2. Surfaces must be essentially smooth.
3. No foreign matter or contamination shall be visually apparent.

E. Cytotoxicity (Agar Overlay):

1. Submit one sample in a sterile pouch per lot for cytotoxicity to a contract laboratory. The sample shall pass this test.

II. Sample/Inspection/Release

A. Perform inspection in the Controlled Environment Area. Wear sterile gloves. Inspect the number of samples equal to the square root plus 1 of the lot size for IB.

B. Test 5 samples at random for IC and 1 for IE.

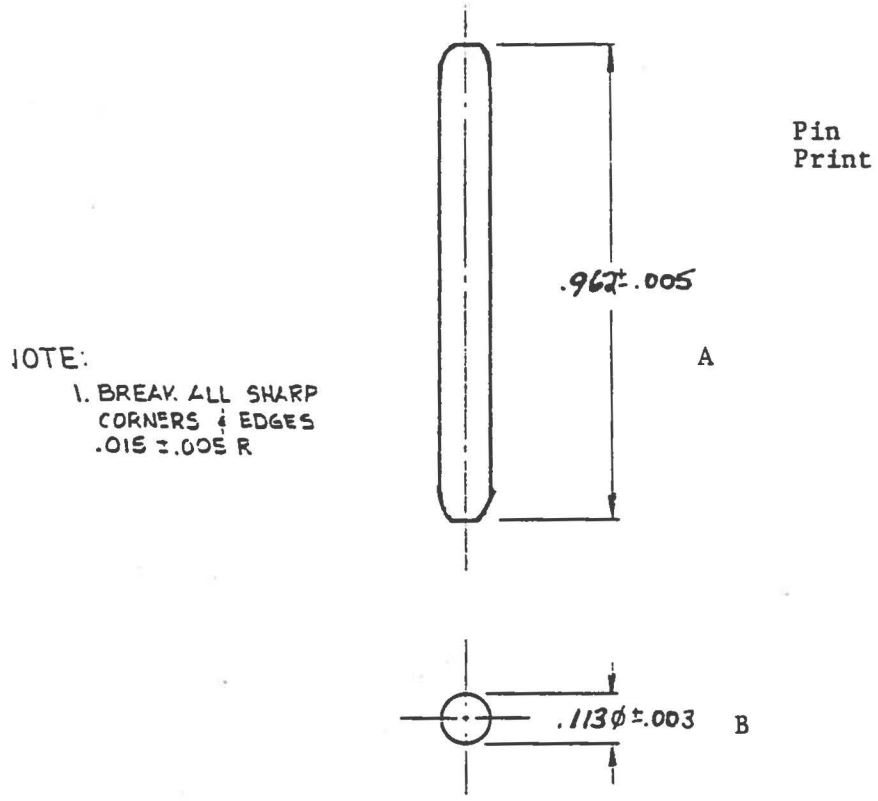
C. Inspect 100% for IA & D.

D. Release the lot if criteria IA-E are met (all defectives found during the 100% inspection must be removed from the lot and the balance released for packaging or sterilization).

III. Storage Requirements

A. Store in sealed sterile pouches at room temperature until packaging.

IV. Print Dimensions



3/1/89

PRODUCT SPECIFICATIONS

Item: Toggle Part No. 5001

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. CRITERIA

A. Description: Black "dumbbell"-like device.

B. Dimensions: Shall conform to dimensions A & B listed on Pin Print (page 2).

C. Mechanical Strength: Samples taken at random shall meet the following test. All must pass test.

1. Pin Shear - not less than 1000 newtons.

Note: This test is conducted by a contract laboratory using an Instron testing machine.

D. Visual Examination:

1. No cracks or voids present.
2. Surfaces must be essentially smooth.
3. No foreign matter or contamination shall be visually apparent.

E. Cytotoxicity (Agar Overlay):

1. Submit one sample in a sterile pouch per lot for cytotoxicity to a contract laboratory. The sample shall pass this test.

II. Sample/Inspection/Release

A. Perform inspection in the Controlled Environment Area. Wear sterile gloves. Inspect the number of samples equal to the square root plus 1 of the lot size for IB.

B. Test 5 samples at random for IC and 1 for IE.

C. Inspect 100% for IA & D.

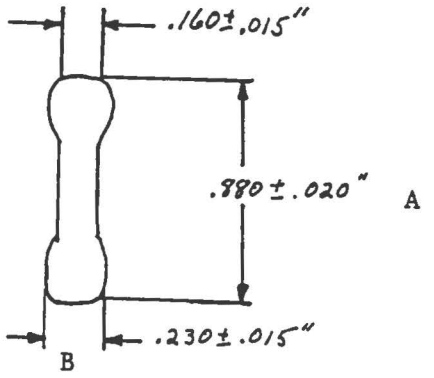
D. Release the lot if criteria IA-E are met (all defectives found during the 100% inspection must be removed from the lot and the balance released for packaging or sterilization.)

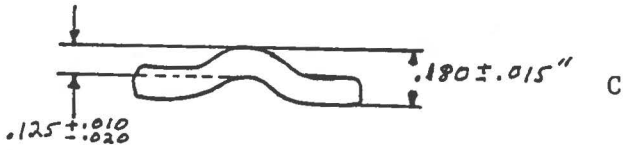
III. Storage Requirements

A. Store in sealed sterile pouches at room temperature until packaging.

IV. Print Dimensions

Toggle Print





STERILIZED FINAL PRODUCT SPECIFICATIONS

Item: Packaged Implant Set Part No. 6000

Date of Issue: _____ Supersedes New

Approvals:

_____ _____

I. CRITERIA

A. Description: A Carbon Fiber Implant, Bollard and Pin and Toggle packaged in a heat sealed foil package overpackaged in a heat sealed film/paper overpackage properly labeled.

B. Coated Fiber Implant: Meets Specifications.

C. Bollard: Meets Specifications.

D. Pin: Meets Specifications.

E. Toggle: Meets Specifications.

F. Pyrogen Test (USP): 10% of lot shall be tested for sterility if spore strips fail test. (Test performed by contract laboratory.)

G. Sterility Test (USP): 10% of lot shall be tested for sterility if spore strips fail test. (Test performed by contract laboratory.)

H. Package Integrity Test: Inner and outer package tested during sealing pass test.

I. Visual Examination:

1. Proper and complete labeling.
2. Satisfactory visual appearance of package and seal (Classification of Defects - Implant Set, PLT-102).
3. No evidence of pin hole leaks.
4. The orange telltale dot has changed to red indicating the package has been subjected to sterilizing radiation.

II. Sample/Inspection/Release:

A. Take 10 samples for IF and 3 per lot for retention.
B. Inspect 100% for IA & I.
C. Release lot for distribution if criteria IA-I have been met.

III. Storage Requirements:

A. Store at room temperature.

STANDARD TEST PROCEDURE

Procedure: Classification of Defects -- Unprinted Pouches

Procedure No. : PLT-100

Revision Record	
Page	**Date**
1	
2	

I. Critical Defects (AQL 0.0% , Mil Std 105, NIIS)

1. Pouch shall be constructed with materials and to dimensions specified on the Purchase Order.

2. Foreign pouch in lot; i.e. same size but bearing another customer's labeling or identification, etc.

II. Serious Defects (AQL 0.65%, Mil Std 105, NIIS)

1. Seals are continuous (free from openings).

2. Seal strength (all seal), shall have a minimum value of 0.75 pounds per linear inch of seal as determined by the test method. Maximum value shall be considered exceeded if, upon peeling, either webs tear or the paper delaminates causing encapsulation of the product.

3. All seals must be uninterrupted and show evidence of sealing all around. An unsealed area that goes completely across a seal that reduces the total seal width by 50% is a defect. Where multiple ribs are used, the total seal width is the combined width of all ribs. For example, if four ribs 1/16" wide, make up the seal width, then a reject would occur if more than two complete ribs were not sealed or the total seal width were less than 1/8". The discontinuity can be no longer in length than 1/4" and more than one discontinuity in a package rejects that package.

4. Finished package is free of holes, openings, tears, delamination, etc., (visual).

Approvals		Date		
Approved By	Q.C.		Approved By Mfg	Effective Date
				Issued By

6000+

STANDARD TEST PROCEDURE

Procedure : Classification of Defects -- Unprinted Pouches

Procedure No. : PLT-100

III. Minor Defects (AQL 2.5%, Mil Std 105, NIIS)

1. Overall pouch shall be within 1/8" of specified dimensions.
2. Seals shall be within 1/8" of specified dimension. If no dimension supplied seal will be 3/8".
3. Pouch shall be cosmetically clean, the outer and inner surfaces to be free from dirt, smudges, foreign marks and materials.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Pouch Integrity Test	**Revision Record** Page	Date
Procedure No.: PLT-101	1	

I. This procedure is used to test the seal integrity of empty pouches sealed in accordance with the proper procedure for heat sealing pouches, PL-137 (Operation of the Impulse Heat Sealer). This procedure is used for testing received lots of pouches and as an inprocess test during packaging.

II. Procedure

Place a vial in the pouch and seal as per PL-137. Totally submerge the sealed pouch in a desiccator containing water. Draw a low vacuum of 5" ± 1". Observe the entire surface for bubbles of escaping air from the seal area or the body of the pouch. The sample fails if a stream of bubbles is observed.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By

STANDARD TEST PROCEDURE

Procedure: Classification of Defects -- Implant Set	**Revision Record** Page / Date
Procedure No.: PLT-102	

I. Critical Defects (AQL 0.0% MIL Std. 105, NIIS)

1. Incorrect labeling.
2. Evidence of contamination
3. Lot number missing.

II. Serious Defects (AQL 0.65%, MIL Std. 105, NIIS)

1. Seal on outer package not continuous.
2. Seal on inner package not continuous.
3. Bollard or toggle appear cracked.

III. Major Defects (AQL 1.0%, MIL Std. 105, NIIS)

1. Carbon fiber implant appears frayed.
2. Shrink sleeve or leader appear unsatisfactory, i.e. split sleeve, no loop on leader, etc.
3. Package label smeared or dirty inner or outer pouch.

IV. Minor Defects (AQL 2.5%, MIL Std. 105, NIIS)

1. Minor smudges, dirt or foreign matter on pouches.
2. Labels crooked.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Date
				Issued By____

INTRODUCTION

The policies, as set forth in this manual, define the Quality Assurance Program as established throughout Plastafil. This document will be revised periodically to reflect changes in policy and/or practices.

Purpose:

This policy and procedure establish the Quality Assurance program to be followed with respect to the manufacture of products to implied and published product standards, Plastafil specifications or government regulation. Responsibility for conformance to the various phases of this Quality Assurance Policy and Procedure are also defined.

Scope:

This policy applies to the manufacture of all Plastafil products or components.

General:

Plastafil, Inc., is a very small company with few employees and with no formal departmental designation. Therefore, the Quality Assurance programs and functions as set forth in this manual are carried out by an individual or individuals assigned by management to perform these functions. Individuals assigned to these and other functions are selected to perform these functions after they have been properly trained and otherwise instructed to perform their assigned tasks.

Where the term manufacturing is used it designates all those activities associated with the fabrication of the product including all steps through the packaging of finished saleable packages, the storage and shipping to customers.

Where the term Quality Assurance is used it designates all those activities designed and necessary to assure that the final product will meet all Plastafil and regulatory agency requirements and that it will perform as intended.

INDEX

STANDARD OPERATING PROCEDURE

Procedure: Plastafil Organizational Structure

Procedure No.: PL-100

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1.0 PURPOSE

To establish and define the manufacturing and Quality Assurance organization and authority.

2.0 SCOPE

The Plastafil manufacturing operating facility.

3.0 APPLICABLE DOCUMENTS

3.1 All Quality Assurance and Manufacturing standard operating procedures.

4.0 GENERAL

4.1 Manufacturing and Quality Assurance operations shall be conducted by individuals qualified by educational background, experience and/or training.

4.2 Quality Assurance shall be performed by individuals assigned to these functions after they have been properly trained and instructed to perform their assigned tasks.

4.3 Individuals assigned to perform Quality Assurance functions shall perform these functions independently and shall be responsible for these functions solely to the President.

4.4 Where a disagreement exists between Manufacturing and Quality Assurance concerning the acceptability of a lot, process, etc. such shall be decided by the President.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Date
				Issued By

STANDARD OPERATING PROCEDURE

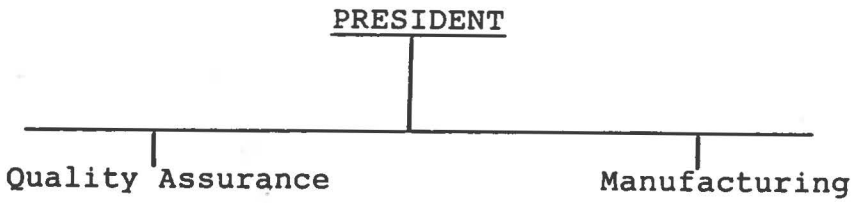
Procedure : Plastafil Organizational Structure

Procedure No. : PL-100

5.0 PROCEDURE

5.1 The Plastafil organizational structure is as follows:

Partial Organizational Structure



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STANDARD OPERATING PROCEDURE

Procedure : General Quality Assurance Program Outline

Procedure No. : PL-101

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1.0 PURPOSE

To describe the general quality assurance program to be followed at Plastafil.

2.0 SCOPE

This program applies to all manufacturing whether in-house or at contract extensions.

3.0 APPLICABLE DOCUMENTS

All standard operating procedures prepared and followed by Quality Assurance.

4.0 GENERAL

4.1 Definition of Quality Assurance: As it applies within Plastafil, Quality Assurance is the sum of all systems and procedures including those which are outlined as follows plus an attitude which has as the objective the assurance that all products and finishd packaged items which are released for distribution are satisfactory for their intended use and conform to labeling statements. Where published standards and/or regulations exist, released items must comply to these also.

4.2 Compliance to Current Good Manufacturing Practices (cGMPs) is required by policy and also by federal law.

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4.3 Each person has a responsibility to:

4.3.1 Know, follow, and remain familiar with Plastafil procedures and cGMP requirements.

4.3.2 Wear proper protective clothing when in an area where such clothing is required and where there may be contact with products such as when sampling, inspecting or working.

4.4 The Quality Assurance system is implemented by written procedures which are maintained current and which are revised as conditions dictate.

4.5 There will be a constant effort exerted by Quality Assurance to encourage quality throughout Plastafil.

4.6 Adequate and appropriate records shall be maintained throughout all stages of in-house manufacturing and at contract extensions so as to provide objective evidence of conformance to procedures.

5.0 PROCEDURE

5.1 Quality Planning

5.1.1 Quality Assurance participates in the planning, specifications development, and new products/processes introduction early in the development cycle and provides quality assurance input and requirements.

5.2 Validation

5.2.1 Quality Assurance validates all non USP, NF, ACS or ASTM test methods, major equipment items and procedures used in the Quality Assurance evaluation of components, intermediate or finished products.

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5.2.2 Quality Assurance participates in and reviews the programs and results of validation of manufacturing procedures and equipment.

5.3 Calibration procedures and equipment.

5.3.1 Quality Assurance is responsible for monitoring the calibration program of those instruments or devices which measure or control a process or procedure and those used for final release of lots.

5.4 Sampling

5.4.1 Representative samples shall be taken from each incoming component, finished product lot and, where appropriate, from intermediates. These are tested or inspected in accordance with specification requirements.

5.4.2 Samples shall be taken in accordance with guidelines using proper equipment and techniques in accordance with approved plans or instructions.

5.4.3 Containers sampled shall be opened and the contents handled properly to prevent contamination of contents. The containers shall be properly sealed after sampling.

5.4.4 The sampling plan indicated in the specification should be adequate to detect possible non-uniformity of the lot to be sampled.

5.5 Testing

5.5.1 All laboratory tests shall be conducted in strict accordance with the item specification and test methods. No deviations shall be permitted from these specifications without the approval of the President or his/her alternate.

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5.5.2 Instruments or devices used for testing which require periodic calibration such as balances, spectrophotometers, thermometers, etc., shall be checked prior to use to insure that they are within te calibration period. If the instruments or devices to be used are past their calibration date, not calibrated or appear to be not performing properly, these shall not be used until properly calibrated and in proper working order.

5.5.3 Samples received shall be logged in as to date taken, date received for testing and date released.

5.5.4 As a general rule, all tests should be performed in at least duplicate with the individual results not significantly different from each other. Where appropriate, a standard or control should be run in parallel as a check on the validity of this test procedure.

5.5.5 Laboratory test records shall indicate the lot represented by the sample, a description of the sample, exact quantity of sample used for each test, the individual readings or results, the calculations, the date the test was performed, and the identification of the person performing the test or inspection. The person performing the test should make a written record of any observations made which would indicate something other than normal was observed either about the sample or the test.

5.5.6 Retention samples should be retained in proper containers and stored under suitable storage conditions for the period indicated. The quantity retained should equal at least two times the quantity needed to perform all tests required in the specification.

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5.5.7 Test results shall be reviewed and checked by a second person prior to lot release. The second person shall initial and date these records.

5.5.8 Testing records, including reagent or equipment standardization records, shall be retained for at least 3 years beyond the expiration date of the lot or 7 years whichever is the longer.

5.6 Labeling Control

5.6.1 Each receipt of every labeling item shall be proofread against an approved text by Quality Assurance and released for use.

5.7 Auditing of Manufacturing

5.7.1 Quality Assurance shall periodically audit the manufacturing areas and procedures both internally and at contractors: (a) to assure compliance with requirements, (b) to assure that agreed-upon procedures, equipment, and practices are being routinely followed, (c) to assure that the planned normal sampling procedures are suitable for monitoring lot acceptability, and (d) to assure that no unusual conditions or circumstances exist which would require a review of quality assurance release procedures.

5.8 Manufacturing Records Review

5.8.1 Quality Assurance shall review all pertinent manufacturing records prior to releasing each lot for distribution to assure that:

5.8.1.1 These records have been completed properly.

5.8.1.2 All required steps have been performed.

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5.8.1.3 No observations have been recorded which would indicate that additional testing or inspections beyond those considered normal are indicated.

5.8.1.4 Yields are within approved guidelines.

5.8.1.5 All required inspections and/or testing, including in-process tests, were performd and the results are satisfactory.

5.8.1.6 Labeling records and a specimen where labels are used are satisfactory.

5.9 Quality Assurance Release

5.9.1 Only material released by Quality Assurance shall be shipped from the plant. The only exceptions are samples sent for laboratory testing or evaluation only or rejected materials returned to suppliers.

5.9.2 Lots or portions of lots shall be released only after a review of all pertinent manufacturing records and Quality Assurance inspection, and test results have been made and this review indicates that the lot is satisfactory for release. The individual making this review should initial and date the records to indicate that the review was made and the lot is satisfactory for release.

5.9.3 Lots or portions of lots found to be either questionable or unsatisfactory shall be promptly so identified and quarantined pending disposition.

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5.10 Product Stability

5.10.1 Quality Assurance performs routine stability studies for the purpose of determining or confirming the expiration dates for all commercially approved products.

5.11 Customer Complaints

5.11.1 Customer complaints concerning all reported adverse reactions, product quality and performance shall be investigated to determine both the probable cause and any other lot or lots likely to be affected by any conditions or deficiency discovered.

5.11.2 Quality Assurance shall act promptly to identify, isolate, retest, and take whatever other actions are indicated and appropriate.

5.12 Quality Assurance Records

5.12.1 Copies of all manufacturing batch records together with quality assurance test and inspection results and other records for each individual lot will be retained by Quality Assurance for at least 3 years after the lot expiration date or for 7 years whichever is the longer.

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Procedure : Item Specifications

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1.0 PURPOSE

To describe the format and the procedure for the development, approval and control of item specifications.

2.0 SCOPE

All materials which require an item specification. Quality Assurance in conjunction with manufacturing is responsible for developing item specifications. Quality Assurance is responsible for document control of item specifications.

3.0 APPLICABLE DOCUMENTS

3.1 Component Specifications

3.2 Product Specifications

3.3 Sterilized Final Product Specifications

3.4 Request for Specification Change

3.5 Part Number Request

4.0 GENERAL

4.1 The following require item specifications:

4.1.1 Raw materials used in the manufacture of final product.

4.1.2 All packaging components and supplies.

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Procedure : Item Specifications

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4.1.3 All finished products.

4.1.4 Sterilized final products.

4.1.5 Quality Assurance may establish specifications for additional materials as required.

4.2 Copying of item specifications by unauthorized personnel is not permitted. All copies must be obtained through Quality Assurance.

4.3 Raw material is defined as any chemical or other substance or materials used in the processing of a final product.

4.4 Packaging supplies are defined as materials which surround, contain or protect the product.

4.5 Product is defined as the finished unit item made for purposes of implanting into patients.

4.6 Packaging items are defined as packaging components which are those items which contain and thus contact or seal the product.

4.7 Sterilized final product is the assembled kit packaged for distribution for use in patients.

5.0 PROCEDURE

5.1 Item Specification Format

5.1.1 The item specification is a two-sided document. The obverse side lists the criteria, container/delivery criteria and general requirements where applicable. The reverse side lists the sampling plan, test strategy and approved suppliers where applicable.

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5.1.2 Each item specification has a heading which lists item name, part number, date of issue, supersedes date and dated approval signatures from Manufacturing and Quality Assurance.

5.2 Item Specification Development

5.2.1 The criteria listed on item specifications are based in part on supplier input and requirements specified by Quality Assurance and Manufacturing.

5.2.2 Initiate item specification development upon receipt of completed Part Number Request Form from Manufacturing.

5.2.3 "Item specification" criteria may be developed from, but not limited to, the following sources:

- Manufacturer
- Manufacturer's certificate or catalog
- Part Number Request Form
- United States Pharmacopeia/National Formulary
- American Chemical Society Test Methodology
- ASTM Test Methodology
- Manufacturing Department Recommendations
- Quality Assurance
- Code of Federal Regulations

5.2.4 "Analytical criteria" may include, but are not limited to, tests for description, purity and identity where applicable.

5.2.5 "Container and Delivery Criteria" may include recommendations for container composition, lot content and container rejection criteria.

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5.2.6 "General Requirements" may include requests of certifications, change notification or any other pertinent requests.

5.2.7 "Sampling Plan" includes sampling frequencies, quantities and method.

5.2.8 "Test Strategy" describes the test requirements for new and approved suppliers.

5.2.9 "Approved Suppliers" includes approved suppliers and suppliers pending approval.

5.2.9.1 A minimum of three consecutive lots must meet all criteria for new suppliers before a supplier is considered an approved supplier.

5.2.9.2 If a lot of purchased component from an approved supplier is rejected, the next three deliveries of the item shall be tested for additional criteria as determined by Quality Assurance. If one of these three lots is rejected, the supplier shall no longer be considered acceptable. If all three deliveries are found to meet specifications, subsequent receipts shall be considered as having been received from an approved supplier.

5.2.10 Prepare a draft of the specification and route it to Manufacturing and Quality Assurance for review and comments.

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5.3 Item Specification Approval

5.3.1 Incorporate any necessary changes into the item specification and route the final copy to Manufacturing and Quality Assurance for approval signatures.

5.3.2 Submit the signed copy of the approved items specification for distribution and filing.

5.4 Item Specification Revision

5.4.1 Complete Request for Specification Change and route to Manufacturing and Quality Assurance for review and approval. Attach a copy of the item specification to be revised.

5.4.2 Once the revision has been approved as indicated by approval signatures, forward the revised draft for typing.

5.4.3 Route the final copy of the revised specification to Manufacturing for approval signatures. Include the approved Request for Specification Change form for reference.

5.4.4 Submit the original, signed copy of the approved item specification along with the signed Request for Specification Change form to Product Security for distribution and filing.

5.5 Control of Item Specifications

5.5.1 File the original signed "Master" copy of the item specification in a locked fire proof file cabinet. File chronologically by Part Number.

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5.5.2 File the original, signed "Master" copy of each revision, along with Request for Item Specification Change, in the appropriate specification file folder in the locked fire proof cabinet.

5.5.3 Make copies for distribution for the following:

President	1 copy
Quality Assurance	1 copy
Manufacturing	1 copy
Receiving	1 copy
Purchasing	1 copy

5.5.4 Prepare a Distribution List. Record the item name, item number, new edition and number of copies issued along with the previous edition and number of copies to be returned.

5.5.5 Issue the item specification to the appropriate department and obtain the signature of the individual receiving the specification. Obtain all issued copies of the previous edition.

5.5.6 Discard all copies of returned obsolete specifications.

5.5.7 File Specification Distribution List in the item specification file cabinet.

5.5.8 Retain Item Specification, change Request Forms and Distribution Lists indefinitely.

5.5.9 Prepare microfilm copies of original and revised specifications on an annual basis and store these off site.

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5.6 Distribution of Specifications to approved suppliers by personnel performing purchasing function.

5.6.1 Forward a copy of the obverse side only of the specifications to suppliers when placing orders for these items. (Where there is a list of approved suppliers on the reverse side of a specification, place the order for an item with one of such approved suppliers.)

5.6.2 Place an order with a new supplier only whem components are not available from an approved supplier in adequate time to meet use requirements (exceptions shall be if an alternate source is being evaluated or for first-time purchase of a new material or grade).

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REQUEST FOR SPECIFICATION CHANGE

ITEM SPECIFICATION: _____

PART NO.: _____ EDITION NO.: _____

REQUESTOR: _____
Date Submitted

REASON FOR CHANGE: _____

REVISION (LIST STEP NO.):

APPROVAL:

_____ _____
Manufacturing Date

_____ _____
Quality Assurance Date

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ITEM SPECIFICATION DISTRIBUTION LIST

Specification(s) Issued To:_____ Date:_____

Item Name	Item No.	Edition Issued	QTY	Edition Returned	QTY

Total No. Issued:_____

Issued By:_____ Date:_____

Received By:_____ Date:_____

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PURCHASED COMPONENT SPECIFICATIONS

Item: _____ Part No. _____

Date of Issue: _____ Supersedes _____

Approvals:

_____ _____

I. Analytical Criteria

A. Description:
B. .
C. .
D. .
E. .
F. .
G. .
H. .
I. .
J. .
K. .

II. Container/Delivery Criteria

A. Shipments shall be in *** containers, with one manufacturer's lot preferred.

B. Containers shall bear appropriate safety, storage, and handling information. Containers showing evidence of leakage or possible contamination shall be rejected.

C. Lots rejected initially shall not be resubmitted without specific written approval from

III. General Requirements

A. The lot(s) supplied should be manufactured in accordance with a quality assurance/quality control system appropriate for the manufacture of this item.

B. Certification or test results for the lot(s) supplied is requested to accompany the lot delivery.

C. No significant changes shall be made in the method of manufacture or control without prior notification to :

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PRODUCT SPECIFICATIONS

Item: _____ Part No. _____

Date of Issue: _____ Supersedes _____

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I. CRITERIA

STERILIZED FINAL PRODUCT SPECIFICATIONS

Item: _____ Part No. _____

Date of Issue: _____ Supersedes _____

Approvals: _____

_____ _____

_____

CRITERIA

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STANDARD OPERATING PROCEDURE

Procedure: QUARANTINE PROCEDURES FOR INCOMING MATERIALS

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1.0 PURPOSE

To provide a procedure for placing incoming materials into quarantine and releasing them from quarantine.

2.0 SCOPE

This procedure applies to all purchased raw material components, packaging supplies and ancillary/adjunct items used in the manufacture, filling or packaging of product.

3.0 APPLICABLE DOCUMENTS

3.1 Incoming components Quarantine Log.

3.2 Raw Material Specifications.
Packaging Component Specifications.
Packaging Supply Specifications.
PL-119 Red Tag Procedures.
PL-122 Quality Review board.

3.3 Inventory Card, Form 6/87-12

3.4 PL-129 Sampling of Incoming Components.

3.5 PL-130 Retention Sampling Procedures.

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Procedure : QUARANTINE PROCEDURES FOR INCOMING COMPONENTS

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4.0 GENERAL

4.1 Materials and Equipment

4.1.1 Yellow Pressure-Sensitive quarantine Labels.

4.1.2 Green Pressure-Sensitive Release Labels.

4.1.3 Red Pressure-Sensitive quarantine Labels.

4.1.4 White Test-Retention Sample Label.

4.2 The Quarantine Area is a limited access facility, and is limited to authorized Quality Assurance Personnel.

4.3 All items placed in quarantine for testing will be stored under the proper storage conditions.

4.4 Only items used for the manufacture, filling or packaging of materials intended for manufacturing use are subjected to these quarantine procedures. The purchase orders for such materials will indicate that these are to be delivered to Quarantine.

4.5 All manufacturing materials are ordered through and by the Manufacturing Department, and are issued a Part Number by

5.0 PROCEDURE

5.1 Items purchased for manufacturing inventory will require testing and release by Quality Assurance.

5.1.1 Received materials which are subject to these procedures for Quarantine will be maintained in a temporary quarantine holding area in the receiving department until delivery to Quarantine.

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5.1.2 These items together with accompanying certifications, test results, or other documents will be delivered to Quality Assurance for disposition.

5.1.3 Inventory cards, one for each item and manufacturer's lot, will be delivered to Quality Assurance with the individual receipt(s).

5.1.3.1 Inventory cards for quarantined components will be filed in the quarantine room until the material is released.

5.1.4 Upon receipt from Receiving, Quality Assurance personnel shall check the item name and grade indicated on the container(s) and part numbers on the inventory card against the item specifications to assure that the correct item has been received.

5.1.4.1 Record the receipt of the material in the Incoming Components Quarantine Log. Record the item specification name, part number, receiving number, quantity, date of receipt in quarantine and initials.

5.1.4.2 If no specifications have been issued at the time of receipt, consult Quality Assurance for guidance.

5.1.5 Sample according to PL-129, Sampling of Incoming Purchased Components. Samples taken will be subtracted from the Inventory Card and the samples delivered to Quality Assurance together with accompanying vendor certifications, etc. for testing.

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5.1.5.1 If no specifications have been issued for the item, sample as directed by Quality Assurance.

5.1.5.2 Test and retention samples will be labeled with a white pressure-sensitive label stating part name, part number, lot number, amount of sample taken, date of sampling and initials of sampler. This information shall also be recorded in a retention sample log and Quality Assurance sample log as stated.

5.1.5.3 Unless specified otherwise, retention samples shall be stored in glass containers with screw cap closures.

5.1.6 Remaining material will be labeled with a yellow pressure-sensitive quarantine label stating the part name, part number, lot number, container number and total number of containers in the lot (ex. 1 of 2, 2 of 2). The sampled container(s) of the quarantined shipment or lot will be marked with the amount of sample removed from the container, date of sampling and initials of sampler.

5.1.6.1 All quarantined materials will be stored in a designated, limited access quarantine area until testing is completed and they are released.

5.1.6.2 Storage conditions shall be as indicated in the specifications. (If no specifications have been issued for the item store at room temperature unless otherwise indicated on the manufacturer's labeling.)

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5.2 All purchased components will meet required specifications as stated in Raw Material Specifications RMS-100 to - , Packaging Component Specifications PCS-100 to - , Packaging Supply Specifications PSS-100 to - .

5.2.1 Test or inspect item in accordance with the item specifications.

5.2.2 Review in-house testing results and manufacturer's test results or certificates for accuracy, thoroughness, and completeness before releasing lots which meet all requirements.

5.3 Quality Assurance personnel shall label each released container with a release label and record the date, initials of the person releasing the materials, and retest date on the label. Assign retest date according to specification instructions. Place the release label directly over th word "quarantine" on the quarantine label. Deliver the released lot to the manufacturing department. Record release date in Incoming Components Quarantine log.

5.3.1 Rejected purchased materials will be returned, or destroyed as per vendors authorization.

5.3.1.1 Rejected in-house manufactured lots will be brought before the Quality Review Board for disposition as appropriate.

5.3.1.2 Stamp containers of rejected materials with a red "Reject" stamp. Stamp each quarantine label with the reject stamp.

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5.3.2 Questionable lots will be Red Tagged and may be brought before the quality Review Board for disposition, as appropriate.

5.3.2.1 Such items will, in general, consist of improperly shipped material, i.e., items requiring refrigeration received at room temperature; or other conditions which may result in lot acceptance upon further review or additional testing.

5.3.2.2 Red tagged materials will be labeled with a Red Quarantine label, stating date quarantined, and initials of person who tagged the materials.

5.4 Released containers are transferred to manufacturing with an inventory card.

5.5 All records pertaining to released or rejected lots will be filed in chronological order by part number.

5.5.1 Release records are maintained in the office area in a file cabinet in accordance with record retention procedures.

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QUARANTINE
Part Name

PN LOT
_____ of ____

RELEASED PN_____
DATE_____ LOT_____

RETEST DATE

_____ _____
INITIALS

QC SAMPLE
Part Name

PN_____ LOT_____

_____ _____
Sample Date Quantity

RETENTION SAMPLE
Part Name

PN_____ LOT_____

_____ _____
Sample Date Quantity

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Procedure: RECEIVING PROCEDURES

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1.0 PURPOSE

This procedure describes the responsibilities of personnel involved with the receiving activities.

2.0 SCOPE

This procedure applies to all employees involved with the receiving of items.

3.0 APPLICABLE DOCUMENTS

3.1 Freight Bills
3.2 Receiving Log
3.3 Purchase Order Form
3.4 Packing List
3.5 Item Certifications
3.6 Returned Goods, PL-110
3.7 Inventory Card

4.0 GENERAL

4.1 Follow all safety rules as they apply to each item received and handled.

4.2 Examples of items received:

4.2.1 Raw Materials
4.2.2 Packaging Materials
4.2.3 Printed Materials
4.2.4 Returned Goods
4.2.5 Office Supplies
4.2.6 Lab Supplies

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4.3 All purchased materials must be processed through Receiving and released by Quality Assurance to assure proper and timely payment to the vendor.

4.4 Refer to Returned Goods, PL-110, for the handling of returned goods.

4.5 Maintain all items in a quarantined area until transferred to the appropriate department.

5.0 PROCEDURE

5.1 At the time a delivery arrives and before accepting the materials, check the shipment against the freight bill.

5.2 Accept the materials unless there is an obvious error in delivery or containers are leaking or there is evidence of possible contamination of contents.

5.3 Check the shipment for visible damage. If any is present, have the driver sign the freight bill and indicate the extent and nature of the damage. Notify a Supervisor for further investigation.

5.4 Contersign the freight bill.

5.5 Give a copy of the freight bill to the driver; this completes the check-in.

5.6 Packing List. Complete the Packing List as follows:

5.6.1 Remove the Packing List from the package and compare it with the actual items received.

5.6.2 Circle items received and verified complete on the Packing List (shipped) column.

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5.6.3 If the (shipped) column does not match the (ordered) column, place a slash next to the number shipped to indicate a partial shipment.

5.6.4 Stamp the Packing List with the date received and initial.

5.6.5 Send the Packing List to Accounting.

5.7 Purchase Order

5.7.1 Obtain the open Purchase Order (P.O.) from the P.O. Files.

5.7.2 Circle items ordered on the P.O if the item is complete and date.

5.7.3 If there is only a partial shipment, place a slash next to the number ordered on the P.O., write in the actual amount received and enter the date.

5.7.4 Send a copy of the P.O. to the Purchasing Department.

5.7.4.1 Send a copy of the P.O. to Quality Assurance for those items described in 4.2.1-4.2.4, which require testing for inspection.

5.7.5 Enter all pertinent information in Receiving Log and note that the P.O. is complete by stamping it with the "Complete" stamp.

5.7.6 Assign an inventory card to each item on any Purchase Order having a Part Number.

5.7.6.1 Assign one inventory card per each receiving number.

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5.7.7 When finished with the Purchase Order, return it to the proper P.O. file located in the Shipping/Receiving Department.

Discrepancy Receipt

Discrepancy receipt is defined as items received not as indicated on the P.O. (e.g., overage, damaged, etc.). These are handled in the following manner:

5.8 Notify the supervisor of significant damages. Provide all information required for filing necessary overcharge, loss or damage claims.

5.9 Continue with rceiving procedures as per steps 5.6 and 5.7.

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INVENTORY CARD

Card Number _____

Part Number _____ Receiving Number _____

Item Name _____

Vendor _____ Vendor Lot _____

P.O. Number _____ Quantity _____ in _____ Containers

Use Before _____ Storage Conditions _____ Inv. Loc. _____

Date	Purpose of Use (Lot Number)	Container Number	Quantity Removed	Balance	Completed By	Checked By

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure : GENERAL CALBRATION PROGRAM REQUIREMENTS

Procedure No.: PL-105

Revision Record	
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1.0 PURPOSE

To describe the program for the calibration of equipment used in the manufacture and Quality Control release testing of bulk and finished drug products.

2.0 SCOPE

This procedure provides basic guidelines. Detailed procedures are described in specific standard operating procedures which apply to particular instruments and equipment. Copies of these, together with specific information concerning equipment identification numbers and location, are maintained by Quality Assurance.

3.0 APPLICABLE DOCUMENTS

3.1 Calibration Programs, Procedure No. P1-106

3.2 Calibration of Equipment by Contractors, Procedure No. PL-107.

3.3 Equipment Installation, Form No. 1001

3.4 Calibration Schedule Card, form No. 1002

4.0 GENERAL

4.1 Equipment refers to measuring, monitoring or controlling devices used in a manufcturing process or system or for Quality Control release testing.

4.2 Attached is a listing of equipment and their recalibration intervals.

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Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No.: PL-105

4.3 Equipment is calibrated upon receipt and at the intervals described in the attachment.

4.4 Before expiration of its calibration period, it is necessary to either replace equipment with a recently calibrated unit or recalibrate existing equipment.

4.5 No item shall be used for critical manufacturing steps or for Quality Assur. release testing if it is past its recalibration date.

4.6 Certain instruments such as pH Meters, for example, which are either calibrated before use or as part of a test procedure are not included in the calibration program.

5.0 PROCEDURE

5.1 All equipment used in Quality Assur. release testing and for critical measuring, monitoring or controlling of a manufacturing process are assigned and labeled with a unique identification number.

5.2 The following information will be maintained on file by Quality Assurance unit for each piece of equipment:

a. equipment identification number
b. description of equipment
c. model number and serial number
d. date of purchase and manufacturer
e. date of installation
f. location

NOTE: This information is recorded on the Equipment Installation Report, and maintained in the Equipment File in Quality Assurance.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No. : PL-105

5.3 Inhouse Calibration

5.3.1 Calibrate equipment according to the method and procedure described in the specific Standard Operating Procedure (SOP). Record information on the form specified in the S.O.P. Information should include:

a. Description of Equipment
b. Identification Numbers
c. Current S.O.P. Issue
d. Identification of calibration equipment used and N.B.S. traceability
e. Readings of the standard
f. Readings of the instrument
g. Adjustments made, if any
h. Any limitations determined during calibration
i. Person calibrating and date of calibration

5.4 Contractor Calibration

5.4.1 Follow procedures listed im Calibration of Equipment by Contractor, Procedure No. PL-107.

5.5 After calibration, affix a calibration sticker in a readily noticeable area of the equipment. Record the date of calibration, initials or other identification of the person performing the calibration and the date that recalibration is due.

5.6 Record the date of calibration, the expiration date and the date of the next scheduled calbration on the Calibration Schedule Card. The scheduled date should provide adequate time to recalibrate before the recalibration due date.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No. : PL-105

5.6.1 Initial the entry and file card by date for the next scheduled calibration in the schedule card file.

5.6.2 Check the schedule card file weekly to determine which instruments are due for recalibration.

5.7 All documentation is filed in the appropriate Equipment File maintained by Quality Assurance.

5.8 If during recalibration, an instrument isfound to be out of calibration, a Report is sent to Manufacturing and Quality Assurance.

The variation from accepted tolerances should be recorded along with an estimate of time the instrument was out of calibration, if possible.

The Report is reviewed by Quality Assurance to determine what products may have been impacted by this occurence. When appropriate, Quality Assurance will present this information to the Quality Review Board for a recommendation concerning what actions, if any, should be taken.

5.9 In the event equipment cannot be recalibrated satisfactorily, affix an "out of service" sticker to the equipment in a readily noticeable area. Such equipment shall be removed from service in Manufacturing and Quality Control operations until appropriate repairs are made and the equipment is successfully recalibrated.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No. : PL-105

EQUIPMENT CALIBRATION INTERVAL

ITEM	RECALIBRATION INTERVAL

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No. : PL-105

CALIBRATION SCHEDULE CARD

Equipment Name _____ Item # _____

Model No. _____ Serial No. _____

Frequency of Calibration _____ SOP Reference _____

Calibration Date	Tech	Expiration Date	Recalibration Schedule Date	Tech

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : GENERAL CALIBRATION PROGRAM REQUIREMENTS

Procedure No.: PL-105

EQUIPMENT INSTALLATION REPORT

ITEM FOR ____ QC ____ MFG
ITEM IDENT. NO. _____

Equipment Description			Warranty Expiration Date
Manufacturer	Model #	Serial #	
Company Installing	Address	Phone #	Contact
Factory Service	Address	Phone #	Contact
Local Service	Address	Phone #	Contact
Comments:			
	Signature		Date

Vendor	Shipper	
P.O. Number	Date Received	
Comments:		

Department	Location Installed	Room #
Sales Rep.		Phone #
Comments:		
	Signature	Date

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Calibration Programs

Procedure No.: PL-106

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1.0 PURPOSE

To describe the program, repoarts and control programs for calibration of manufacturing and quality assurance equipment.

2.0 SCOPE

All equipment and instruments which either measure or control products or processes and those used for the final release of products.

3.0 APPLICABLE DOCUMENTS

3.1 General Calibration Requirements, PL-105
3.2 Calibration of Equipment by Contractors, PL-107
3.3 Preventative Maintenance Program, PL-148
3.4 Calibration Sticker
3.5 Recalibration Notice
3.6 Calibration Schedule Card, Form 1002
3.7 Equipment Installation, Form 1001
3.8 Calibration Report

4.0 GENERAL

4.1 A specific calibration method is prepared for each item to be calibrated. These procedures are usually as recommended by the manufacturer of the item.

4.2 Calibration is usually performed by outside contractors under the supervision or monitoring by Quality Assurance.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By____

STANDARD OPERATING PROCEDURE

Procedure : Calibration Programs

Procedure No. : PL-106

4.3 Equipment is calibrated upon initial receipt or installation and at intervals described in standard operating procedure, PL-105, and/or other applicable standard operating procedures, this includes loaned equipment.

4.4 All equipment to be calibrated must be assigned and labeled with a unique identification number for identification purposes.

4.5 For systems which are comprised of more than one unit or module requiring calibration, the system is considered within calibration only if all units are within calibration.

4.6 Each equipment item must be operating within operational parameters before it can be calibrated (see PL-148).

4.7 Quality Assurance shall be responsible for performing all procedures indicated unless otherwise stated.

5.0 PROCEDURE

5.1 New Equipment Installation

5.1.1 Upon receipt of a copy of the Equipment Installation Report on a new piece of equipment determine whether it requires calibration. Review the operation/owner's manual, consult with the department supervisor(s) in which the equipment will be used and determine whether it meets the description for equipment in Scope.

5.1.2 If calibration is required, consult with the equipment manufacturer to determine the appropriate calibration procedure, recalibration intervals, and responsibility for calibrating the equipment and specifications or tolerances to calibrate to.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : Calibration Programs

Procedure No.: PL-106

5.1.3 Prepare a standard operating procedure for calibrating the equipment.

5.1.3.1 The standard operating procedure shall include:

- A description of the standards to be used. The standards shall be traceable to the NBS or other recognizable source.
- Frequency or recalibration.
- Acceptable tolerances or acceptance criteria based on product quality requirements.
- Retest requirements or action to be taken for out-of-tolerance results.
- The approximate form to be used to document the calibration.

5.1.4 Prepare a calibration schedule card for the equipment. Record the name, assigned number and system numbers, model and serial number, frequency of calibration and the Index number of the calibration standard operating procedure.

5.1.5 If the equipment is not already listed on the calibration frequency list update the list with the new type of equipment and the calibration frequency interval.

5.1.6 Prepare a Calibration Report for each instrument. This will be provided to the person/company performing the calibration or recalibration.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Calibration Program

Procedure No.: PL-106

5.2 Calibrations by Outside Contractors

Note: Calibrations are done by an approved qualified contractor or equipment manufacturer's representative. A list of these is maintained by Quality Assurance.

5.2.1 The contractor shall contact the individual responsible for the equipment prior to calibrating equipment if the calibration is to be done on the premises.

5.2.2 The contractor must provide a written copy of the Calibration Report properly completed.

5.2.3 Obtain the contractor's calibration report.

5.2.4 Review the calibration report to ensure that the calibration procedure has been properly performed and that calibration requirements have been met. Verify by signature and date.

5.2.5 If the calibration has been successfully completed and the calibration acceptance criteria have been met, remove the previous calibration sticker and affix a new sticker. Record equipment number, initials and date of calibration and the next calibration due date.

5.2.5.1 If necessary, describe any limitations for use on a label and affix the label to a readily noticeable part of the equipment.

5.2.6 Forward the appropriate calibration report to Quality Assurance.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Calibration Program

Procedure No.: PL-106

5.2.7 Record the date of calibration, the calibration expiration date and the recalibration schedule date on the Calibration Schedule Card. The next scheduled date should provide adequate time to recalibrate the equipment before the expiration or due date.

5.2.8 Initial the entry and file the card by date for the next scheduled calibration in the schedule card file.

5.2.9 Check the schedule card file weekly to determine which instruments are due for recalibration.

5.2.10 Notify the appropriate department when recalibration is due by issuing a Recalibration Notice.

5.3 If during recalibration, an instrument is found to be out of calibration, complete a report and send it to Manufacturing.

5.3.1 The variation from accepted tolerances should be recorded along with an estimate of time the instrument was out of calibration, if possible.

5.3.2 Determine what products may have been impacted by this occurrence. When appropriate, Quality Assurance will present this information to the Quality Review Board for a recommendation concerning what actions, if any, should be taken.

5.3.3 In the event equipment cannot be recalibrated satisfactorily, affix an "out of service" sticker to the equipment in a readily noticeable area. Record that the equipment is "Out of Service" in the calibration log or equipment use log if one exists for that unit. Such equipment shall be removed from service in Manufacturing and Quality Assurance until appropriate repairs are made and the equipment is successfully recalibrated.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Calibration Program

Procedure No. : PL-106

Recalibration Notice

To:_____

This is notification that the _____
(Equipment)
MIS No. _____ is within _____ days of
(Number of days)
its recalibration due date of_____.
(Date)

Please note that if this equipment is not recalibrated before this date it will be labeled "Out of Sevice".

_____ _____
Quality Assurance Date

CALIBRATION

EQUIP. #_____

By_____Date_____

Due_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Calibration Program

Procedure No. : PL-106

CALIBRATION REPORT

				App. By Date	
		Freq.	Next Due Date	Work By Date	
ID No.	Description		Manufacturer	Model No.	Serial No.
Location	Range	Calibration Procedure SOP # ( )See Comments		Equipment User	

Environment Conditions: ( )Ambient
( )Other_____

CALIBRATION STANDARD USED:

ID No.	MFG	MODEL	SERIAL NO.	CERT. BY	TEST DATE	DUE DATE

INSTRUMENT AS-FOUND READINGS:

STD SHOWED	IN. SHOWED	ERROR	NOTES

( ) WITHIN INSTRUMENT ACCURACY
( ) NOT WITHIN INSTRUMENT ACCURACY, BUT WITHIN MAXIMUM PROCESS TOLERANCE
( ) NOT WITHIN MAXIMUM PROCESS TOLERANCE

INSTRUMENT CORRECTED READINGS:

STD SHOWED	IN. SHOWED	ERROR	NOTES

( ) IN. CORRECTED TO WITHIN INSTRUMENT ACCURACY
( ) IN. CORRECTED TO WITHIN MAXIMUM PROCESS TOLERANCE
( ) IN. REQUIRES CORRECTIVE ACTION (Repair, rejection, etc.)_____
( ) CALIBRATION LABEL PLACED ON INSTRUMENT:_____
( ) LABEL "DO NOT USE - CALIBRATION REQUIRED" PLACED ON INSTRUMENT
( ) "INSTRUMENT OUT OF TOLERANCE NOTIFICATION" SENT OUT
( ) SPARE PARTS TO BE ACQUIRED:_____

COMMENTS:_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: CALIBRATION OF EQUIPMENT BY CONTRACTORS

Procedure No.: PL-107

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1.0 PURPOSE

To describe the procedure for the calibration of equipment by outside contractors.

2.0 SCOPE

This procedure applies to all equipment used for quality assurance release testing or for manufacturing processes which cannot be calibrated inhouse because of lack of proper equipment, personnel or expertise. It is the responsibility of Quality Assurance personnel to monitor the calibration of such equipment and to maintain calibration documentation.

3.0 APPLICABLE DOCUMENTS

3.1 S.O.P. Procedure No. PL-105, General Calibration Program Requirements.

3.2 S.O.P. Procedure No. PL-106, Calibration Programs.

4.0 GENERAL

4.1 All equipment used for Quality Assurance release testing or to monitor or control critical manufacturing processes must be within the calibration period to be used in the testing or manufacture of product.

4.2 Before expiration of its calibration period, it is necessary to either replace equipment with a recently calibrated unit or recalibrate existing equipment.

4.3 See 4.0 General in Procedure No. 106, Calibration Programs for additional general information.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By

STANDARD OPERATING PROCEDURE

Procedure: CALIBRATION OF EQUIPMENT BY CONTRACTORS

Procedure No.: PL-107

5.0 PROCEDURE

5.1 Calibrations are done by an approved qualified outside contractor. A list of these contractors is maintained by Quality Assurance.

5.2 The contractor must provide a written copy of the following documentation:

5.2.1 Adequate description of the equipment being calibrated including model, serial number and equipment number.

5.2.2 Description of the calibration system used including measuring and test equipment and their N.B.S. traceability.

5.2.2.1 Contractor must supply proper documentation of NBS traceability for all equipment used during calibration.

5.2.3 Record any adjustments made to the equipment on Service/History Report, as well as a copy of contractor's documentation.

5.2.4 Provide the date the test was conducted and the signature or initials of the technician performing the calibration.

5.2.5 Indicate all limitations for use discovered during the recalibration.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : CALIBRATION OF EQUIPMENT BY CONTRACTORS

Procedure No.: PL-107

5.3 Equipment sent to the contractor for calibration shall have a calibration sticker affixed as in SOP Procedure NO. PL-106, Calibration Programs, where the contractor can record the recalibration date and the calibrator's initials. Upon receipt of the calibrated equipment, the expiration date is assigned according to the date the calibration was performed per Procedure PL-106.

5.4 The above docmentation is maintained in the appropriate equipment file by Quality Assurance.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: WASHING LABWARE TO BE HEAT STERILIZED

Procedure No.: PL-108

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1.0 PURPOSE

To describe the method for manually cleaning glassware and other small lab equipment and subsequent heat drying.

2.0 SCOPE

This procedure applies to all qualified personnel involved with the cleaning and autoclaving of glassware and small lab equipment.

3.0 GENERAL EQUIPMENT AND MATERIALS REQUIRED

3.1 Cleaning Utensils, e.g., Brushes, etc.

3.2 Approved Detergent, e.g., Liquinox.

3.3 Glassware is defined as all glass items used for the various manufacturing processes.

3.4 Small equipment consists of spatulas, stir bars, and other small nonglass items for manufacturing use.

3.5 All glassware and equipment are manually washed using the sink located in manufacturing area.

3.6 Aluminum Foil.

3.7 Distilled Water.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure : WASHING LABWARE TO BE HEAT STERILIZED

Procedure No.: PL-108

3.8 All glassware and equipment are heat sterilized using the hot air oven located in the manufacturing area.

3.9 As a safety measure, gloves shall be worn when cleaning all small equipment and lab glassware and when handling hot items.

4.0 PROCEDURE

4.1 Fill the sink with hot tap water and add the appropriate quantity of an approved detergent (e.g., Liquinox). Refer to the manufacturer's directions for detergent used.

4.2 Wash all glassware and small equipment by immersing into the cleaning solution and scrubbing with a suitable brush.

4.3 Rinse thoroughly with warm tap water three times or more until all evidence of detergent is no longer present.

4.4 Rinse three times with distilled water and drain.

4.5 Immediately close or cover all apertures with a layer of aluminum foil. This cover must be adequate to maintain the status of the item after completion of the hot air drying process.

4.6 Wrap all small equipment individually with aluminum foil. Assure that the item is wrapped so as to maintain the status after completion of the drying process.

4.6.1 Place the date of sterilization on the aluminum foil that covers the equipment using a suitable marking device.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : WASHING LABWARE TO BE HEAT STERILIZED

Procedure No.: PL-108

4.7 Load the wrapped glassware, spatulas, stir bars and other small equipment into the oven. Place each wrapped item such that there is ample room between items to assure circulation of air between and around each item.

4.7.1 Either place a heat indicator on each piece. of equipment or place the equipment/glassware in a tray and place the indicator on the tray.

Dry using the approved cycle.

4.9 Make all appropriate entries in the Equipment Cleaning and Use Log for the oven. Be sure to enter process parameters.

4.10 When the process is complete, review the chart and verify that the process parameters have been satisfied. Sign and date the chart for approval.

4.10.1 If the required parameters have not been satisfied, notify the supervisor for corrective action.

4.11 Remove the chart and submit it to the supervisor or manager for approval.

4.12 Review chart and sign/date if approved. File in the appropriate file.

4.13 Remove sterilized labware and place in the designated location for sterilized labware.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : WASHING LABWARE TO BE HEAT STERILIZED

Procedure No. : PL-108

4.14 Any labware that has been stored for a period of longer than 30 days from the indicated date of sterilization is not to be used and is to be reprocessed per this procedure.

4.14.1 Periodic checks are to be made of all lab glassware and small equipment to remove any items that have exceeded the 30 day storage parameter. This labware will be resterilized. The foil will be removed to prevent the possibility of mix-ups.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Writing Standard Operating Procedures

Procedure No. : PL-109

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1.0 PURPOSE

To provide a simple, concise, and uniform format and procedure for the writing of Standard Operating Procedures (SOPs).

2.0 SCOPE

2.1 The writing and use of all SOPs applies to all departments involved with the manufacture and quality assurance of products.

2.1.1 Manufacture denotes all aspects of receiving, processing, storage, and distribution.

2.1.2 Product is defined as all components, intermediates, batches (in process), and finished goods.

2.1.3 Quality Assurance denotes all aspects of the quality function.

2.2 These SOPs serve as a written reference for future operations, thereby reducing errors and omissions by providing a standard protocol.

2.3 SOPs provide a training medium to assure that all affected understand exactly what is required and how functions are to be performed.

3.0 APPLICABLE DOCUMENTS

3.1 SOP Form No. 600Q+
3.2 Document Control, PL-151

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Writing Standard Operating Procedures

Procedure No. : PL-109

4.0 GENERAL

4.1 SOPs are written by designated personnel from each section.

4.2 SOPs become effective after the indicated effective date.

5.0 PROCEDURE

5.1 Write the procedure in active voice using present tense.

5.2 Select a title for the SOP that is specific and concise.

5.3 Identify the SOP by Procedure Number. Obtain these numbers from person responsible for Document Control.

5.4 Write the body of each SOP according to the following format:

NOTE: Enter N/A for any section that is not applicable.

5.4.1 Purpose (1.0) is the "why" of the SOP. It is the reason for the procedure and how it applies to the operation.

5.4.2 Scope (2.0) details the personnel and areas that the SOP encompasses.

5.4.3 Applicable Documents (3.0) are any forms or other SOPs referenced in a particular procedure.

5.4.3.1 Attach a copy of any form referenced in the SOP.

5.4.4 General (4.0) identifies items that include any additional information pertaining to the SOP not covered under other headings. Include any sketches or diagrams. Examples from this category are as follows:

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STANDARD OPERATING PROCEDURE

Procedure: Writing Standard Operating Procedures

Procedure No.: PL-109

5.4.4 General (4.0) (continued)

- Equipment Required
- Descriptions
- Materials Required
- Tools Required
- Specifications
- Safety Precautions
- Reagents
- Limitations
- Interferences
- Data Interpretation

5.4.5 Procedure (5.0) describes in detail the step-by-step process of completing the task.

- Use the decimal system when outlining the procedure.
- Write the procedure in such a way that it can be easily understood and followed.

5.5 Submit the rough draft for typing and routing to appropriate personnel for comments.

5.6 Review any suggestions and comments; rewrite the SOP, if necessary, and resubmit it for typing of the final draft.

5.7 Review the final copy and sign. Submit for final approval signatures.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Writing Standard Operating Procedures

Procedure No.: PL-109

STANDARD OPERATING PROCEDURE

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1.0 PURPOSE

2.0 SCOPE

3.0 APPLICABLE DOCUMENTS

4.0 GENERAL

5.0 PROCEDURE

5.1

5.1.1

5.1.1

5.2

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Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By____

600Q+

Effective Date

Issued By_____

600Q÷

STANDARD OPERATING PROCEDURE

Procedure: Returned Goods

Procedure No.: PL-110

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1.0 PURPOSE

To describe the procedures for receiving and controlling and determining the disposition of returned goods.

2.0 SCOPE

This procedure applies to all products shipped under Plastafil labeling which is subsequently returned to Plastafil.

3.0 APPLICABLE DOCUMENTS

3.1 Receiving Procedures, PL-104
3.2 Quality Review Board, PL-133
3.3 Notice of Returned Goods Form
3.4 Packing List
3.5 Customer Complaint, PL-153

4.0 GENERAL

4.1 Return authorization number is a sequential numerical code assigned by Customer Service consisting of RG- and four digits.

4.2 Follow all safety procedures when handling returned items.

5.0 PROCEDURE

5.1 Sales or other authorized personnel authorizes return of an item and assigns return authorization number. Document authorization number, reason for return, part number, quantity, and lot number. This provides notification to Manufacturing and Ouality Assurance of pending return.

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Approved By	Q.C.		Approved By Mfg.	Effective Dat
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STANDARD OPERATING PROCEDURE

Procedure: Returned Goods

Procedure No.: PL-110

5.2 Manufacturing personnel shall receive returned goods according to Pl-104. Record the condition of packaging upon receipt. Transfer the item to Quality Assurance along with a copy of Notice of Returned Goods.

5.2.1 A return authorization is required for accepting returned goods.

5.2.2 Notify sales and finance.

5.3 Quality Assurance shall transfer the item to the quarantine area.

5.4 Determine disposition of the item. Returned goods are returned to manufacturing inventory only if all of the following criteria are met:

5.4.1 Product must be received at Plastafil within three days of the date of shipment to the customer.

5.4.2 Product must be received under the same packaging conditions as it was originally shipped. Package must be unopened.

5.4.3 The reason for return is either a duplicate shipment or an incorrect order was placed or shipped.

5.4.4 An inspection of the return by Quality Assurance indicates that the material is satisfactory for return to stock.

5.5 If all of 5.4.1-5.4.4 apply, Quality Assurance releases the product to Manufacturing for return to inventory.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Returned Goods

Procedure No.: PL-110

5.6 If the reason for return is a duplicate shipment or an incorrect order was placed or shipped, however the product was received after the three-day time limitation or was shipped under adverse shipping conditions, Quality Assurance shall prepare a report for Quality Review Board action.

5.7 Quality Assurance shall record final disposition of the item on Notice of Returned Goods form.

5.8 Reasons for return which concern the quality of the product should be brought to the attention of the Quality Review Board. Issues of concern include but are not limited to:

- Customer complaints
- Damaged or illegible labeling
- Physical defects in the immediate product container
- Appearance of product
- Items may have been held at improper storage or shipping temperatures

Retain the returned item in Quarantine in the event that testing of the material is required.

5.9 The Quality Review Board shall review all documentation referenced above and conduct investigation according to PL-133.

5.10 Based on results of investigation, the Board shall determine whether returned item is to be destroyed or maintained in Quarantine in the event that further evaluation would be required or salvaged. Record final disposition of the item on the Notice of Returned Goods form.

5.11 Quality Assurance shall maintain file of all returned goods documentation. Documentation is reviewed quarterly to determine any trends or patterns in returned goods.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Returned Goods

Procedure No.: PL-110

NOTICE OF RETURNED GOODS

AUTHORIZATION NO._____

AUTHORIZED BY:_____

PART NO._____ LOT NUMBER_____

PRODUCT NAME_____

QUANTITY TO BE RETURNED_____DATE RETURNED_____

RETURNED FROM_____

RECEIVING

RECEIVING NUMBER_____DATE RECEIVED_____

QUANTITY RECEIVED_____BY_____

COMMENTS_____

QUALITY ASSURANCE USE ONLY

DATE OF SHIPMENT TO CUSTOMER_____

CONDITION OF PACKAGE ON RECEIPT_____

REASON FOR RETURN_____

RETURNED GOODS DISPOSITION

/ / RELEASED FOR RETURN TO FINISHED GOODS INVENTORY

/ / REJECTED

/ / RETAIN FOR FURTHER TESTING

_____ _____

QUALITY ASSURANCE DATE

cc: Finance
Marketing

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: CERTIFICATION OF MANUFACTURING SYSTEMS, PROCESSES AND EQUIPMENT

Procedure No.: PL-111

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1.0 PURPOSE

To define the program for validation and certification of manufacturing process equipment, processes or systems which are an integral part in the manufacture of implantable medical devices. Validation of manufacturing processes and process controls assures a high probability that successive batches of finished product will consistently meet its quality and design specifications.

2.0 SCOPE

This protocol defines the guidelines in designing and implementing Validation procedures. Detailed procedures are described in specific protocols and standard operating procedures which apply to a particular system or process.

A validation program is developed and implemented for any process which has a significant impact on the quality, safety and effectiveness of a product.

3.0 APPLICABLE DOCUMENTS

3.1 Validation Change Control, PL-112.

3.2 Certification Document.

4.0 GENERAL

4.1 Installation Qualification:

Documented verification that the process equipment is suitable for its intended function, that it has been properly installed and that its design requirements for installation have been met.

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4.2 Operational Qualification:

Documented demonstration that the system or process equipment functions as intended and is capable of consistently operating within its design specification.

4.3 Process Validation:

Documented series of studies in which a process is challenged so that it can be reliably demonstrated that the process is consistently doing what it purports to do within defined limits of acceptability.

4.4 Performance qualification is conducted when a process does not require challenges to demonstrate its effectiveness. Instead, the end product of the process can be evaluated by appropriate test methods to determine its acceptability.

4.5 Certification:

Documented verification by qualified persons that a process validation has been accomplishd with acceptable results.

4.6 Validation Review Board is a group of two or more who are responsible for the following:

- The review of protocols, and the acceptance criteria set forth in them. They evaluate whether the protocols meet the standards set forth in the FDA guidelines for process validation.
- The review of data collected to assure that the previously approved acceptance criteria have been met and that the validation package is complete.
- Evaluating any discrepancies encontered during validated procedures and what action should be taken to rectify a problem.

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- The review of proposed changes in procedures, equipment, and processes to evaluate their possible impact on the validated status of a process and how this change could best be validated.

- Evaluates new products and how they will be impacted by presently validated systems and whether new validations will be required.

- Issues final certification of a process.

4.7 Equipment, systems or processes should not be used for manufacturing unless properly certified.

5.0 PROCEDURE

Depending on the nature of the equipment or process to be evaluated, the validation procedures will follow this outline where applicable..

5.1 An installation qualification for process equipment or systems is prepared and will include:

5.1.1 Identification of the Equipment/System.

5.1.2 Design characteristics.

5.1.3 Utilities Supplying the Equipment.

5.1.4 Identification of controllers, monitoring devices associated with equipment.

5.1.5 The Validation Review Board reviews the installation qualification and verifies by signature that the installation satisfies the manufacturer's recommendations, local and state codes, OSHA standards, and cGMPs.

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5.2 Operational qualification studies shall be designed in such a way that they will demonstrate:

5.2.1 Operational qualification includes calibration of any controllers, gauges, temperature or monitoring devices that are associated with the process under evaluation.

5.2.2 Measuring devices used for qualification studies and validation are calibrated prior to initiating the studies.

5.2.3 Variabilities detected during the test runs are evaluated by the Validation Review Board to determine whether the acceptance limits established prior to conducting the study are reasonable and what factors may be contributing to the variability in the process.

5.2.4 If any changes to the process result from the above evaluation, the studies should be repeated to determine the acceptability of these changes.

5.2.5 The above findings are documented along with any action taken to rectify problems and the results of these actions in a chronological format.

5.3 Validation studies are designed to demonstrate that a process operating under given parameters will produce an end result within approved acceptance criteria. These studies shall include the following elements:

5.3.1 The process should be challenged under conditions that simulate actual production situations. Operation of equipment and process procedures should follow current standard operating procedures.

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5.3.2 The study should include a "worst case" challenge to define the maximum operating limit at which a process can produce acceptable results. "Worst case" is defined as a set of conditions encompassing upper and lower processing limits and circumstances, including those written standard operating procedures which pose the greatest chance of process or product failure when compared to ideal conditions. If this limit is exceeded under subsequent manufacturing operations there is no assurance that the process will produce a product that meets its required quality specifications.

An evaluation of the material or product affected by the process under study may be required to determine what this worse case challenge should be. Information obtained during operational qualification may also be used to determine critical aspects of the system and how it could best be challenged.

5.3.3 At least three consecutive validation test runs should be conducted.

5.3.4 Acceptance criteria for evaluating the success of a test run should be determined prior to conducting the tests.

5.3.5 The test results are reviewed by the Validation Review Board; and if all of the acceptance criteria are satisfied for three consecutive runs, the process is certified.

5.3.6 If one or more of the test runs fails to meet the acceptance criteria, the Validation Review Board investigates the possible reasons for failure, outlines action to rectify the problem and the validation process is repeated.

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5.3.7 If an unsuccessful run occurs due to human error or mechanical failure indirectly related to the equipment or system, the validation run may be repeated without disrupting the sequence of validation. The incident should be reviewed by the Validation Review Board to determine whether it is acceptable to repeat the run.

5.3.8 The above findings are docmented along with the actions taken and the repeat test results in a chronological format.

5.4 For those processes not applicable to validation challenge studies, a performance qualification program is designed to evaluate the end result of a process. Test methods and sampling plans for the end product of the process shall provide adequate information as to the effectiveness and reliability of the process.

5.4.1 Performance qualifications are conducted and reviewed as in Steps 5.3.4 to 5.3.8.

5.5 Certification

5.5.1 When the studies are complete, the Validation Review Board reviews the data. When all reviewers agree that all requirements for validation have been met, a Certification Document, is prepared.

5.5.2 At this time the equipment, process or system is available for use in manufacturing. All standard operating procedures, process parameters, and configurations must remain identical to those during the validation procedure in order to maintain a validated status. Changes can only be initiated according to procedures set forth in PL-112.

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5.5.3 All data and reports accumulated during validation procedures are kept on file in the appropriate folder for each process, system or equipment.

5.6 Revalidation

5.6.1 In the event there is a need for a system or process to be altered, equipment to be changed, or equipment needs a major repair to a part critical to its function, Pl-112 Validation Change Control procedure is followed to implement the change.

5.6.2 An investigation will be conducted if a change in the quality of an intermediate or final product is detected through in-process or release testing. Based on the findings of the investigation, the Validation Review Board will determine whether the original validation status has changed and whether revalidation is necessary.

5.6.3 If no changes are made to the equipment system or process, the Validation Review Board will conduct a review of all pertinent SOPs, monitoring results, product release test results and equipment recalibrations annually. The Validation Review Board will determine, based on the findings of this review, whether revalidation is necessary. If monitoring results, product release test results or recalibrations indicate the equipment or process continues to operate within the previously validated parameters and no SOP or equipment changes are required, a Certificate of Validation is reissued. Otherwise, the Validation Review Board, based on the findings of the review will make recommendations as to the requirements for revalidating a system.

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CERTIFICATION DOCUMENT

This is to certify that the _____

operates within the limits specified in Validation

Protocol _____ Edition No. _____

Review of this certification is due _____

_____.

_____ _____
Date

_____ _____
Date

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Validation Change Control

Procedure No.: PL-112

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1.0 PURPOSE

To describe the procedures for initiating a change to validated manufacturing equipment, systems, or processes. This procedure ensures that changes cannot be made and implemented without prior approval by the Validation Review Board.

2.0 SCOPE

This procedure applies to all proposed changes to equipment, systems, or processes prior to use in manufacturing operations.

This procedure is to be followed by Manufacturing and Quality Assurance personnel.

3.0 APPLICABLE DOCUMENTS

3.1 Request for Change
3.2 Certification Document
3.3 Certification of Equipment/Systems/Process, PL-111

4.0 GENERAL

4.1 Changes to equipment, systems, or processes refers to any procedural changes in standard operating procedures, changes in process operating parameters, or replacements of equipment parts with parts other than those having similar specifications.

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4.2 After a change has been made the process or equipment must not be used to produce product until the system has been revalidated.

4.3 The Validation Review Board shall be made up of the same members as the Quality Review Board. This Board shall review and approve all proposed validation protocols and shall certify and approve all validations.

5.0 PROCEDURE

5.1 In the event a change must be made to a validated system, process, or item of equipment, the requesting department submits a Request for Change to the Validation Review Board. The request should include a specific description of the change, the reason for the change, and which systems, products, and SOPs are affected by this change.

5.2 The Validation Review Board reviews this information and determines whether to authorize the change and outlines what validation procedures will be required to update the validation documentation. If the change or the validation protocol are not approved, the Validation Review Board will provide recommendations on what changes can or should be made and the appropriate validation procedures required.

5.3 Upon approval of the change, the Validation Review Board notifies the requesting department. The requesting department initiates the change.

5.4 Validation studies are conducted and the results are reviewed by the Validation Review Board,

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5.5 Upon successful validation, the system is certified. The certification authorizes use of the system or process for use in manufacturing operations.

5.6 All documentation is added to the appropriate validation folder as a supplement.

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REQUEST FOR CHANGE

Requesting Department:_____ Requestor:_____

Priority: /7 Emergency /7 Non-Emergency

Equipment:_____ Equipment No._____

SOP Title:_____ No._____

Description of Change:_____

Equipment/Systems/Process Affected by Change:_____

Validation SOP for this Equipment/Process:
Title:_____ No._____

SOPs Affected by Change:_____

Change Approved: /7 Not Approved: /7

By:_____ _____
Manufacturing Date

_____ _____
Quality Assurance Date

_____ _____
President Date

Effective Date
Issued By_____

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STANDARD OPERATING PROCEDURE

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1.0 PURPOSE

To describe the procedures and test methods used to evaluate the performance of the controlled environment air system. This evaluation comprises the operational qualification of the controlled environment areas.

2.0 PRINCIPLE

Controlled environment refers to rooms in which the air supply is filtered through High Efficiency Particulate Air (HEPA) filters and distributed in order to control airborn particle concentrations. Materials used in the construction of the area and procedures followed while working in the area are designed to aid in the maintenance of the appropriate cleanliness level required for Manufacturing operations.

The controlled environment areas are evaluated for three parameters in this study. Air flow velocity and uniformity is evaluated to determine the average airflow velocity and the uniformity of the velocity throughout the controlled environment area. An installation leak test is conducted to verify the absence of bypass leakage in the filter installation and to detect defects or leaks in the filter medium. A room pressurization test is conducted to determine the ability of the controlled environment system to maintain the specified pressure differentials from one room to its adjoining rooms.

3.0 SCOPE

This procedure is applicable to the controlled environment areas in Manufacturing. The following tests may be conducted by an approved outside contractor according to these procedures.

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Procedure: CERTIFICATION OF THE CONTROLLED ENVIRONMENT AREA

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4.0 APPLICABLE DOCUMENTS

4.1 PL-111: Certification of Equipment, System and Processes

4.2 PL-115: Environmental Monitoring of the Controlled Environment Area

4.3 Federal Standard 209-D, Clean Room and Work Station Requirements for Controlled Environment

4.4 Testing Clean Rooms, Recommended Practice, Institute of Environmental Sciences, 1984

5.0 SAFETY PRECAUTIONS

Dioctyl phthalate is potentially carcinogenic to man. Wear an OSHA/MSHA approved respirator, protective clothing, gloves and safety goggle while working with this chemical.

6.0 MATERIALS AND EQUIPMENT

6.1 Hot wire or vane-type anemometer, accurate to within ± 3% of the scale reading over the range of velocity to be measured. Instrument should be within current calibration.

6.2 Aerosol generator.

6.3 Aerosol photometer with a logarithmic or linear readout. The sampling flow rate should be 1.0 (± 0.1) ft^3/minute. Instrument should be within current calibration.

7.0 PROCEDURE

7.1 Air Flow Velocity and Uniformity Test

7.1.1 Use a support stand to position the anemometer under the filter to be measured. The anemometer should be no closer than one inch or no more than 12 inches from the filter face.

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7.1.2 Take the measurement for not less than five seconds. Use the average of the measurements during the period as the reported value.

7.1.3 Measure each filter as in 7.1.1 - 7.2.3.

7.1.4 Record the measurement for each filter on a schematic diagram of the room.

7.2 HEPA Filter Installation Leak Test

7.2.1 Use an aerosol generation to blow air through liquid diotyl phthalate. Introduce the aerosol into the plenum upstream of the HEPA filters.

7.2.2 Adjust the generator to provide the concentration required for the photometer to be used. For linear readout, photometers adjust the generator to read 10-20 ugrams of air. Sample the upstream concentration with the photometer and adjust the photometer, to read 100%. For a logarthmic readout, photometer adjust the aerosol generator to a concentration 1.0×10^4 above the minimum sensitivity of the photometer.

7.2.3 Hold the photometer sampling probe approximately one inch from the filter face. Scan the entire face of the filter using overlapping passes. Scan along the bond between the filter pack and the frame, between the filter frame gasket and the filter bank supporting frames and between the supporting frames and the walls or ceiling.

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7.3 Room Pressurization Test

7.3.1 Close the doors to all rooms undergoing the evaluation.

7.3.2 Measure the pressure differential between the innermost room and the next adjoining room. Continue from this room to the next adjoining room and so on until the last room has been measured against the exterior ambient. Record the pressure differentials on a schematic diagram of the area and indicate direction of air flow.

8.0 DATA ANALYSIS

8.1 Air Flow Velocity and Uniformity Test

8.1.1 Calculate the arithmetic mean of all readings in the room and report as average airflow velocity in feet/minute.

8.1.2 Calculate the limits for airflow uniformity equal to the average airflow velocity ± 20%.

8.1.3 Acceptance Criteria

Velocity not less than 90 feet/minute and uniformity ± 20% of the average velocity.

8.2 HEPA Filter Installation Leak Test

8.2.1 For a linear readout photometer, a reading greater than 0.01% of the upstream challenge concentration indicates a leak. For a logarthmic readout, a reading greater than one scale division indicates a leak.

8.2.2 Record the location of any leaks detected.

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8.2.3 HEPA filters may be repaired by caulking, however, not more than 5% of the filter area may be caulked, and the dimensions of each repair may not exceed 1.5 inches.

8.3 Room Pressurization Test

8.3.1 Determine that there is a positive airflow from the Controlled Environment Area to the adjacent areas.

9.0 RECORDING AND REPORTING OF DATA

9.1 Compile all data obtained in a permanent folder along with a summary of the results. Describe any problems that were encountered during conducting these studies and what actions were taken to correct them. Obtain a Validation Task report Number and submit the report to the Validation Review Board for review and approval.

9.2 On review of the above,if the Validation Review Board finds that the documentation reflects that the controlled environment areas meet the acceptance criteria specified above, verify the approval by signature on the Certification Document.

9.3 On completion of the above, the controlled environment is considering operational and is certified for use in manufacturing operations.

9.4 The controlled environment area is recertified annually ± 30 days.

9.5 An ongoing performance qualification is conducted on a continuous basis. Temperatue, relative humidity, and room pressure differentials are monitored at regular intervals. The data is reviewed daily to note any deviation from the limits specified in PL-115.

9.6 Monitoring is conducted according to PL-115.

Effective Date

Issued By

FED-STD-209D
June 15, 1988
SUPERSEDING
FED-STD-209C
October 27, 1987

FEDERAL STANDARD

CLEAN ROOM AND WORK STATION

REQUIREMENTS, CONTROLLED ENVIRONMENT

This standard is approved by the Commissioner, Federal Supply Service, General Services Administration, for the use of all Federal Agencies.

FSC 3694

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FSC 3694

APPENDIX A

PARTICLE MONITORING - MANUAL COUNTING AND SIZING METHODS

APPENDIX B

OPERATION OF OPTICAL PARTICLE COUNTERS

APPENDIX A

PARTICLE MONITORING - MANUAL COUNTING AND SIZING METHODS

APPENDIX B

OPERATION OF OPTICAL PARTICLE COUNTERS

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APPENDIX C

STATISTICAL ANALYSIS

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SOURCES OF SUPPLEMENTAL INFORMATION

APPENDIX E

GLOSSARY

1. Scope and limitations.

1.1 Scope. This document establishes standard classes of air cleanliness for airborne particulate levels in cleanrooms and clean zones. It prescribes methods for class verification and monitoring of air cleanliness. It also addresses certain other factors, but only as they affect control of airborne particulate contamination.

1.2 Limitations. The requirements of this document do not apply to equipment or supplies for use within cleanrooms or clean zones. Except for size classification and population, this document is not intended to characterize the physical, chemical, radiological, or viable nature of airborne particulate contamination. No definitive relationship between airborne particulate cleanliness classifications and the level of viable airborne particles has been established. In addition to the need for a clean air supply monitored for total particulate contamination and meeting established limits, special requirements are necessary for monitoring and controlling microbial contamination.

2. Referenced document.

For further information on Student's t, see: Johnson, Norman L. and Leone, Fred C., Statistics and Experimental Design in Engineering and the Physical Sciences, Volume I (New York, London, Sydney: John Wiley & Sons, Inc., 1964).

3. Definitions.

3.1 Airborne particulate cleanliness class. The statistically allowable number of particles equal to or larger than 0.5 micrometer in size per cubic foot of air.

3.2 Calibration. Comparison of a measurement standard or instrument of unknown accuracy with another standard or instrument of known accuracy to detect, correlate, report, or eliminate by adjustment any variation in the accuracy of the unknown standard or instrument.

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APPENDIX C

STATISTICAL ANALYSIS

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SOURCES OF SUPPLEMENTAL INFORMATION

APPENDIX E

GLOSSARY

3.3 Clean zone. A defined space in which the concentration of airborne particles is controlled to specified limits.

3.4 Cleanroom. A room in which the concentration of airborne particles is controlled to specified limits.

3.4.1 As-built cleanroom (facility). A cleanroom (facility) that is complete and ready for operation, with all services connected and functional, but without production equipment or personnel within the facility.

3.4.2 At-rest cleanroom (facility). A cleanroom (facility) that is complete and has the production equipment installed and operating, but without personnel within the facility.

3.4.3 Operational cleanroom (facility). A cleanroom (facility) in normal operation with all services functioning and with production equipment and personnel present and performing their normal work functions in the facility.

3.5 Unidirectional airflow. (commonly known as laminar flow) Air flowing in a single pass in a single direction through a cleanroom or clean zone with generally parallel streamlines.

3.6 Nonunidirectional airflow. (commonly known as turbulent flow) Airflow which does not meet the definition of unidirectional airflow by having either multiple pass circulating characteristics or a nonparallel flow direction.

3.7 Condensation nucleus counter. An instrument for counting small airborne particles, approximately 0.01 micrometer and larger, by optically detecting droplets formed by condensation of a vapor upon the small particles.

3.8 Optical particle counter. A light-scattering instrument with display and/or recording means to count and size discrete particles in air.

3.9 Particle. A solid or liquid object generally between 0.001 and 1000 micrometers in size.

3.10 Particle size. The apparent maximum linear dimension of the particle in the plane of observation as observed with an optical microscope, or the equivalent diameter of a particle detected by automatic instrumentation. The equivalent diameter is the diameter of a reference sphere having known properties and producing the same response in the sensing instrument as the particle being measured.

3.11 Particle concentration. The number of individual particles per unit volume of air.

3.12 Student's t distribution. The distribution:

t = [(population mean) - (sample mean)]/[standard error]

obtained from sampling a Gaussian ("normal") distribution. (Available in tables in statistics texts.)

3.13 Upper confidence limit (UCL). An upper limit of the estimate of the mean, calculated in such a way that in a given percentage of cases (here, 95%) the upper limit of the estimate would be more than the true mean, if the means were sampled from a Gaussian ("normal") distribution.

4. Airborne particulate cleanliness classes.

4.1 Determination of class limits. Airborne particulate cleanliness classes listed in Table I shall be determined as follows:

3.10 Particle size. The apparent maximum linear dimension of the particle in the plane of observation as observed with an optical microscope, or the equivalent diameter of a particle detected by automatic instrumentation. The equivalent diameter is the diameter of a reference sphere having known properties and producing the same response in the sensing instrument as the particle being measured.

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3.12 Student's t distribution. The distribution:

t = [(population mean) - (sample mean)]/[standard error]

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4. Airborne particulate cleanliness classes.

4.1 Determination of class limits. Airborne particulate cleanliness classes listed in Table I shall be determined as follows:

3.3 Clean zone. A defined space in which the concentration of airborne particles is controlled to specified limits.

3.4 Cleanroom. A room in which the concentration of airborne particles is controlled to specified limits.

3.4.1 As-built cleanroom (facility). A cleanroom (facility) that is complete and ready for operation, with all services connected and functional, but without production equipment or personnel within the facility.

3.4.2 At-rest cleanroom (facility). A cleanroom (facility) that is complete and has the production equipment installed and operating, but without personnel within the facility.

3.4.3 Operational cleanroom (facility). A cleanroom (facility) in normal operation with all services functioning and with production equipment and personnel present and performing their normal work functions in the facility.

3.5 Unidirectional airflow. (commonly known as laminar flow) Air flowing in a single pass in a single direction through a cleanroom or clean zone with generally parallel streamlines.

3.6 Nonunidirectional airflow. (commonly known as turbulent flow) Airflow which does not meet the definition of unidirectional airflow by having either multiple pass circulating characteristics or a nonparallel flow direction.

3.7 Condensation nucleus counter. An instrument for counting small airborne particles, approximately 0.01 micrometer and larger, by optically detecting droplets formed by condensation of a vapor upon the small particles.

3.8 Optical particle counter. A light-scattering instrument with display and/or recording means to count and size discrete particles in air.

3.9 Particle. A solid or liquid object generally between 0.001 and 1000 micrometers in size.

TABLE I

Class limits in particles per cubic foot of size equal to or greater than particle sizes shown (micrometers)[a]

Class	Measured Particle Size (Micrometers)				
	0.1	0.2	0.3	0.5	5.0
1	35	7.5	3	1	NA.
10	350	75	30	10	NA.
100	NA.	750	300	100	NA.
1,000	NA.	NA.	NA.	1,000	7
10,000	NA.	NA.	NA.	10,000	70
100,000	NA.	NA.	NA.	100,000	700

(NA. - not applicable)

[a]The class limit particle concentrations shown in Table I and Figure 1 are defined for class purposes only and do not necessarily represent the size distribution to be found in any particular situation.

4.2 Particle sizes measured to determine Classes 100 and greater. Airborne particulate cleanliness classes shall be determined by measurement at any one of the particle sizes listed for the class in Table I. The class is considered met if the measured particle concentration is within the limits specified, at any one of the particle sizes shown in Table I, as determined by the statistical analysis of Paragraph 5.4.

4.3 Particle sizes measured to determine Classes less than 100. Airborne particulate cleanliness classes shall be determined by measurement at one or more of the particle sizes in Table I, as specified[1], and determined by the statistical analysis of Paragraph 5.4.

[1]When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

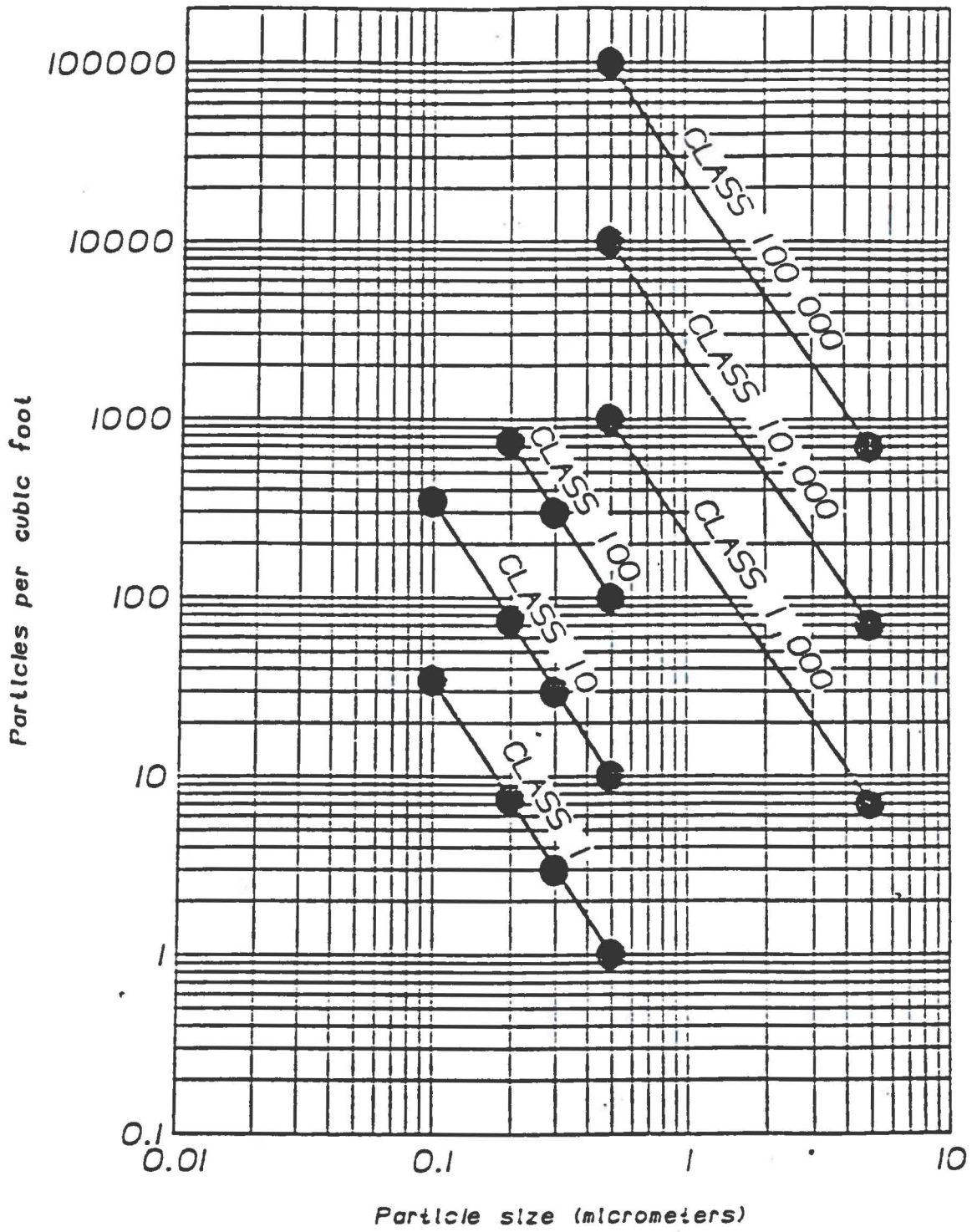

Figure 1. Class limits in particles per cubic foot of size equal to or greater than particle sizes shown*

*The class limit particle concentrations shown on Table I and Figure 1 are defined for class purposes only and do not necessarily represent the size distribution to be found in any particular situation.

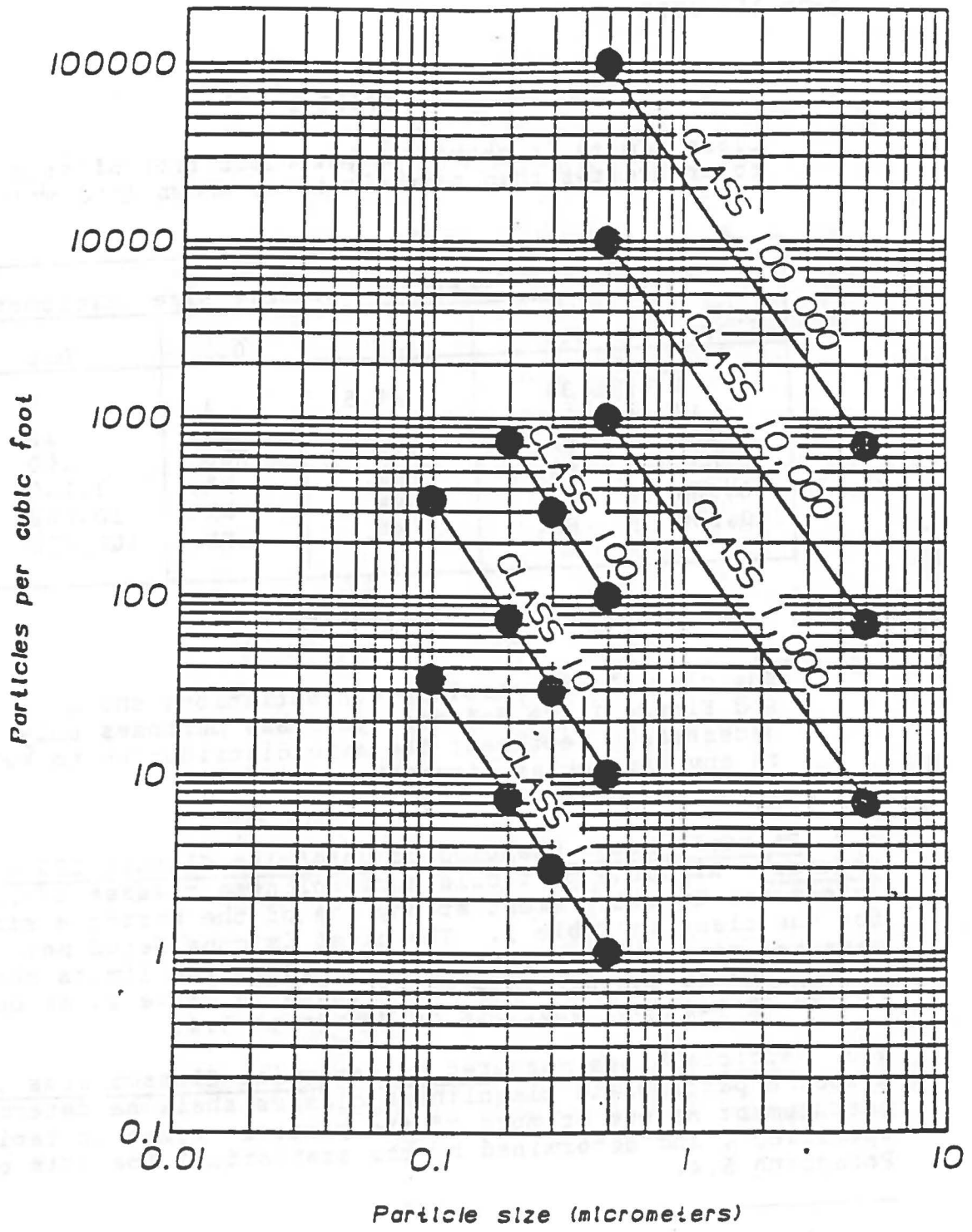

Figure 1. Class limits in particles per cubic foot of size equal to or greater than particle sizes shown*

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TABLE I

Class limits in particles per cubic foot of size equal to or greater than particle sizes shown (micrometers)[a]

Class	Measured Particle Size (Micrometers)				
	0.1	0.2	0.3	0.5	5.0
1	35	7.5	3	1	NA.
10	350	75	30	10	NA.
100	NA.	750	300	100	NA.
1,000	NA.	NA.	NA.	1,000	7
10,000	NA.	NA.	NA.	10,000	70
100,000	NA.	NA.	NA.	100,000	700

(NA. - not applicable)

[a]The class limit particle concentrations shown in Table I and Figure 1 are defined for class purposes only and do not necessarily represent the size distribution to be found in any particular situation.

4.2 Particle sizes measured to determine Classes 100 and greater. Airborne particulate cleanliness classes shall be determined by measurement at any one of the particle sizes listed for the class in Table I. The class is considered met if the measured particle concentration is within the limits specified, at any one of the particle sizes shown in Table I, as determined by the statistical analysis of Paragraph 5.4.

4.3 Particle sizes measured to determine Classes less than 100. Airborne particulate cleanliness classes shall be determined by measurement at one or more of the particle sizes in Table I, as specified[1], and determined by the statistical analysis of Paragraph 5.4.

[1]When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

4.4 Classification by measurement at other particle sizes. A classification of air cleanliness by measurement at particle sizes other than those specified herein may be performed with the following limitation: Particle counts may be interpolated between points but under no conditions may counts be extrapolated beyond the end points of Table I or Figure 1. The particle count limit for the next larger particle size in Table I must not be exceeded.

4.5 Provision for alternative airborne particulate cleanliness classes. Classes other than those stated in Table I (for example, 50, 300, 50,000, etc.) may be defined where special conditions dictate their use. Such classes will be defined by the intercept point on the 0.5-micrometer line in Figure 1, with a curve parallel to the established curves. Any curves that are used for these other classifications shall not be extrapolated to indicate concentrations for particles outside the following limits:

(a) Classes greater than 1,000 shall be determined by measurement at either 0.5 or 5 micrometers, as specified[1].

(b) Classes greater than 10 and less than 1,000 shall be determined by measurement at 0.2, 0.3, or 0.5 micrometer, as specified[1].

(c) Classes less than 10 shall be determined by measurement at one or more of the following particle sizes: 0.1, 0.2, 0.3, or 0.5 micrometer, as specified[1].

4.6 Particle counts for the determination of cleanliness classes. To determine an airborne particulate cleanliness class, particle counts shall be made in accordance with Section 5.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

5. Verification and monitoring of airborne particulate cleanliness classes.

5.1 Verification of airborne particulate cleanliness classes. The airborne particulate cleanliness class as defined in Section 4 shall be verified for a cleanroom or clean zone by measurement of airborne particle concentration under the following conditions.

5.1.1 Frequency. Verification tests shall be performed initially and at periodic intervals, or as specified[1].

5.1.2 Environmental test conditions. Verification of air cleanliness class shall be determined by particle concentration measurement under specified[1] operating conditions.

5.1.2.1 Conditions of test. The conditions of test of the cleanroom or clean zone shall be recorded as "as-built," "at-rest," "operational," or as otherwise specified[1].

5.1.2.2 Environmental and use parameters. The applicable environmental and use parameters of the cleanroom or clean zone shall be recorded. These conditions of measurement may include (but are not limited to) air velocity, air volume change rate, room air pressure, makeup air volume, unidirectional airflow parallelism, temperature, humidity, vibration, equipment, and personnel activity.

5.1.3 Particle counting. Particle counting shall be performed using a method specified in Paragraph 5.3 for verification of all classifications of cleanrooms and clean zones.

5.1.3.1 Sample locations and number - unidirectional airflow. For unidirectional airflow, the clean zone is identified by an entrance and an exit plane perpendicular to the airflow. The entrance plane shall be immediately upstream of the work activity

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

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5.1.2 Environmental test conditions. Verification of air cleanliness class shall be determined by particle concentration measurement under specified[1] operating conditions.

5.1.2.1 Conditions of test. The conditions of test of the cleanroom or clean zone shall be recorded as "as-built," "at-rest," "operational," or as otherwise specified[1].

5.1.2.2 Environmental and use parameters. The applicable environmental and use parameters of the cleanroom or clean zone shall be recorded. These conditions of measurement may include (but are not limited to) air velocity, air volume change rate, room air pressure, makeup air volume, unidirectional airflow parallelism, temperature, humidity, vibration, equipment, and personnel activity.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

4.4 Classification by measurement at other particle sizes. A classification of air cleanliness by measurement at particle sizes other than those specified herein may be performed with the following limitation: Particle counts may be interpolated between points but under no conditions may counts be extrapolated beyond the end points of Table I or Figure 1. The particle count limit for the next larger particle size in Table I must not be exceeded.

4.5 Provision for alternative airborne particulate cleanliness classes. Classes other than those stated in Table I (for example, 50, 300, 50,000, etc.) may be defined where special conditions dictate their use. Such classes will be defined by the intercept point on the 0.5-micrometer line in Figure 1, with a curve parallel to the established curves. Any curves that are used for these other classifications shall not be extrapolated to indicate concentrations for particles outside the following limits:

(a) Classes greater than 1,000 shall be determined by measurement at either 0.5 or 5 micrometers, as specified[1].

(b) Classes greater than 10 and less than 1,000 shall be determined by measurement at 0.2, 0.3, or 0.5 micrometer, as specified[1].

(c) Classes less than 10 shall be determined by measurement at one or more of the following particle sizes: 0.1, 0.2, 0.3, or 0.5 micrometer, as specified[1].

4.6 Particle counts for the determination of cleanliness classes. To determine an airborne particulate cleanliness class, particle counts shall be made in accordance with Section 5.

---

[1]When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

area within the clean zone. The minimum number of sample locations required for classification of a clean zone shall be the lesser of (a) the area of the entrance plane (in square feet) divided by 25, or (b) the area of the entrance plane (in square feet) divided by the square root of the airborne particulate cleanliness class designation.

5.1.3.2 Sample locations and number - nonunidirectional airflow. For nonunidirectional airflow, the number of sample locations shall be uniformly spaced horizontally, and as specified[1] vertically, throughout the clean zone, except as limited by equipment within the clean zone. The minimum number of sample locations shall be equal to the square feet of floor area of the clean zone divided by the square root of the airborne particulate cleanliness class designation.

5.1.3.3 Sample location restrictions. No fewer than two locations shall be sampled for any clean zone. The number of sample locations shall be uniformly spaced throughout the clean zone except as limited by equipment within the clean zone. At least one sample shall be taken at each of the sampling locations specified in Paragraph 5.1.3.1 or 5.1.3.2. A total of at least five samples shall be taken. More than one sample may be taken at each location and different numbers of samples may be taken at different locations.

5.1.3.4 Sample volume and sampling time. Table II lists the minimum volume per sample for various airborne particulate cleanliness classes and measured particle sizes. The sample time is calculated by dividing the sample volume by the sample flow rate. A larger sample volume will improve the precision of the concentration measurements, decreasing the amount of variation between samples; however, the volume should not be so large as to render the sample time impractical. The particle concentration shall be reported in terms of particles per cubic foot of air regardless of the sample volume size. The sample volume size shall also be reported.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

TABLE II

Minimum volume per sample in cubic feet for the air cleanliness class and measured particle size shown

Class	Measured Particle Size (Micrometers)				
	0.1	0.2	0.3	0.5	5.0
1	0.6	3.0	7.0	20.0	NA.
10	0.1	0.3	0.7	2.0	NA.
100	NA.	0.1	0.1	0.2	NA.
1,000	NA.	NA.	NA.	0.1	3.0
10,000	NA.	NA.	NA.	0.1	0.3
100,000	NA.	NA.	NA.	0.1	0.3

(NA. - not applicable)

5.1.3.5 Sample volume at other classes or particle sizes. Sample volume for other classes or particle sizes not specified herein shall be the same as that specified for the next lower class or particle size.

5.1.4 Interpretation of the data. A statistical evaluation of particle concentration measurement data shall be performed according to Paragraph 5.4 to verify the airborne particulate cleanliness class level.

5.2 Monitoring of airborne particulate cleanliness. After verification, if specified, the airborne particulate cleanliness shall be monitored during operations. Monitoring shall consist of particle concentration measurements. Other environmental parameters as suggested in Paragraph 5.1.2.2 may also be monitored as specified[1] to indicate trends in airborne particulate cleanliness.

[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

TABLE II

Minimum volume per sample in cubic feet for the air cleanliness class and measured particle size shown

Class	Measured Particle Size (Micrometers)				
	0.1	0.2	0.3	0.5	5.0
1	0.6	3.0	7.0	20.0	NA.
10	0.1	0.3	0.7	2.0	NA.
100	NA.	0.1	0.1	0.2	NA.
1,000	NA.	NA.	NA.	0.1	3.0
10,000	NA.	NA.	NA.	0.1	0.3
100,000	NA.	NA.	NA.	0.1	0.3

(NA. - not applicable)

5.1.3.5 Sample volume at other classes or particle sizes. Sample volume for other classes or particle sizes not specified herein shall be the same as that specified for the next lower class or particle size.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

area within the clean zone. The minimum number of sample locations required for classification of a clean zone shall be the lesser of (a) the area of the entrance plane (in square feet) divided by 25, or (b) the area of the entrance plane (in square feet) divided by the square root of the airborne particulate cleanliness class designation.

5.1.3.2 Sample locations and number - nonunidirectional airflow. For nonunidirectional airflow, the number of sample locations shall be uniformly spaced horizontally, and as specified[1] vertically, throughout the clean zone, except as limited by equipment within the clean zone. The minimum number of sample locations shall be equal to the square feet of floor area of the clean zone divided by the square root of the airborne particulate cleanliness class designation.

5.1.3.3 Sample location restrictions. No fewer than two locations shall be sampled for any clean zone. The number of sample locations shall be uniformly spaced throughout the clean zone except as limited by equipment within the clean zone. At least one sample shall be taken at each of the sampling locations specified in Paragraph 5.1.3.1 or 5.1.3.2. A total of at least five samples shall be taken. More than one sample may be taken at each location and different numbers of samples may be taken at different locations.

5.1.3.4 Sample volume and sampling time. Table II lists the minimum volume per sample for various airborne particulate cleanliness classes and measured particle sizes. The sample time is calculated by dividing the sample volume by the sample flow rate. A larger sample volume will improve the precision of the concentration measurements, decreasing the amount of variation between samples; however, the volume should not be so large as to render the sample time impractical. The particle concentration shall be reported in terms of particles per cubic foot of air regardless of the sample volume size. The sample volume size shall also be reported.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

5.2.1 Monitoring plan. A monitoring plan shall be established based on the airborne particulate cleanliness class and the degree of cleanliness control necessary for work activity or product protection. The monitoring plan shall specify frequency, operating conditions, the method of counting particles, the locations, number, and volume of samples, and some method for interpretation of the sample data.

5.2.2 Particle counting. Particle counting shall be performed using one of the test methods in Paragraph 5.3, as specified[1]. Particle concentration measurements shall be taken at locations throughout the clean zone or where the cleanliness level is particularly critical or where the higher particle concentration levels are found during verification testing. The air shall be sampled as it reaches the clean zone.

5.3 Methods and equipment for measuring airborne particle concentration. The method and equipment to be used for measuring the airborne particle concentration shall be selected on the basis of the particle size of interest. The following methods are suitable for class verification and monitoring of air cleanliness unless otherwise specified[1]. Other particle counting methods and equipment may be used if demonstrated to have accuracy and repeatability equal to or better than the methods listed below[2,3].

---

[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

[2] For example, for particle size approximately 0.01 micrometer in diameter and larger, a condensation nucleus counter, which optically detects particles which have been grown by condensation of a supersaturated vapor, may be used. The counter must detect single particles.

[3] For monitoring purposes only, evaluation of particles by sedimentation methods may be carried out by allowing the particles to deposit on the surface of an appropriate medium and then counting them using optical microscopy.

5.3.1 Counting particles 5 micrometers and larger. For particle sizes 5 micrometers and larger, a manual sizing and counting method or an optical particle counting instrument shall be used. The manual sizing and counting method shall be in accordance with Appendix A, and the optical particle counting instrument shall be in accordance with Appendix B.

5.3.2 Counting particles 0.1 micrometer and larger. For particle sizes 0.1 micrometer and larger, an optical particle counting instrument shall be used in accordance with Appendix B. The instrument must count single particles. Only information obtained with a periodically calibrated and properly maintained particle counter shall be used in conducting airborne particle concentration measurements. Particle size data shall be reported in terms of equivalent diameter as calibrated against reference standard particles.

5.3.3 Limitations of particle counting methods.

5.3.3.1 Optical particle counters. Optical particle counters with unlike geometry or different operating principles may give different results when counting the same particles. Even recently calibrated instruments of like design may show differences in measurement results when sampling the same air. Caution should be used when comparing measurements from different instruments.

5.3.3.2 Microscopic evaluation. Since the microscopically measured size of a particle is the apparent longest linear dimension, and the size of particles measured by optical particle counters is based upon the diameter of a reference particle, microscopic counts will generally differ from counts obtained by optical particle counters.

5.3.3.3 Upper limits. Particle counters shall not be used to count particle concentrations or particle sizes greater than the upper limits specified by the manufacturer.

5.3.1 Counting particles 5 micrometers and larger. For particle sizes 5 micrometers and larger, a manual sizing and counting method or an optical particle counting instrument shall be used. The manual sizing and counting method shall be in accordance with Appendix A, and the optical particle counting instrument shall be in accordance with Appendix B.

5.3.2 Counting particles 0.1 micrometer and larger. For particle sizes 0.1 micrometer and larger, an optical particle counting instrument shall be used in accordance with Appendix B. The instrument must count single particles. Only information obtained with a periodically calibrated and properly maintained particle counter shall be used in conducting airborne particle concentration measurements. Particle size data shall be reported in terms of equivalent diameter as calibrated against reference standard particles.

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5.2.1 Monitoring plan. A monitoring plan shall be established based on the airborne particulate cleanliness class and the degree of cleanliness control necessary for work activity or product protection. The monitoring plan shall specify frequency, operating conditions, the method of counting particles, the locations, number, and volume of samples, and some method for interpretation of the sample data.

5.2.2 Particle counting. Particle counting shall be performed using one of the test methods in Paragraph 5.3, as specified[1]. Particle concentration measurements shall be taken at locations throughout the clean zone or where the cleanliness level is particularly critical or where the higher particle concentration levels are found during verification testing. The air shall be sampled as it reaches the clean zone.

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---

[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

[2] For example, for particle size approximately 0.01 micrometer in diameter and larger, a condensation nucleus counter, which optically detects particles which have been grown by condensation of a supersaturated vapor, may be used. The counter must detect single particles.

[3] For monitoring purposes only, evaluation of particles by sedimentation methods may be carried out by allowing the particles to deposit on the surface of an appropriate medium and then counting them using optical microscopy.

5.3.4 Calibration of particle counting instrumentation. All instruments shall be calibrated against known reference standards at regular intervals as specified[1]. Parameters which may need calibration include, but are not limited to, air flow rate and particle size.

5.4 Statistical analysis. The collection and analysis of airborne particle concentration data for verification of an airborne particulate cleanliness class shall be performed in accordance with the following requirements. This statistical analysis deals only with random errors (lack of precision), not errors of a nonrandom nature ("bias"), such as erroneous calibration.

5.4.1 Acceptance criteria. The cleanroom or clean zone shall meet the acceptance criteria for an airborne particulate cleanliness class if 1) the average of the particle concentrations (see Table I) measured at each location falls at or below the class limit, and 2) the mean of these averages falls at or below the class limit with a 95% confidence limit. The confidence limit shall be based on a one-tailed Student's t distribution, as follows.

5.4.1.1 Average particle concentration. The average particle concentration (A) at a location is the sum of the individual sample particle counts (C_i) divided by the number of samples taken at the location (N), as shown in Equation (5-1). If only one sample is taken, the average particle concentration is the same as the particle count measured.

$$A = (C_1 + C_2 + \ldots + C_N) / N \qquad (5\text{-}1)$$

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[1]When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet the requirements will be specified by the user or contracting agency.

5.4.1.2 Mean of the averages. The mean of the averages (M) is the sum of the individual averages (A_i) divided by the number of locations (L), as shown in Equation (5-2). All locations are weighted equally, regardless of the number of samples taken.

$$M = (A_1 + A_2 + \ldots + A_L) / L \qquad (5\text{-}2)$$

5.4.1.3 Standard deviation. The standard deviation (SD) of the averages is the square root of the sum of the squares of differences between each of the individual averages and the mean of the averages $(A_i-M)^2$ divided by the number of locations (L) minus one, as shown in Equation (5-3).

$$SD = \sqrt{\frac{(A_1 - M)^2 + (A_2 - M)^2 + \ldots + (A_L - M)^2}{L - 1}} \qquad (5\text{-}3)$$

5.4.1.4 Standard error. The standard error (SE) of the mean of the averages (M) is determined by dividing the standard deviation (SD) by the square root of the number of locations, as shown in Equation (5-4).

$$SE = SD/\sqrt{L} \qquad (5\text{-}4)$$

5.4.1.5 Upper confidence limit (UCL). The 95% UCL of the mean of averages (M) is determined by adding to the mean the appropriate UCL factor (see Table III for UCL factor) times the standard error (SE), as shown in Equation (5-5).

$$UCL = M + (UCL\ Factor \times SE) \qquad (5\text{-}5)$$

TABLE III

UCL factor for 95% upper control limit

No. of locations(L)	2	3	4	5-6	7-9	10-16	17-29	>29
95% UCL factor	6.3	2.9	2.4	2.1	1.9	1.8	1.7	1.65

5.4.1.2 Mean of the averages. The mean of the averages (M) is the sum of the individual averages (A_i) divided by the number of locations (L), as shown in Equation (5-2). All locations are weighted equally, regardless of the number of samples taken.

$$M = (A_1 + A_2 + \ldots + A_L) / L \qquad (5\text{-}2)$$

5.4.1.3 Standard deviation. The standard deviation (SD) of the averages is the square root of the sum of the squares of differences between each of the individual averages and the mean of the averages $(A_i-M)^2$ divided by the number of locations (L) minus one, as shown in Equation (5-3).

$$SD = \sqrt{\frac{(A_1 - M)^2 + (A_2 - M)^2 + \ldots + (A_L - M)^2}{L - 1}} \qquad (5\text{-}3)$$

5.4.1.4 Standard error. The standard error (SE) of the mean of the averages (M) is determined by dividing the standard deviation (SD) by the square root of the number of locations, as shown in Equation (5-4).

$$SE = SD/\sqrt{L} \qquad (5\text{-}4)$$

5.4.1.5 Upper confidence limit (UCL). The 95% UCL of the mean of averages (M) is determined by adding to the mean the appropriate UCL factor (see Table III for UCL factor) times the standard error (SE), as shown in Equation (5-5).

$$UCL = M + (UCL\ Factor \times SE) \qquad (5\text{-}5)$$

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UCL factor for 95% upper control limit

No. of locations(L)	2	3	4	5-6	7-9	10-16	17-29	>29
95% UCL factor	6.3	2.9	2.4	2.1	1.9	1.8	1.7	1.65

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5.3.4 Calibration of particle counting instrumentation. All instruments shall be calibrated against known reference standards at regular intervals as specified[1]. Parameters which may need calibration include, but are not limited to, air flow rate and particle size.

5.4 Statistical analysis. The collection and analysis of airborne particle concentration data for verification of an airborne particulate cleanliness class shall be performed in accordance with the following requirements. This statistical analysis deals only with random errors (lack of precision), not errors of a nonrandom nature ("bias"), such as erroneous calibration.

5.4.1 Acceptance criteria. The cleanroom or clean zone shall meet the acceptance criteria for an airborne particulate cleanliness class if 1) the average of the particle concentrations (see Table I) measured at each location falls at or below the class limit, and 2) the mean of these averages falls at or below the class limit with a 95% confidence limit. The confidence limit shall be based on a one-tailed Student's t distribution, as follows.

5.4.1.1 Average particle concentration. The average particle concentration (A) at a location is the sum of the individual sample particle counts (C_i) divided by the number of samples taken at the location (N), as shown in Equation (5-1). If only one sample is taken, the average particle concentration is the same as the particle count measured.

$$A = (C_1 + C_2 + \ldots + C_N) / N \qquad (5\text{-}1)$$

---

[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet the requirements will be specified by the user or contracting agency.

5.4.1.6 Sample calculation. A sample calculation is shown in Appendix C.

6. Changes. When a Federal agency considers that this standard does not provide for its essential needs, written request for changing or adding to the standard, supported by adequate justification, shall be sent to the Administration. This justification shall explain wherein the standard does not provide for esssential needs. The request shall be sent to the General Services Administration, Federal Supply Service, Engineering Division, 819 Taylor Street, Fort Worth, TX 76102. The Administration will determine the appropriate action to be taken and will notify the agency.

7. Conflict with referenced specifications. Where the requirements stated in this standard conflict with any requirement in a referenced specification, the requirements of this standard shall apply. The nature of conflict between the standard and the referenced specification shall be submitted in duplicate to the General Services Administration, Federal Supply Service, Engineering Division, 819 Taylor Street, Fort Worth, TX 76102.

8. Federal agency interests.

Department of Commerce
Department of Defense, Office of the Assistant Secretary of Defense (Installations and Logistics)
Army
Navy
Air Force
Department of Energy
Department of Health and Human Services
Department of Transportation
General Services Administration
National Aeronautics and Space Administration
Nuclear Regulatory Commission

APPENDIX A

PARTICLE MONITORING - MANUAL COUNTING AND SIZING METHODS

A10. Scope. This appendix describes procedures for determining airborne particulate contamination levels of particles 5 micrometers and greater in size in cleanrooms and clean zones by a membrane filtration and particle count method.

A20. Summary of method.

A20.1 Description of the basic method. At the sampling point, air is passed through a membrane filter using a vacuum to effect the filtration. The air flow rate is controlled by means of a limiting orifice or an air flowmeter, and the total volume of air sampled is controlled by the sampling time. The membrane filter is examined microscopically, using a high-intensity oblique incident light source, to determine the number of particles 5 micrometers and greater collected from the air sample.

A20.2 Alternatives to optical microscopy. Image analysis or projection microscopy can replace direct optical microscopy for sizing and counting, provided that the accuracy and reproducibility are equal to or better than those of the direct optical microscopic method.

A20.3 Acceptable sampling procedures. There are two acceptable procedures for this method as described herein: (a) Aerosol Monitor Method, and (b) Open Filter Holder Method. They differ primarily in the apparatus used and in the time required for performance.

A30. Equipment.

A30.1 Equipment common to both methods.

A30.1.1 Microscope. Binocular microscope with ocular-objective combinations for 100X to 250X magnifications. These combinations are chosen such that the ultimate smallest division of the ocular reticle, at the highest magnification, is less than or equal to 5 micrometers. The latter objective should have a numerical aperture of at least 0.25.

A30.1.2 Ocular micrometer scale: 5- or 10-millimeter linear scale with 100 divisions, dependent upon ocular-objective combinations, or micrometer eyepiece with movable scale.

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A30.1.1 Microscope. Binocular microscope with ocular-objective combinations for 100X to 250X magnifications. These combinations are chosen such that the ultimate smallest division of the ocular reticle, at the highest magnification, is less than or equal to 5 micrometers. The latter objective should have a numerical aperture of at least 0.25.

A30.1.2 Ocular micrometer scale: 5- or 10-millimeter linear scale with 100 divisions, dependent upon ocular-objective combinations, or micrometer eyepiece with movable scale.

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5.4.1.6 Sample calculation. A sample calculation is shown in Appendix C.

6. Changes. When a Federal agency considers that this standard does not provide for its essential needs, written request for changing or adding to the standard, supported by adequate justification, shall be sent to the Administration. This justification shall explain wherein the standard does not provide for esssential needs. The request shall be sent to the General Services Administration, Federal Supply Service, Engineering Division, 819 Taylor Street, Fort Worth, TX 76102. The Administration will determine the appropriate action to be taken and will notify the agency.

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8. Federal agency interests.

Department of Commerce
Department of Defense, Office of the Assistant Secretary of Defense (Installations and Logistics)
- Army
- Navy
- Air Force

Department of Energy
Department of Health and Human Services
Department of Transportation
General Services Administration
National Aeronautics and Space Administration
Nuclear Regulatory Commission

A30.1.3 Stage micrometer: standard 0.01- to 0.1-millimeter-per-division scale.

A30.1.4 External microscope illuminator.

A30.1.5 Vacuum pump capable of maintaining a vacuum of 500 torr while pumping at a rate of at least 1 cubic foot per minute.

A30.1.6 Electrical timer or timing device, 60-minute range.

A30.1.7 Flowmeter or limiting orifice calibrated with the vacuum pump, filter holder, and filter to collect a sample of sufficient volume. See Paragraph A50.1.

A30.1.8 Manual tally counter.

A30.1.9 Filter storage holders for membrane filters after sampling; Petri plates or Petri slides with covers.

A30.1.10 Rinse fluid: purified water prefiltered to 0.45 to 1.2 micrometers.

A30.1.11 Forceps: flat, with unserrated tips.

A30.2 Equipment for aerosol monitor method.

A30.2.1 Aerosol monitors: dark, 0.8-micrometer mean pore size, with imprinted grid.

A30.2.2 Aerosol adapter.

A30.3 Equipment for open filter holder method.

A30.3.1 Filter holder: aerosol, open type.

A30.3.2 Membrane filter: dark, 0.8-micrometer or smaller pore size, with imprinted grid.

A30.3.3 Membrane filters: white (for evaluating dark particles), 0.8-micrometer or smaller pore size, with imprinted grid.

A30.4 Optional equipment.

A30.4.1 Image analyzer.

A30.4.2 Projection microscope and screen.

A40. Preparation of equipment.

A40.1 Preparation for both methods.

A40.1.1 All equipment preparation should be performed within a clean zone having an airborne particulate cleanliness class equal to or less than that of the clean zone to be monitored.

A40.1.2 All equipment should be maintained at maximum cleanliness and should be stored with protective covers, cases, or other suitable enclosures when not in use in a location having an airborne particulate cleanliness class equal to or less than that of the clean zone of lowest class number where sampling is performed.

A40.1.3 Personnel performing sampling, sizing, and counting operations should be equipped with garments consistent with the airborne particulate cleanliness class of the clean zone being monitored.

A40.1.4 Thoroughly rinse with purified water all internal surfaces of the Petri slide holders or Petri plates used to hold the exposed membranes for counting. Rinse in cascading action, as with the membrane holders. After rinsing, leave the lid open in a unidirectional airflow clean zone until the interior surfaces are dry.

A40.2 Preparation for aerosol monitor method.

A40.2.1 Establish a filter background count in the following manner. Where the manufacturer of aerosol monitors has indicated an average background count for a package of monitors (in the particle size ranges of concern), examine and establish the average background count for 5% of the filters in the package. If the average background count determined is equal to or less than the manufacturer's indication, use the indication as the background count for all filters in the package. If the determined count is higher than the manufacturer's indication, or if there is no such indication, establish a background count for each filter used.

A30.4.2 Projection microscope and screen.

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A30.1.4 External microscope illuminator.

A30.1.5 Vacuum pump capable of maintaining a vacuum of 500 torr while pumping at a rate of at least 1 cubic foot per minute.

A30.1.6 Electrical timer or timing device, 60-minute range.

A30.1.7 Flowmeter or limiting orifice calibrated with the vacuum pump, filter holder, and filter to collect a sample of sufficient volume. See Paragraph A50.1.

A30.1.8 Manual tally counter.

A30.1.9 Filter storage holders for membrane filters after sampling; Petri plates or Petri slides with covers.

A30.1.10 Rinse fluid: purified water prefiltered to 0.45 to 1.2 micrometers.

A30.1.11 Forceps: flat, with unserrated tips.

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A30.3.3 Membrane filters: white (for evaluating dark particles), 0.8-micrometer or smaller pore size, with imprinted grid.

A30.4 Optional equipment.

A30.4.1 Image analyzer.

A40.2.2 Background counts for individual filters are determined by following the microscopic procedures of Paragraph A70.

A40.2.3 After the background count has been established, package the aerosol monitors in a particle-free container or place into their appropriate sampling devices and transport them to the sampling location.

A40.2.4 Except for purposes of making background counts, aerosol monitors should be opened only when in the sampling location or the counting area.

A40.3 Preparation for open filter holder method.

A40.3.1 Disassemble the filter holder and wash in liquid soap and water. After washing, rinse and store in the unidirectional airflow clean zone until dry. (DO NOT WIPE DRY.) Deionized water or distilled water are the rinse media of choice.

A40.3.2 After the filter holder is completely dry, mount a membrane filter in the filter holder, with the grid exposed. After mounting the membrane filter, invert the filter holder assembly and thoroughly flush the filter surface area and exposed filter holder parts with purified water using a cascade rinsing action, starting at the top and progressing to the bottom of the filter face. Place in the unidirectional airflow clean zone and allow to dry.

A40.3.3 Establish a filter background count for each membrane filter to be used by following the procedures of Paragraph A70.

A40.3.4 After the interior surfaces of the filter storage holders are dry, apply a small piece of double-sided cellophane tape or stopcock grease to the bottom surface.

A40.3.5 After the filter holder and membrane are clean and dry, package them in a particle-free container.

A40.3.6 Transport the prepared filter holder, with membrane filter and vacuum source, to the sampling location. DO NOT EXPOSE THE FILTER SURFACE UNTIL THE APPARATUS IS ASSEMBLED AND READY FOR SAMPLING.

A50. Sampling.

A50.1 Sampling orientation and flow. For unidirectional airflow cleanrooms and clean zones, the aerosol monitor or filter holder should be oriented to face into the airflow. For non-unidirectional airflow cleanrooms and clean zones, orient the aerosol monitor or filter holder so that the opening faces upward, unless otherwise specified[1]. Airflow into the filter should be adjusted to be isokinetic for unidirectional airflow. For nonunidirectional airflow, the airflow into the filter should be adjusted to be 0.25 cubic foot per minute for a 25-millimeter filter or 1 cubic foot per minute for a 47-millimeter filter. The minimum sample volume should be 10 cubic feet for Class 1000 and 1 cubic foot for Class 10,000 and greater.

A50.2 Sampling by aerosol monitor method.

A50.2.1 At the sampling location, attach the aerosol monitor to the aerosol adapter and the adapter to the vacuum source. Have in line either a limiting orifice or a flowmeter. Isolate the vacuum pump exhaust from the area being sampled, as it may be a source of extraneous airborne contamination.

A50.2.2 Adjust the flowmeter, if used, for the flow rate at the operating vacuum pressure where it is used.

A50.2.3 Connect a timer to the vacuum pump power source.

A50.2.4 Remove the bottom plug from the aerosol monitor and attach it to the free end of the aerosol adapter. Position the aerosol monitor as required, pry off the top portion of the aerosol monitor, and store it in a clean location.

A50.2.5 Turn on the pump, adjust the flowmeter, and operate for a time which will provide the required sample at the chosen flow rate.

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[1] When the terms "as specified" or "shall be specified" are used without further reference, the degree of control needed to meet requirements will be specified by the user or contracting agency.

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A40.2.2 Background counts for individual filters are determined by following the microscopic procedures of Paragraph A70.

A40.2.3 After the background count has been established, package the aerosol monitors in a particle-free container or place into their appropriate sampling devices and transport them to the sampling location.

A40.2.4 Except for purposes of making background counts, aerosol monitors should be opened only when in the sampling location or the counting area.

A40.3 Preparation for open filter holder method.

A40.3.1 Disassemble the filter holder and wash in liquid soap and water. After washing, rinse and store in the unidirectional airflow clean zone until dry. (DO NOT WIPE DRY.) Deionized water or distilled water are the rinse media of choice.

A40.3.2 After the filter holder is completely dry, mount a membrane filter in the filter holder, with the grid exposed. After mounting the membrane filter, invert the filter holder assembly and thoroughly flush the filter surface area and exposed filter holder parts with purified water using a cascade rinsing action, starting at the top and progressing to the bottom of the filter face. Place in the unidirectional airflow clean zone and allow to dry.

A40.3.3 Establish a filter background count for each membrane filter to be used by following the procedures of Paragraph A70.

A40.3.4 After the interior surfaces of the filter storage holders are dry, apply a small piece of double-sided cellophane tape or stopcock grease to the bottom surface.

A40.3.5 After the filter holder and membrane are clean and dry, package them in a particle-free container.

A40.3.6 Transport the prepared filter holder, with membrane filter and vacuum source, to the sampling location. DO NOT EXPOSE THE FILTER SURFACE UNTIL THE APPARATUS IS ASSEMBLED AND READY FOR SAMPLING.

A50.2.6 When the sampling time has elapsed, release the vacuum, replace the top portion of the aerosol monitor, and remove the aerosol monitor from the aerosol adapter. The bottom plug need not be replaced. Identify the aerosol monitor with a sample identification tag. Transport the aerosol monitor to a counting area which should be a clean zone of airborne particulate cleanliness class at least equal to that of the clean zone sampled.

A50.3 Sampling by open filter holder method.

A50.3.1 When in the sampling area, place the filter holder in position. With the aid of vacuum tubing, connect the filter holder to the vacuum train which includes the filter holder, either a limiting orifice or a flowmeter, and a source of vacuum (vented outside the sampling area or filtered to prevent contamination of the area sampled).

A50.3.2 Adjust the flowmeter, if used, for the flow rate at the operating vacuum pressure where it is used.

A50.3.3 Remove the protective cover from the membrane filter holder and turn on the vacuum source. Turn on the pump, adjust the flowmeter, and operate for a time which provides the required sample at the chosen flow rate.

A50.3.4 At the end of the sampling period, turn off the vacuum source and carefully re-cover the filter holder with a precleaned cover. Return the covered sample filter holder to the counting area, which should be a clean zone of airborne particulate cleanliness class at least equal to that of the clean zone sampled.

A60. Microscope calibration.

A60.1 IF CALIBRATION OF THE MICROSCOPE HAS BEEN PERFORMED PREVIOUSLY BY THE OPERATOR, OMIT THIS SECTION.

A60.2 Place the stage micrometer on the mechanical stage; focus and adjust the light to give an even and full illumination in the field of view.

A60.3 Verify that the proper eyepiece and objective combination is in place to provide total magnification equal to 100X to 250X, as required.

A60.4 Assure that the microscope is properly focused by focusing each eyepiece to achieve a sharp stage micrometer image.

A60.5 If an image analyzer or projection microscope is used, perform a similar calibration.

A60.6 Using the entire length of the ocular reticle scale, record the number of stage micrometer divisions the eyepiece reticle covers.

(a) Compute the ocular micrometer scale calibration for a particular magnification by the formula:

$$\text{Micrometers per ocular scale division} = \frac{(\text{No. of Stage Micrometer Div.}) \times (\text{Size of One Stage Micrometer Div.})}{(\text{No. of Eyepiece Divisions})}$$

Example:

At 100X: 100 eyepiece divisions equals 100 stage divisions, each 5.0 micrometers in length.

Thus: Micrometers/Eyepiece Division =

$$\frac{(100 \text{ Divisions}) \times (5.0 \text{ Micrometers})}{(100 \text{ Divisions})} = 5.0 \text{ Micrometers}$$

(b) Calculate the number of linear divisions required to measure each range.

Example:

At 100X: each eyepiece division equals 5 micrometers, so for a 16- to 20-micrometer range, 3 to 4 divisions would be examined.

Note: If the microscope is equipped with a zoom adjustment, this may be employed to adjust the calibration to the nearest integer (X micrometers/division, instead of X.Y micrometers/division), provided the adjustment is noted in the calculations.

NOTE: A CHANGE IN INTERPUPILLARY DISTANCE BETWEEN OPERATORS CHANGES FOCAL DISTANCE, HENCE CALIBRATION.

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A50.2.6 When the sampling time has elapsed, release the vacuum, replace the top portion of the aerosol monitor, and remove the aerosol monitor from the aerosol adapter. The bottom plug need not be replaced. Identify the aerosol monitor with a sample identification tag. Transport the aerosol monitor to a counting area which should be a clean zone of airborne particulate cleanliness class at least equal to that of the clean zone sampled.

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A50.3.1 When in the sampling area, place the filter holder in position. With the aid of vacuum tubing, connect the filter holder to the vacuum train which includes the filter holder, either a limiting orifice or a flowmeter, and a source of vacuum (vented outside the sampling area or filtered to prevent contamination of the area sampled).

A50.3.2 Adjust the flowmeter, if used, for the flow rate at the operating vacuum pressure where it is used.

A50.3.3 Remove the protective cover from the membrane filter holder and turn on the vacuum source. Turn on the pump, adjust the flowmeter, and operate for a time which provides the required sample at the chosen flow rate.

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A70. Microscopic counting and sizing of particles.

A70.1 In the clean zone where the particles upon the membrane filters are counted and sized, remove the membrane filter from the aerosol monitor or the open filter holder with unserrated flat forceps.

A70.2 Place the membrane filter, grid side up, in a precleaned Petri slide holder or Petri plate, allowing the filter to adhere to the sticky surface of the storage holder. Tightly seal the carrier to prevent contamination of the sample filter.

A70.3 The microscope should be clean so as not to add particulate contamination to the sample. Carefully place the covered Petri slide or Petri plate on the microscope stage and adjust the angle and focus of the illuminator to provide optimum particle definition at the magnification used for counting. Use an oblique lighting angle of 10 to 20 degrees to cast a shadow of the particle, thereby effectively separating the particle image from the filter background.

A70.4 Select a field size so that there are no more than about 50 particles larger than 5 micrometers in the field. Optional fields are: a grid square; a rectangle defined by the width of a grid square and the calibrated length of the ocular micrometer scale; a rectangle defined by the width of the grid square and a portion of the length of the ocular micrometer scale.

A70.5 Estimate the number of particles in the greater-than-5-micrometer range over the effective filtering area by scanning one unit area of the field size selected. If the total number of particles in this range is estimated to be less than 500, count the number of particles in this range over the entire effective filtering area. If the number is greater, the counting procedure in Paragraph A70.8.1 applies.

A70.6 In scanning for particles, manipulate the stage so that particles to be counted pass under the ocular scale. Only the maximum dimension of the particle is regarded as significant. The eyepiece containing the ocular micrometer may be rotated to accommodate specific particles, if necessary.

A70.7 Using a manual tally counter, record all particles in the selected field that are equal to or exceed the dimension as indicated by the ocular micrometer scale. Record the number of particles in each field counted, in order to establish uniformity of distribution and to have a record of the number of fields counted.

A70.8 Statistical particle counting.

A70.8.1 When the estimated number of particles over the effective filtering area exceeds 500, the method entails the selection of a unit area for statistical counting, counting all particles in the unit area, and then similarly counting additional unit areas until the following statistical requirement is met:

$$F \times N > 500$$

where:

F = number of grid squares or unit areas counted, and

N = total number of particles counted in F areas.

A70.8.2 Calculate the total number of particles on the filter as follows:

$$P = N \times \frac{A}{n \times a}$$

where:

P = total number of particles of a size range on the filter.

(When a background count is obtained, subtract this from the P value after calculation, but prior to dividing by sample volume.)

N = total number of particles counted in n unit areas.

n = number of unit areas counted.

a = unit area in square millimeters.

A = effective total filter area in square millimeters.

A70.7 Using a manual tally counter, record all particles in the selected field that are equal to or exceed the dimension as indicated by the ocular micrometer scale. Record the number of particles in each field counted, in order to establish uniformity of distribution and to have a record of the number of fields counted.

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A70.6 In scanning for particles, manipulate the stage so that particles to be counted pass under the ocular scale. Only the maximum dimension of the particle is regarded as significant. The eyepiece containing the ocular micrometer may be rotated to accommodate specific particles, if necessary.

A80. Reporting.

A80.1 Subtract the background count for a filter from the total count obtained for the filter in accordance with Paragraph A70.

A80.2 Results should be expressed for each size range of specific interest, including 5-micrometer particles, in particles per cubic foot of sample by dividing the number of particles, P, by the sample volume (V).

$$\text{Particles per cubic foot} = P/V$$

A80.3 Final results are expressed in particles per cubic foot of sampled air, 5 micrometers and greater.

A90. Factors affecting precision and accuracy.

A90.1 The precision and accuracy of this method can be no higher than the sum total of the variables. In order to minimize the variables attributable to an operator, a trained microscopist technician is required. Variables of equipment are recognized by the experienced operator, thus further reducing possible error. The operator should have adequate basic training in microscopy and the techniques of particle sizing and counting.

A90.2 For training personnel, low- to medium-concentration specimens may be prepared on a grid filter and preserved between microslides as standards for a given laboratory. Standard counting specimens are available for this purpose.

A90.3 Accuracy for a sampling location can be increased by increasing the number of samples taken and processed at that sampling location.

A90.4 Accuracy for a sampling location can be increased by increasing the volume of air per sample and by increasing the time of sampling.

A90.5 Accuracy can be increased by establishing and using background counts for filters.

APPENDIX B

OPERATION OF OPTICAL PARTICLE COUNTERS

B10. Scope.

B10.1 Application. Optical particle counters provide data on airborne particle concentration and size distribution on a near-real-time basis. This appendix describes methods for the operation, use, and testing of optical particle counters used to satisfy requirements of this Federal Standard. Guidelines are given which should aid in standardization of optical airborne particle monitoring procedures for defining air cleanliness.

B10.2 Limitations. Particle size data are referenced to the particle system used to calibrate the optical particle counter; however, differences in optical, electronic, and sample handling systems among the various optical particle counters may contribute to variations in counting results. Care must be exercised in attempting to compare data from samples which vary significantly in particle composition or shape from the calibration base. Variations may also occur between instruments using particle sensing systems with different operating parameters. These effects should be recognized and minimized by using standardized methods for counter calibration and operation.

B10.3 Qualifications of personnel. Individuals performing the procedures described herein should be trained in the use of the optical particle counter and understand its operation, capabilities, and limitations.

B20. Applicable references.

B20. 1 ASTM F 328 Determining Counting and Sizing Accuracy of an Airborne Particle Counter Using Near-Monodisperse Spherical Particulate Materials.

B20.2 ASTM F 649 Secondary Calibration of Airborne Particle Counter Using Comparison Procedures, American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

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B20.2 ASTM F 649 Secondary Calibration of Airborne Particle Counter Using Comparison Procedures, American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

A80. Reporting.

A80.1 Subtract the background count for a filter from the total count obtained for the filter in accordance with Paragraph A70.

A80.2 Results should be expressed for each size range of specific interest, including 5-micrometer particles, in particles per cubic foot of sample by dividing the number of particles, P, by the sample volume (V).

$$\text{Particles per cubic foot} = P/V$$

A80.3 Final results are expressed in particles per cubic foot of sampled air, 5 micrometers and greater.

A90. Factors affecting precision and accuracy.

A90.1 The precision and accuracy of this method can be no higher than the sum total of the variables. In order to minimize the variables attributable to an operator, a trained microscopist technician is required. Variables of equipment are recognized by the experienced operator, thus further reducing possible error. The operator should have adequate basic training in microscopy and the techniques of particle sizing and counting.

A90.2 For training personnel, low- to medium-concentration specimens may be prepared on a grid filter and preserved between microslides as standards for a given laboratory. Standard counting specimens are available for this purpose.

A90.3 Accuracy for a sampling location can be increased by increasing the number of samples taken and processed at that sampling location.

A90.4 Accuracy for a sampling location can be increased by increasing the volume of air per sample and by increasing the time of sampling.

A90.5 Accuracy can be increased by establishing and using background counts for filters.

B20.3 IES-RP-CC-013 Recommended Practice for Equipment Calibration or Validation Procedures, Institute of Environmental Sciences, 940 East Northwest Highway, Mt. Prospect, IL 60056.

B30. Summary of method.

B30.1 Calibration. Primary calibration of optical particle counters is performed with spherical isotropic particles of refractive index 1.6. Secondary calibration may be performed with atmospheric particles for correlation with a reference particle counter. In addition, stable operation should be assured by standardizing against internal references built into the counter or by other approved methods.

B30.2 Operation. The air to be classified is sampled at a known flow rate from the sample point or points of concern. Particles contained in the sampled air pass through the sensing zone of the optical particle counter and produce a signal which is related to particle size. An electronic discriminator circuit sorts and counts the pulses in relation to particle size and displays or prints out the particle count in the sample volume.

B40. Apparatus and related documentation.

B40.1 Optical particle counting system. The optical particle counting system may include a recorder or printer; alternatively, data may be transmitted to a remote location for additional processing and computing.

B40.2 Sample air flow system. The sample air flow system consists of an intake tube, a sensing chamber, an air flow metering or control system, and an exhaust system. The exhaust system may consist of either a built-in vacuum source or an external vacuum supply with a separate flow control element for the optical particle counter in use. If a built-in vacuum source is used, and the optical particle counter is to be used where the exhaust air could affect either the particle counts being measured or operations in the cleanroom or clean zone, then the exhaust should be suitably filtered.

B40.3 Sensing system. The sensing system of the optical particle counter is formed by intersecting the sample air flow with a fixed sensing volume of such dimension so that the probability of more than one particle being present at any time (the coincidence error) is less than 5%. The signal produced from each particle passage through the sensing volume is received and processed by the electronic system in real time. The instrument should be designed to maintain its stated accuracy despite variations in the specified operating line voltage and ambient temperature. The operating line voltage and temperature ranges should be specified.

B40.4 Electronic system. The electronic system includes a pulse analyzer and counter, along with a system for registering particle counts in relation to particle size.

B40.4.1 The pulse analyzer may operate in either one or both of two modes: (1) in response to all particles within discrete size ranges, or (2) in response to all particles larger than the predetermined lower threshold size limit(s). Air cleanliness classification data, however, should be reported in terms of mode (2). Particle size ranges or limits may be either selectable or fixed.

B40.4.2 The counting circuits during a known time interval may accumulate information generated by the pulse analyzer in response to particle passages. Pulse count accumulation in one or more size ranges may be provided.

B40.4.3 For determination of the airborne particulate cleanliness class, the counting circuit is allowed to accumulate data for a preset time interval before reporting. The time interval is selected to yield a known sample volume, so that particle concentration can be readily calculated.

B40.4.4 The registering system indicates the number of particles or the particle concentration with respect to the selected particle size range(s) or size limit(s). Counts may be recorded or displayed on the optical particle counter, or may be transmitted to a remote location for recording, display, or computer processing.

B40.3 Sensing system. The sensing system of the optical particle counter is formed by intersecting the sample air flow with a fixed sensing volume of such dimension so that the probability of more than one particle being present at any time (the coincidence error) is less than 5%. The signal produced from each particle passage through the sensing volume is received and processed by the electronic system in real time. The instrument should be designed to maintain its stated accuracy despite variations in the specified operating line voltage and ambient temperature. The operating line voltage and temperature ranges should be specified.

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B40.4.4 The registering system indicates the number of particles or the particle concentration with respect to the selected particle size range(s) or size limit(s). Counts may be recorded or displayed on the optical particle counter, or may be transmitted to a remote location for recording, display, or computer processing.

B20.3 IES-RP-CC-013 Recommended Practice for Equipment Calibration or Validation Procedures, Institute of Environmental Sciences, 940 East Northwest Highway, Mt. Prospect, IL 60056.

B30. Summary of method.

B30.1 Calibration. Primary calibration of optical particle counters is performed with spherical isotropic particles of refractive index 1.6. Secondary calibration may be performed with atmospheric particles for correlation with a reference particle counter. In addition, stable operation should be assured by standardizing against internal references built into the counter or by other approved methods.

B30.2 Operation. The air to be classified is sampled at a known flow rate from the sample point or points of concern. Particles contained in the sampled air pass through the sensing zone of the optical particle counter and produce a signal which is related to particle size. An electronic discriminator circuit sorts and counts the pulses in relation to particle size and displays or prints out the particle count in the sample volume.

B40. Apparatus and related documentation.

B40.1 Optical particle counting system. The optical particle counting system may include a recorder or printer; alternatively, data may be transmitted to a remote location for additional processing and computing.

B40.2 Sample air flow system. The sample air flow system consists of an intake tube, a sensing chamber, an air flow metering or control system, and an exhaust system. The exhaust system may consist of either a built-in vacuum source or an external vacuum supply with a separate flow control element for the optical particle counter in use. If a built-in vacuum source is used, and the optical particle counter is to be used where the exhaust air could affect either the particle counts being measured or operations in the cleanroom or clean zone, then the exhaust should be suitably filtered.

B40.5 Calibration. An internal secondary calibration system or a means of ensuring stability should be provided in the instrument. The internal secondary calibration system should be capable of validation with respect to primary calibration in accordance with the methods of ASTM F 328 and ASTM F 649. The secondary calibration system is used for checking the sizing and counting stability of the optical particle counter and to provide a stable reference for any necessary sensitivity adjustment of the instrument.

B40.6 Documentation. Instructions which should be supplied with the instrument by the manufacturer include:

(a) Brief description of the operating principles of the instrument.

(b) Description of major components.

(c) Environmental conditions (ambient temperature, relative humidity, and pressure) and line voltage range required for stable operation.

(d) Particle size and concentration ranges for accurate measurement.

(e) Suggested maintenance procedure and recommended intervals for routine maintenance.

(f) Operating procedure for particle counting and sizing.

(g) Secondary calibration procedure (where applicable).

(h) Primary calibration procedure (a factory primary calibration facility should be available for calibration of the counter upon customer request), and field primary calibration capability and procedures.

(i) Suggested intervals for primary calibration.

B50. Preparations for sampling and counting. The procedures described in the following paragraphs should be performed or verified before the optical particle counter is used for determination of airborne particulate cleanliness classes. Each of the procedures has its own requirements regarding frequency interval.

B50.1 Primary calibration. Particle sizing and air sample volume require primary calibration. The comments in the following paragraphs are intended as a general guideline for primary calibration to be considered in interpreting ASTM F 328, ASTM F 649, or IES-RP-CC-013. Deviations may be necessary to achieve a specific objective. It is, however, the duty of the manufacturer to include in the operating instructions a description of the appropriate primary calibration method for the optical particle counter.

B50.1.1 Particle sizing. Primary calibration of the particle sizing function of the optical particle counter is carried out by registering the response of the counter to a monodisperse homogeneous and isotropic controlled aerosol containing predominantly spherical particles of known size and refractive index, and by adjusting the calibration control until the correct sizing response is obtained. Thereafter, the internal secondary calibration system is adjusted, if necessary, for correct response to the reference aerosol. Nonspherical particles may be used for primary calibration for specific applications. In these cases, the particle size is defined in terms of an appropriate dimension for the reference particles. Means of generating the reference particles has been extensively described in the literature[1].

B50.1.2 Air sample volume. The air sample volume is calibrated by measuring the flow rate and the duration of the sampling

[1]For instance, Liu, B.Y.H., "Methods for Generating Monodisperse Aerosols." 1967. Publication #104, Particle Technology Laboratory, Department of Mechanical Engineering, University of Minnesota.

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B40.5 Calibration. An internal secondary calibration system or a means of ensuring stability should be provided in the instrument. The internal secondary calibration system should be capable of validation with respect to primary calibration in accordance with the methods of ASTM F 328 and ASTM F 649. The secondary calibration system is used for checking the sizing and counting stability of the optical particle counter and to provide a stable reference for any necessary sensitivity adjustment of the instrument.

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(c) Environmental conditions (ambient temperature, relative humidity, and pressure) and line voltage range required for stable operation.

(d) Particle size and concentration ranges for accurate measurement.

(e) Suggested maintenance procedure and recommended intervals for routine maintenance.

(f) Operating procedure for particle counting and sizing.

(g) Secondary calibration procedure (where applicable).

(h) Primary calibration procedure (a factory primary calibration facility should be available for calibration of the counter upon customer request), and field primary calibration capability and procedures.

(i) Suggested intervals for primary calibration.

interval[2]. To avoid erroneous readings, equipment used for this measurement should not introduce an additional static pressure drop to the optical particle counter flow system. All flow measurements should be referenced to ambient conditions of temperature and pressure or as otherwise specified.

B50.2 Sampling setup.

B50.2.1 Sample location. In-place sample locations and orientation of the sample inlet tube should be established in accordance with Section 5 of this standard.

B50.2.2 Extension of sample inlet tube. Any extension of the sample inlet tube may affect the sampling results. The effects may be of little significance for particles in the size range from approximately 0.1 to 1 micrometer for sample tube extensions up to approximately 30 meters. Outside of this range, extensions of the sample inlet tube are used only if no other method is possible for sample acquisition. The sample tube extensions should be configured to maintain the sample flow Reynolds number in the range from 5,000 to 10,000 and the sample residence time in the extension below 5 seconds; no radius of curvature below 10 centimeters should be used. Where air sampling requires data on particles larger than 3 micrometers in diameter, no extension tube longer than 3 meters should be used.

B50.2.3 Particle counter exhaust air. The particle counter should be located and used so that air vented does not contaminate the sample or clean zone. The exhaust air should be filtered to a level consistent with the ambient airborne particulate cleanliness class or else vented outside of the cleanroom.

B50.3 Field calibration procedure. Perform secondary calibration or standardization (if applicable) in accordance with the manufacturer's instructions.

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[2]See Baker, W.C. and Pouchot, J.F., "The Measurement of Gas Flow Part I," 1983, Journal of Air Pollution Control Association, January, Vol. 33, No. 1 and Baker, W.C. and Pouchot, J.F., "The Measurement of Gas Flow Part II," 1983, Journal of Air Pollution Control Association, February, Vol. 33, No. 2.

B50.4 Zero count check. The absence of spurious counts is verified by a zero count check, as described in the following paragraphs.

B50.4.1 Place an appropriate filter on the counter sample inlet tube to prevent the passage of particles larger than the smallest size particle the counter can count.

B50.4.2 Turn on the sample air flow system; adjust for the specified sample air flow rate, if necessary.

B50.4.3 Turn on the counting circuits.

B50.4.4 Verify that the instrument reads zero counts for particles 0.5 micrometer and larger. If counts are registered, permit the counter to purge itself with the filter in place until a zero count level is reached.

B50.4.5 For counters capable of detecting particles smaller than 0.5 micrometer, zero counts may not be achievable for the smallest particles detectable. For such instruments, a tare concentration less than 10% of the airborne particulate cleanliness class concentration of such smaller particles (e.g., 0.1, 0.2, 0.3 micrometer) should be achieved.

B60. Counting procedure.

B60.1 Perform the field (secondary) calibration and zero count check, in accordance with Paragraphs B50.3 and B50.4.

B60.2 Check and adjust to the specified air flow rate (if applicable).

B60.3 Turn on the counting circuits, if necessary; read and record the particle count displayed for the particle size(s) of interest.

B70. Reporting.

B70.1 Record the particle size range(s), the volume of air sampled, the particle count, the time, and the sample point location.

B70.2 Report particle count data in terms of the number of particles per cubic foot of air sampled.

B50.4 Zero count check. The absence of spurious counts is verified by a zero count check, as described in the following paragraphs.

B50.4.1 Place an appropriate filter on the counter sample inlet tube to prevent the passage of particles larger than the smallest size particle the counter can count.

B50.4.2 Turn on the sample air flow system; adjust for the specified sample air flow rate, if necessary.

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interval[2]. To avoid erroneous readings, equipment used for this measurement should not introduce an additional static pressure drop to the optical particle counter flow system. All flow measurements should be referenced to ambient conditions of temperature and pressure or as otherwise specified.

B50.2 Sampling setup.

B50.2.1 Sample location. In-place sample locations and orientation of the sample inlet tube should be established in accordance with Section 5 of this standard.

B50.2.2 Extension of sample inlet tube. Any extension of the sample inlet tube may affect the sampling results. The effects may be of little significance for particles in the size range from approximately 0.1 to 1 micrometer for sample tube extensions up to approximately 30 meters. Outside of this range, extensions of the sample inlet tube are used only if no other method is possible for sample acquisition. The sample tube extensions should be configured to maintain the sample flow Reynolds number in the range from 5,000 to 10,000 and the sample residence time in the extension below 5 seconds; no radius of curvature below 10 centimeters should be used. Where air sampling requires data on particles larger than 3 micrometers in diameter, no extension tube longer than 3 meters should be used.

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APPENDIX C

STATISTICAL ANALYSIS

C10. Sample calculation. The data and calculations presented in the following paragraphs are intended to serve as a working example, illustrating the statistical procedures involved in determination of acceptance criteria for cleanrooms and clean zones. The data and calculations are based upon a 1-cubic-foot sample volume and testing at 0.3-micrometer measured particle size for Class 10. (Note: Table 1 indicates that the UCL is to be less than or equal to 30 particles per cubic foot 0.3 micrometer and larger to meet Class 10.)

C10.1 Tabulation of particle count data.

Location	Particle Counts (C_i)					Total No. of Samples (N)	($\sum C_i$) Total Count	(A_i) Average Counts
	1	2	3	4	5			
A	15	NR	NR	NR	NR	1	15	15.00
B	33	24	9	15	NR	4	81	20.25
C	18	3	12	24	NR	4	57	14.25
D	39	18	9	33	6	5	105	21.00
E	0	27	6	0	NR	4	33	8.25

(NR - no reading taken)

C10.2 Mean of averages (M).

$$M = (A_1 + A_2 + \ldots + A_L) / L \quad \text{(Equation 5-2)}$$

$$M = (15.00 + 20.25 + 14.25 + 21.00 + 8.25)/5 = 15.75$$

L = (Number of sample locations)

C10.3 Standard deviation of averages (SD).

(Equation 5-3)

$$SD = \sqrt{\frac{(A_1 - M)^2 + (A_2 - M)^2 + \ldots + (A_L - M)^2}{L - 1}}$$

$$SD = \sqrt{[(15.00-15.75)^2 + (20.25-15.75)^2 + (14.25-15.75)^2 + (21.00-15.75)^2 + (8.25-15.75)^2] / [5-1]}$$

SD = 5.17

C10.4 Standard error of mean of averages (SE).

$$SE = SD/\sqrt{L} \qquad \text{(Equation 5-4)}$$

$$SE = 5.17/\sqrt{5} = 2.31$$

C10.5 Upper 95% confidence limit (UCL).

For 5 locations, UCL factor = 2.1

UCL = M + (UCL Factor x SE) (Equation 5-5)

UCL = 15.75 + (2.1 x 2.31) = 20.6

C20. Conclusion. Since the upper 95% confidence limit (UCL) is less than 30 and all location average particle concentrations (A_i) were less than 30, the above data meet the acceptance criteria for Class 10, although some of the individual particle counts were above 30.

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APPENDIX C

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D	39	18	9	33	6	5	105	21.00
E	0	27	6	0	NR	4	33	8.25

(NR - no reading taken)

C10.2 Mean of averages (M).

$$M = (A_1 + A_2 + \ldots + A_L) / L \quad \text{(Equation 5-2)}$$

$$M = (15.00 + 20.25 + 14.25 + 21.00 + 8.25)/5 = 15.75$$

L = (Number of sample locations)

APPENDIX D

SOURCES OF SUPPLEMENTAL INFORMATION

D10. Scope. The purpose of this appendix is to list references for supplemental information which may provide instruction or guidance in the preparation of documents related to the design, acquisition, testing, operation, and maintenance of cleanrooms and clean zones. This listing of sources and documents emphasizes that information contained in such sources is not part of this standard and is not mandatory for compliance with this standard.

D20. Source references.

D20.1 AFWP - Headquarters, AFLC/DAPD, Wright-Patterson AFB, OH 45433

D20.2 AFWR - Warner Robins ALD/MMEDT, Robins AFB, GA 31098

D20.3 ANSI - American National Standards Institute, 1430 Broadway, New York, NY 10018

D20.4 ASHRAE - American Society of Heating, Refrigerating, and Air-Conditioning Engineers, 1791 Tullie Circle Northeast, Atlanta, GA 30329

D20.5 ASME - American Society of Mechanical Engineers, 345 East 47th Street, New York, NY 10017

D20.6 ASTM - American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103

D20.7 DOE - Nuclear Standards Management Center, Oak Ridge National Laboratory, Building 9204.1, Room 321, MS/10, P. O. Box Y, Oak Ridge, TN 37830

D20.8 IES - Institute of Environmental Sciences, 940 East Northwest Highway, Mount Prospect, IL 60056

D20.9 MSFC - Marshall Space Flight Center, NASA, Marshall Space Flight Center, AL 35812

D20.10 NPFC - The Naval Publications and Forms Center, 5801 Tabor Avenue, Philadelphia, PA 19120

D20.11 NRC - U.S. Nuclear Regulatory Commission, Attn: Director, Division of Document Control, P-130A, Washington, DC 20555

D20.12 NSF - National Sanitation Foundation, 3465 Plymouth Road, P. O. Box 1468, Ann Arbor, MI 48106

D20.13 NTIS - National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161

D30. Document references.

D30.1 Document No. AFM 88-4 Chapter 5 Source AFWP & AFWR
Title Criteria for Air Force Clean Facility Design and Construction
Abstract Prescribes criteria for the design and construction of Air Force clean facilities. It specifies the real property standards for meeting the requirements of Air Force T.O. 00-25-203.

D30.2 Document No. T.O. 00-25-203 Source AFWP & AFWR
Title Contamination Control of Aerospace Facilities, U.S. Air Force
Abstract This document specifies cleanroom design, operating, and test procedures. It also includes recommended cleanliness levels for typical operations.

D30.3 Document No. ASHRAE Std. 52-76 Source ASHRAE
Title Method of Testing Air-Cleaning Devices Used in General Ventilation for Removing Particulate Matter
Abstract This standard defines unified test procedures and apparatus for evaluating filters with efficiencies below that of HEPA filters.

D30.4 Document No. F 25 Source ASTM
Title Standard Method for Sizing and Counting Airborne Particulate Contamination in Clean Rooms and Other Dust-Controlled Areas Designed for Electronic and Similar Applications

D20.11 NRC - U.S. Nuclear Regulatory Commission, Attn: Director, Division of Document Control, P-130A, Washington, DC 20555

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D20.9 MSFC - Marshall Space Flight Center, NASA, Marshall Space Flight Center, AL 35812

D20.10 NPFC - The Naval Publications and Forms Center, 5801 Tabor Avenue, Philadelphia, PA 19120

	Abstract	Procedures are given for membrane filter sampling and microscope counting in clean areas.
D30.5	Document No.	F 50 Source ASTM
	Title	Standard Practice for Continuous Sizing and Counting of Airborne Particles in Dust-Controlled Areas Using Instruments Based upon Light Scattering Principles
	Abstract	Methods are given for sampling, particle counting, and data evaluation using light-scattering particle counters in cleanrooms.
D30.6	Document No.	F 91 Source ASTM
	Title	Standard Recommended Practice for Testing for Leaks in the Filters Associated with Lar nar Flow Clean Rooms and Clean Work Stations by the Use of a Condensation Nuclei Detector
	Abstract	Provides a method of testing the integrity of HEPA filter installations in laminar flow cleanrooms and clean work stations.
D30.7	Document No.	F 328 Source ASTM
	Title	Standard Practice for Determining Counting and Sizing Accuracy of an Airborne Particle Counter Using Near-Monodisperse Spherical Particulate Materials
	Abstract	Counting and sizing accuracy determination procedures are given for certifying operation of an optical airborne particle counter.
D30.8	Document No.	F 649 Source ASTM
	Title	Standard Practice for Secondary Calibration of Airborne Particle Counter Using Comparison Procedures
	Abstract	Procedures are given for fine-tuning the response of an airborne particle counter to match that of a standard

instrument for defining atmospheric dust, following calibration with monodisperse latex particles.

D30.9 Document No. F 661 Source ASTM
Title Standard Practice for Particle Count and Size Distribution Measurements in Batch Samples for Filter Evaluation Using an Optical Particle Counter
Abstract Procedures are given for sample handling, sample evaluation, and particle count and size analysis in batch samples for use in an optical single particle counter. The method is directed at samples obtained in filter testing, but can be used for any samples.

D30.10 Document No. IES-RP-CC-002 Source IES
Title Laminar Flow Clean Air Devices
Abstract Covers definitions, procedures for evaluating performance, and major requirements of laminar flow clean air devices. Sixteen test and performance criteria are considered.

D30.11 Document No. IES-RP-CC-001 Source IES
Title HEPA Filters
Abstract Recommends basic provisions for HEPA filters for use in clean air devices and cleanrooms. Five levels of performance and two grades of construction are included.

D30.12 Document No. IES-RP-CC-006 Source IES
Title Testing Clean Rooms
Abstract Describes test methods for characterizing the performance of cleanrooms. Performance tests are recommended for three types of cleanrooms at three operational phases.

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D30.11 Document No. IES-RP-CC-001 Source IES
Title HEPA Filters
Abstract Recommends basic provisions for HEPA filters for use in clean air devices and cleanrooms. Five levels of performance and two grades of construction are included.

D30.12 Document No. IES-RP-CC-006 Source IES
Title Testing Clean Rooms
Abstract Describes test methods for characterizing the performance of cleanrooms. Performance tests are recommended for three types of cleanrooms at three operational phases.

	Abstract	Procedures are given for membrane filter sampling and microscope counting in clean areas.
D30.5	Document No.	F 50 Source ASTM
	Title	Standard Practice for Continuous Sizing and Counting of Airborne Particles in Dust-Controlled Areas Using Instruments Based upon Light Scattering Principles
	Abstract	Methods are given for sampling, particle counting, and data evaluation using light-scattering particle counters in cleanrooms.
D30.6	Document No.	F 91 Source ASTM
	Title	Standard Recommended Practice for Testing for Leaks in the Filters Associated with Laminar Flow Clean Rooms and Clean Work Stations by the Use of a Condensation Nuclei Detector
	Abstract	Provides a method of testing the integrity of HEPA filter installations in laminar flow cleanrooms and clean work stations.
D30.7	Document No.	F 328 Source ASTM
	Title	Standard Practice for Determining Counting and Sizing Accuracy of an Airborne Particle Counter Using Near-Monodisperse Spherical Particulate Materials
	Abstract	Counting and sizing accuracy determination procedures are given for certifying operation of an optical airborne particle counter.
D30.8	Document No.	F 649 Source ASTM
	Title	Standard Practice for Secondary Calibration of Airborne Particle Counter Using Comparison Procedures
	Abstract	Procedures are given for fine-tuning the response of an airborne particle counter to match that of a standard

D30.13	Document No.	IES-RP-CC-013 Source IES
	Title	Recommended Practice for Equipment Calibration or Validation Procedures
	Abstract	This Recommended Practice covers definitions and procedures for calibrating instruments used for testing cleanrooms and clean air devices, and for determining intervals of calibration.
D30.14	Document No.	NHB 5340.2 Source MSFC
	Title	NASA Standards for Clean Rooms and Work Stations for the Microbially Controlled Environment
	Abstract	Establishes standard classes of air conditions (both total particles and viable particles) within cleanrooms and clean work stations for the microbially controlled environment.
D30.15	Document No.	IES-CC-009 Source IES
	Title	Compendium of Standards, Practices, Methods and Similar Documents Relating to Contamination Control
	Abstract	Listing of documents.
D30.16	Document No.	MIL-STD-45622 Source NPFC
	Title	Calibration Systems Requirements
	Abstract	Prescribes requirements for establishment and maintenance of a calibration system used to control the accuracy of measuring and test equipment.
D30.17	Document No.	MIL-F-51068 Source NPFC
	Title	Military Specification: Filter, Particulate, High-Efficiency, Fire Resistant
	Abstract	Covers design, construction, and performance of HEPA filters in six sizes and seven types.
D30.18	Document No.	MIL-F-51079 Source NPFC
	Title	Military Specification: Filter Medium, Fire-Resistant, High-Efficiency

	Abstract	Provides requirements and test methods for determining compliance for one grade of HEPA filter medium.
D30.19	Document No.	MIL-F-51477 Source NPFC
	Title	Military Specification: Filters, Particulate, High-Efficiency, Fire Resistant, Biological Use
	Abstract	Covers general requirements for particulate filters for use in air cleaning or air filtration systems involving chemical, carcinogenic, radiogenic, or hazardous biological particles.
D30.20	Document No.	NE: F3-41 Source DOE
	Title	In-Place Testing of HEPA Filter Systems by the Single-Particle, Particle-Size Spectrometer Method
	Abstract	Procedures are described for in-place testing of single and tandem HEPA filter installations with DOP challenge and an optical particle counter with sensitivity to 0.1 micrometer.
D30.21	Document No.	NASA SP-5045 Source NTIS
	Title	Contamination Control Principles
	Abstract	Broad overview and guidelines to those designing or planning cleanroom facilities.
D30.22	Document No.	NASA SP-5074 Source NTIS
	Title	Clean Room Technology
	Abstract	Considerable information on history, need, nature, and type of cleanrooms with details of cleanroom environment and operation.
D30.23	Document No.	NASA SP-5076 Source NTIS
	Title	Contamination Control Handbook
	Abstract	Extensive detail on contaminants and their control and cleaning methods.

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	Title	Military Specification: Filter Medium, Fire-Resistant, High-Efficiency

D30.24	Document No.	F 24 Source ASTM
	Title	Measuring and Counting Particulate Contamination on Surfaces
	Abstract	A method for size distribution analysis of particulate contamination, 5 micrometers and larger, either on, or washed from, surfaces of small electronic device components.
D30.25	Document No.	F 51 Source ASTM
	Title	Sizing and Counting Particulate Contaminant In and On Clean Room Garments
	Abstract	A membrane filter/microscope method for determining detachable particulate contaminants, 5 micrometers and larger, on cleanroom garments.
D30.26	Document No.	MIL-HDBK-406 Source NPFC
	Title	Contamination Control Technology - Cleaning Materials for Precision Precleaning and Use in Clean Rooms and Clean Work Stations
	Abstract	Extensive information on selection and use of cleaning materials developed by DOD.
D30.27	Document No.	MIL-HDBK-407 Source NPFC
	Title	Contamination Control Technology - Precision Cleaning Methods and Procedures
	Abstract	Extensive information on cleaning methods used by the military services for gross and precision cleaning of work processed under controlled environment conditions.

APPENDIX E

GLOSSARY

E10. Scope. This appendix lists terms used in the other appendixes, for which further explanation in the context of such use may benefit the user.

E20. List of terms.

E20.1 Isokinetic. A term describing a condition of sampling, in which the velocity of gas into the sampling device (at the opening or face of the inlet) has the same velocity rate and direction as the ambient atmosphere being sampled.

E20.2 Isotropic particles. Particles with equal, uniform physical and chemical properties along all axes.

E20.3 Membrane filter. Porous membrane composed of pure and biologically inert cellulose esters, polyethylene, or other materials through which the air stream is passed for the purposes of filtration.

E20.4 Reynolds number. A dimensionless number which is significant in the design of a model of any system in which the effect of viscosity is important in controlling the velocities or the flow pattern of a fluid: equal to the density of a fluid times its velocity, times a characteristic length, divided by the fluid viscosity.

PREPARING ACTIVITY:

GSA-FSS

APPENDIX E

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PREPARING ACTIVITY:

GSA-FSS

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STANDARD OPERATING PROCEDURE

Procedure: Product Recall Field Correction and Withdrawal

Procedure No.: PL-114

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1.0 PURPOSE

To provide a uniform, consistent, and comprehensive action plan for dealing with those situations where action may be required with respect to materials which have left Plastafil's control. This procedure concerns those decisions and actions with respect to recall of product from distribution channels, field correction, and market withdrawal.

2.0 SCOPE

All products bearing Plastafil labeling in distribution

3.0 APPLICABLE DOCUMENTS

3.1 Market Withdrawal Request
3.2 Product Recall Request
3.3 Product Field Correction Request
3.4 Product Recall Notice
3.5 Field Correction Notice
3.6 Product Withdrawal Notice
3.7 Failure Reporting, PL-154
3.8 Failure Investigation, PL-157
3.9 Customer Complaints, PL-153

4.0 GENERAL

4.1 Definitions:

4.1.1 Recall -- removal of a marketed product from the customer or from distribution channels beyond Plastafil's control.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By

STANDARD OPERATING PROCEDURE

Procedure : Product Recall Field Correction and Withdrawal

Procedure No.: PL-114

4.1.2 Field Correction -- relabeling, inspection, modification, or destruction without return to Plastafil with such actions taken at the initiation of Plastafil.

4.1.3 Market Withdrawal -- discontinue product.

4.2 Recalls are classified by FDA into three classes. These are:

Class I - A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

Class II - A situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Class III - A situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.

4.3 Recall communications can be by telegrams, mailgrams, or first class letters conspicuously marked in bold type on the letter and envelope in red "Medical Device Recall (or Correction)". If a letter is sent, the letter should be marked "Urgent" for Class I and II recalls and for Class III when appropriate. Telephone or other personal contacts should be confirmed by the above appropriate method.

4.4 No recall, field correction, or market withdrawal action whether verbally or in writing shall be initiated without the approval of the President.

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STANDARD OPERATING PROCEDURE

Procedure : Product Recall Field Correction and Withdrawal

Procedure No. : PL-114

5.0 PROCEDURE

5.1 A Recall/Field Correction Review Board shall be established. This Board shall consist of the same members as constitute the Quality Review Board. Other appropriate disciplines may be asked to participate in the decision of the Board.

5.2 The purpose of the Board is to review all information concerning individual lots or products which may require recall or field correction, decide whether such actions are necessary or appropriate, initiate such actions, oversee these actions, and assure effectiveness. This review shall be documented as appropriate.

5.3 Lots or products requiring review as a potential recall or field correction situation are:

5.3.1 Lot(s) or portions of lots in distribution which subsequent information indicates have a potential for failure to meet a critical specification or usage requirement.

5.3.2 Lot(s) or portions of lots in distribution where real or suspected injury or damage through use of the item has been reported or is suspect.

5.3.3 Lot(s) or portions of lots in distribution which is confirmed or is suspect of being in violation of statutory, labeling, or regulatory regulations or requirements

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Procedure: Product Recall Field Correction and Withdrawal

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5.3.4 Lot(s) or portions of lots in distribution which subsequent information indicates may contain individual product which may be mislabeled, misbranded, adulterated, or contain an incorrect component, an improper component, or have a component missing where such incorrect, improper, or missing component could result in a significant performance, safety, regulatory, or statutory issue.

5.3.5 Lot(s) or portions of lots in distribution which have been manufactured using equipment or techniques subsequently found or believed to be suspect.

5.3.6 Lot(s) or portions of lots in distribution where subsequent information indicates that such was manufactured or held under questionable environmental conditions.

5.3.7 Lot(s) in distribution which are the subject of significant number of confirmed complaints.

5.3.8 A management decision concerning the Plastafil image.

5.4 All personnel shall be constantly on the alert for indications or evidence when investigating and evaluating customer complaints and failure investigations and when evaluating lot failures or problems or indications that the conditions under 5.3 above may exist.

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STANDARD OPERATING PROCEDURE

Procedure : Product Recall Field Correction and Withdrawal

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5.5 As promptly as is practical after plant personnel discover or believe that a potential recall situation exists, such personnel shall immediately notify Quality Assurance.

5.6 Quality Assurance shall make a preliminary investigation of the report and if the information appears to support the belief that a recall or field correction is necessary, promptly call a meeting of the Recall/Field Correction Review Board, initiates Product Recall Request, or Product Field Correction Request as appropriate. If no action is determined to be necessary as the result of this investigation, Quality Assurance documents the findings and circulates a report to all Board members and files a copy with the records for the subject lot.

5.7 The Board shall promptly review information and data and determine a course of action. Such actions may include but not be limited to:

5.7.1 Request additional testing, investigations, or other to confirm the problem and to determine corrective actions required.

5.7.2 Initiate product recall, market withdrawal, or field correction after obtaining approval from the President. These decisions shall also include the depth and extent of such actions to be initiated and the timeframe.

5.7.3 Advise customers or users of the suspected or real condition(s) with or without recommending action(s) to be taken by the customer or user.

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Procedure : Product Recall Field Correction and Withdrawal

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5.7.4 Determine, based on information and/or data, that a significant situation does not exist and that no action with respect to material which has left Plastafil's control is warranted.

5.8 Product Recall

5.8.1 Product recall shall normally be indicated for the most serious types of deficiencies where the continued presence of product in the hands of a customer or user presents a significant risk or hazard. It also may be indicated if corrections in the field are impossible, unacceptable, difficult, or inappropriate.

5.8.2 Should product recall be indicated, the Board shall appoint a Recall Manager. This individual shall determine the number and kinds of personnel necessary to assist in carrying out the recall.

5.8.3 The Recall Manager shall establish a task force which shall obtain customer lists and generate the means for notifying customers or users as shall be appropriate for the extent and depth of the recall. Such means shall include letter (Product Recall Notice), telephone, telegram, etc. as appropriate. (Recalls based on conditions likely to cause serious or imminent hazards require appropriate means for notification.)

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Procedure : Product Recall Field Correction and Withdrawal

Procedure No. : PL-114

5.8.4 The Recall Manager shall reconcile amounts by batch/lot of product to manufactured amounts to amounts shipped to amounts returned. This will be reported weekly or at appropriate intervals to the President.

5.8.5 Quality Assurance shall audit the recall to assure that it has been effective in notifying all consignees and will report to the Board the results of this audit.

5.8.6 The Recall Manager shall report completion of the recall to the President.

5.8.7 Quality Assurance shall determine final disposition of the recovered material.

5.8.8 Finance shall report total cost to the President.

5.9 Field Correction

5.9.1 Manufacturing, Quality Assurance, and Marketing shall agree on the method and mechanism for field correction.

5.9.2 Marketing shall be responsible for initiating and implementing the field correction within the timeframe specified in accordance with 5.7.2 above, sends out Field Correction Notice, to the field sales force indicating what actions are necessary, how to carry out the task and the reporting requirements. Marketing shall issue periodic and timely reports on the status and effectiveness of the field correction. These reports shall be made to the Board.

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5.9.3 Quality Assurance shall audit the effectiveness of the field correction and shall report to the Board the results of the audit.

5.9.4 The Finance shall report total cost to the President.

5.10 Market Withdrawal

5.10.1 Marketing shall be responsible for all aspects of a market withdrawal, including but not limited to customer notification, replacement, where appropriate, etc. Marketing shall issue periodic and timely reports as to status and effectiveness.

5.11 The President

5.11.1 The President shall determine if federal, state and/or local agencies shall be notified concerning actions and contemplated actions and make a recommendation to the Recall/Field Correction Review Board (see Failure Reporting, PL-154).

5.11.2 The President shall initiate such notifications and provide the necessary reports during the action and at completion concerning its effectiveness to the Board.

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Request No._____

MARKET WITHDRAWAL REQUEST

Product	Package Size(s)	Est. Quantity Distributed

1. Reason for request:

2. Recommended procedure:

3. Approvals:

Marketing	President

Requestor	Signature	Date

cc: Quality Assurance
Marketing
President

PRR No._____

QA Use Only
Date Instituted
Date Int Rpt to FDA
Date Completed
Date of Audit by QA

PRODUCT RECALL REQUEST

Product	Lot No.	Pkg Size	Quan in Distribution

1. Description of problem/condition:

2. Details of investigation (cause, extent, etc.):

3. Recommended action (extent and depth of recall):

4. Review Board action:

Review Date_____
Recommendation_____

_____
Review Board Chairman

5. Action approved:

_____
President

Requestor	Signature	Date

cc: President
Quality Assurance
Marketing
Manufacturing

Request No._____

QA Use Only
Date Instituted
Date Int Rpt to FDA
Date Completed
Date of Audit by QA

PRODUCT FIELD CORRECTION REQUEST

Product	Lot No.	Pkg Size	Quan in Distribution

1. Description of problem/condition:

2. Details of investigation (cause, extent, etc.):

3. Recommended action:

4. Review Board action:

Review Date_____
Recommendation_____

_____
Review Board Chairman

5. Action approved:

_____
President

Requestor	Signature	Date

cc: President
Quality Assurance
Marketing
Manufacturing

PRODUCT RECALL NOTICE

IMPORTANT: MEDICAL DEVICE RECALL

RE: _____

Attention:

This is to advise you that _____

The reason for this recall is _____

_____

Please examine your stocks for lot _____ and discontinue use immediately. Determine your inventory and complete and return the attached self-addressed, postage-paid card.

Promptly return your inventory to _____. Appropriate credit will be issued for all packages returned.

Please check your distribution records and advise us promptly as to which of your customers has received this lot.

This action is voluntary on the part of Plastafil and is made with the knowledge of the Food and Drug Administration.

Your prompt asistance is appreciated.

Sincerely,

Quality Assurance

RE: FIELD CORRECTION NOTICE

TO: Field Sales Force

Lot_____ of Product _____ has been shipped to the following customers in your territory:

Customers	Location

Please arrange to visit these customers at your earliest convenience, examine all stock still in inventory of the above Lot and perform the following actions:

1. Action to be Taken:

2. Method to be Used:

3. Records to be Maintained:

Your prompt action is requested.

Sincerely,

Marketing

PRODUCT WITHDRAWAL NOTICE

RE: _____

Attention:

This is to advise you that Plastafil has decided to discontinue the distribution of _____.

This action is taken because _____

_____

_____

Sincerely,

Marketing

STANDARD OPERATING PROCEDURE

Procedure : Environmental Monitoring of Controlled Environment Area

Procedure No.: PL-115

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1.0 PURPOSE

To describe the program and procedures for monitoring the controlled environment areas for the environmental parameters described below.

2.0 SCOPE

2.1 This procedure applies to the controlled environment areas in manufacturing and the laminar flow work sations in these areas.

2.2 Quality Assurance personnel are responsible for monitoring the controlled environment areas and maintaining this program.

2.3 The controlled environment areas are monitored for temperature, relative humidity, air pressure and particulates. Non-viable particulates are monitored by an approved contractor.

2.4 Warehouse, laboratory, general office and shipping areas are not monitored under this procedure.

3.0 APPLICABLE DOCUMENTS

3.1 Daily Monitoring Record

3.2 Plate Count Records

3.3 Contractor Reports

3.4 P1-128, Performing Air Pressure Differential Test

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By

STANDARD OPERATING PROCEDURE

Procedure: Environmental Monitoring of Controlled Environment Area

Procedure No.: PL-115

4.0 GENERAL

4.1 Controlled environment area refers to manufacturing areas in which the air supply is filtered through high efficiency particulate air (HEPA) filters. The air pressure in relation to adjacent areas, temperature and relative humidity are controlled.

4.2 Materials required:

4.2.1 Thermometers
4.2.2 Petri Dishes
4.2.3 Humidity Gage

4.3 These procedures are performed and followed only when products are being processed in these areas.

4.4 Personnel performing monitoring shall conform to the gowning and other requirements before entry into each area.

5.0 PROCEDURE

5.1 Temperature, Relative Humidity, Air Pressure

5.1.1 Record the temperature in the controlled environment each day in the afternoon.

5.1.1.1 Acceptable temperature range is 15-25°C

5.1.2 Record the relative humidity reading each day in the afternoon.

5.1.2.1 Acceptable range is 20-60%

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STANDARD OPERATING PROCEDURE

Procedure: Environmental Monitoring of Controlled Environment Area

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5.1.3 Check for proper air pressure differential between the controlled environment area and the adjacent area daily. (Follow Procedure PL-128, Performing Air Pressure Differential Test). Record results.

5.1.4 In the event a parameter is out of range, notify the appropriate supervision. Investigate and evaluate effects on products in process during period of deviation.

5.2 Non-viable Particulates

5.2.1 Maintains list of approved contractors.

5.2.2 Schedules, coordinates and accompanies the contractor during monitoring. Assures contractor adheres to gowning requirements.

5.2.3 Measures airborne particulates according to the following:

5.2.3.1 Manufacturing laminar flow work stations and surrounding area are monitored at least every three months. This monitoring takes place during use.

5.2.3.2 Performs particulate counting in accordance with the instructions for the specific unit.

5.2.3.3 Reports results to Quality Assurance and the President.

5.2.3.4 Limits:

Laminar Flow Work Stations: approximately 100 particles per cubic foot greater than 5 microns in size.

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STANDARD OPERATING PROCEDURE

Procedure : Enviromental Monitoring of Controlled Environment Area

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Surrounding Area: approximately 10,000 particles per cubic foot greater than 5 microns in size.

5.3 Viable Particulate Monitoring

5.3.1 Sample Sites

5.3.1.1 Divide each room into grids of equal size. Assign coordinate numbers along the longer wall and letters for coordinate designations along the shorter wall.

5.3.1.2 Any particular site may not be sampled consecutively. Alternate sample sites so each area is sampled over a period of time. Sample at the approximate working level in the room.

5.3.1.3 For sampling conducted in laminar flow work stations during manufacturing operations, sample within one foot of critical operations.

5.3.2 Sampling Frequency

5.3.2.1 For controlled environment areas, sample each room on a monthly basis. Take two samples per room.

5.3.2.2 For laminar flow work stations, sample once per week. Take two samples per work station.

5.3.2.3 During aseptic operations, sample in the vicinity of the operations. Sample during the entire process.

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STANDARD OPERATING PROCEDURE

Procedure: Environmental Monitoring of Controlled Environment Area

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5.3.3 Sampling Procedure

5.3.3.1 Use 100 x 15 mm petri dishes containing sterile Trypticase Soy Agar.

5.3.3.2 Place agar plate in sampling location and remove cover for 30 minutes.

5.3.3.3 Replace cover and incubate at 30-35°C for 72 hours and then at 20-25°C for 96 hours.

5.3.3.4 Count colonies. Record results on the testing report.

5.3.3.5 Plot results using graph paper to establish trending for each room and work station.

5.3.4 Limits

5.3.4.1 Counts in controlled environment areas should not exceed 25 colonies/plate.

5.3.4.2 Counts in Laminar Flow Work Stations should not exceed 5 colonies/plate.

5.4 In the event that limits for viable or non-viable particulates are exceeded, notify the President of the deviation.

5.4.1 Re-sample area. If results continue to exceed limits, discontinue work in the area until the problem can be corrected. Possible action may include, but is not limited to:

- Changing work flow patterns or activities
- Cleaning and sanitizing equipment and work areas
- Repairing leak in filter
- Replacing filter

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Procedure: Environmental Monitoring of Controlled Environment Area

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Document action taken and demonstrate that the problem has been resolved by further sampling

5.4.2 In the event limits are exceeded during manufacturing operations in the laminar flow work station, issue a report to the Quality Review Board. The possible cause of the deviation should be investigated and the impact on the product evaluated. The above are documented.

5.4.3 All sampling data and monitoring results and accompanying documentation are maintained permanently in the Quality Assurance files.

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STANDARD OPERATING PROCEDURE

Procedure : Environmental Monitoring of Controlled Environment Area

Procedure No. : PL-115

Month _____ Year _____

DAILY MONITORING RECORD

Day	Temperature	Humidity	Air Pressure	Monitor
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
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STANDARD OPERATING PROCEDURE

Procedure: CERTIFICATION OF LAMINAR FLOW WORK STATIONS

Procedure No.: PL-116

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1.0 PURPOSE

To describe the procedures and test methods used to evaluate the performance of laminar flow work stations.

2.0 PRINCIPLES

A laminar flow work station refers to an enclosed work bench in which its air supply is filtered through high efficiency particulate air (HEPA) filters and makes a single pass through the work area in a parallel flow pattern.

The laminar flow work station is evaluated for two parameters in this study. Air flow velocity and uniformity is evaluated to determine the average air flow velocity and the uniformity of the velocity through the filters. An installation leak test is conducted to verify the absence of bypass leakage in the filter installation and to detect leaks in the filter medium.

3.0 SCOPE

This procedure is applicable to all laminar flow work stations. The following tests may be conducted by an approved outside contractor according to these procedures.

4.0 APPLICABLE DOCUMENTS

4.1 PL-111: Certification of Equipment, System and Process.

4.2 PL-113: Certification of Controlled Environment Area.

4.3 PL-115: Environmental Monitoring of Controlled Environment Areas.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By

STANDARD OPERATING PROCEDURE

Procedure: CERTIFICATION OF LAMINAR FLOW WORK STATIONS

Procedure No.: PL-116

4.4 Federal Standard 209-D, Clean Room and Work Station Requirements for Controlled Environment.

4.5 Testing Clean Rooms, Recommended Practice, Institute of Enviromental Sciences, 1984.

5.0 SAFETY PRECAUTIONS

Diocytl Phthalate is potentially carcinogenic for man. Wear an OSHA/MSHA approved respirator, protective clothing, gloves, and safety goggles while working with this chemical.

6.0 MATERIALS AND EQUIPMENT

6.1 Hot wire or vane-type anemometer, accurate to within ± 3% of the scale reading over the range of velocity to be measured. Instrument should be within current calibration.

6.2 Aerosol Generator.

6.3 Aerosol photometer with a logarithmic or linear readout. The sampling flow rate should 1.0 (± 0.1) ft^3/min. Instrument should be wihin current calibration.

7.0 PROCEDURE

7.1 Air flow velocity and uniformity test.

7.1.1 Divide the filter face area into grids of equal area. The area of each grid should not exceed 4 ft^2.

7.1.2 Position the anemometer at the approximate center of each grid point. The probe should be no closer than one inch or no more than 12 inches from the filter face.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: CERTIFICATION OF LAMINAR FLOW WORK STATIONS

Procedure No.: PL-116

7.1.3 Take the measurement for not less than five seconds. Use the average of the measurements during the period as the reported value.

7.1.4 Record the measurement for each grid point on a schematic diagram.

7.2 HEPA Filter Installation Leak Test

7.2.1 Conduct test according to PL-113, 7.2.1 - 7.2.3

8.0 DATA ANALYSIS

8.1 Air Flow Velocity and Uniformity Test

8.1.1 Calculate the arithmetic mean of all readings across the filter face and report as average airflow velocity in feet/min.

8.1.2 Calculate the limits for airflow uniformity equal to the average airflow velocity ± 20%.

8.1.3 Acceptance Criteria

Airflow velocity at not less than 90 feet/minute and uniformity ± 20% of the average velocity across the filter face.

8.2 HEPA Filter Installation Leak Test

8.2.1 For a linear readout photometer a reading greater than 0.01% of the upstream challenge concentration indicates a leak. For a logarithmic readout, a reading greater than one scale division indicates a leak.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: CERTIFICATION OF LAMINAR FLOW WORK STATIONS

Procedure No.: PL-116

8.2.2 Record the location of any leaks detected.

8.2.3 HEPA filters may be repaired by caulking; however, not more than 5% of the filter area may be caulked and the dimensions of each repair may not exceed 1.5 inches.

9.0 RECORDING AND REPORTING OF DATA

9.1 Compile all data obtained in a permanent folder along with a summary of the results. Describe any problems that were encountered during conducting these studies and what actions were taken to correct them. Obtain a Validation Task Report Number and submit the report to the Validation Review Board for review and approval.

9.2 Upon review of the above, if the Validation Review Board finds that the documentation reflects that the acceptance criteria have been met, verify the approval by signature on the Certification Document.

9.3 Upon completion of the above, the laminar flow work station is considered operational and is certified for use in manufacturing operations.

9.4 The controlled environment area if recertified annually ± 30 days.

9.5 Monitoring is conducted according to PL-115.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Assigning Receiving Numbers

Procedure No.: PL-117

Revision Record	
Page	**Date**
1	
2	
3	

1.0 PURPOSE

1.1 To describe the procedures used when assigning a receiving number.

2.0 SCOPE

2.1 This procedure applies to personnel in the Receiving Area.

2.2 This procedure applies only to items with an assigned part number otherwise referred to as inventoried items.

3.0 APPLICABLE DOCUMENTS

3.1 Receiving Number Log

3.2 Inventory Card Form

3.3 Receiving Log

3.4 Receiving Procedures, PL-104

4.0 GENERAL

4.1 A receiving number is defined as a control or lot number for inventoried items received at Plastafil and used to provide traceability back to the vendor.

4.2 Every individual inventoried item received shall have a receiving number assigned to it.

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure: Assigning Receiving Numbers

Procedure No.: PL-117

4.3 Only inventory items will have an inventory card form initiated for the material.

4.4 Inventory items will be identified on the purchase order by a part number.

4.5 Receiving numbers will be assigned sequentially beginning with A1000 to A9999, B1000 to B9999 until Z9999 is reached.

4.6 The Material Name for inventory items shall be consistent with the item specifications.

4.7 No receiving number will be reissued once assigned.

4.8 Identical materials of the same manufacturers' lot number and received at the same time will be given the same receiving number. Both conditions must be met otherwise a new receiving number will be given.

5.0 PROCEDURE

5.1 Receive the materials according to PL-104 Receiving Procedure.

5.2 Record the inventoried item name in the receiving number assignment log beside the next number in the sequential order and enter the date received.

5.3 Record the part number in the appropriate space.

5.4 Fill out an inventory card with the proper information.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Assigning Receiving Numbers

Procedure No.: PL-117

INVENTORY CARD

Card Number _____

Part Number _____ Receiving Number _____

Item Name _____

Vendor _____ Vendor Lot _____

P.O. Number _____ Quantity _____ in _____ Containers

Use Before _____ Storage Conditions _____ Inv. Loc. _____

Date	Purpose of Use (Lot Number)	Container Number	Quantity Removed	Balance	Completed By	Checked By

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure: Requesting a Part Number

Procedure No.: PL-118

Revision Record	
Page	Date
1	
2	
3	

1.0 PURPOSE

1.1 To detail the procedure for requesting a part number for a new item to be inventoried and used in product for which a part number has not been previously assigned.

2.0 SCOPE

2.1 This procedure applies to personnel who have determined the need for a new part number.

3.0 APPLICABLE DOCUMENTS

3.1 Request for Part Number Form

3.2 Part Number Assignment, PL-119

4.0 GENERAL

4.1 An individual appointed by Management will assign the part number and its classification.

4.2 This individual will make all entries on the side of the request form with the heading of "Part Number Assignment".

4.3 Item specifications are not required for part number assignment but can be developed subsequently.

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure: Requesting A Part Number

Procedure No.: PL-118

5.0 PROCEDURE

5.1 Obtain the Part Number Request Form.

5.2 Fill out the top part of the request form with the heading "Part Number Request Form".

5.2.1 Fill out the request form completely making sure all entries are accurate. Avoid leaving blanks as all information requested is essential for both purchasing and quality testing.

5.3 Obtain an approval signature from your immediate supervisor.

5.4 Submit the completed form to your supervisor.

5.5 Follow PL-119 to assign a part number.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Requesting A Part Number

Procedure No.: PL-118

PART NUMBER REQUEST

Requested By:_____ Date Needed:_____

Description: _____

_____

Where Used (be specific):_____

_____

Primary Vendor/Catg. #:_____

Alternate Vendor/Catg. #:_____

Grades Recommended:_____

Special Concerns:_____

Storage Conditions:_____

Synonyms:_____

Safety Concerns:_____

_____

Originating Approval:_____Date:_____

Assigned P/N:_____

Official Description:_____

_____

_____

Assigned By:_____Date:_____

Approval:_____Date:_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Part Number Assignment

Procedure No.: PL-119

Revision Record	
Page	Date
1	
2	
3	
4	

1.0 PURPOSE

To detail the procedure for consistently assigning part numbers.

2.0 SCOPE

This procedure applies to Manufacturing supervision.

3.0 APPLICABLE DOCUMENTS

3.1 Part Number Assignment Log Book

3.2 Completed Part Number Request

4.0 GENERAL

4.1 Part Item specifications can be developed before or after a part number is assigned, as long as a vendor and catalog number has been provided.

4.2 Part Item specifications will be defined by Quality Assurance, although input from others may be necessary.

4.3 Part numbers are not to be reused.

5.0 PROCEDURE

5.1 Review the completed Part Number Request form for appropriate information.

5.1.1 Verify that the request form has been approved.

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Approved By	Q.A.		Approved By	Mfg	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure: Part Number Assignment

Procedure No.: PL-119

5.2 Classify material for part number assignment according to table below.

Part Numbers	Inventory Type
0100 to 0999	Product Components
1000 to 1999	Packaging Material with Product Contact
2000 to 2999	Packaging Material without Product Contact
3000 to 3999	Labels
4000 to 4999	Intermediate, and subassemblies -- primarily inhouse
5000 to 5999	Product
6000 to 6999	Final Packaged Product

5.3 Determine the next sequential number within that classification and assign it to that item.

5.4 In the Part Number Assignment Log Book, record the item name next to the assigned number with any qualifiers which could segregate this material from a similar item (e.g., USP, anhydrous or heptahydrate, fill volumes, concentration, etc.)

5.5 Record the item name and part number on the Part Number Request form.

5.6 Inform the requestor of the assigned part number by forwarding a photocopy of the front page of the assignment form.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Part Number Assignment

Procedure No.: PL-119

5.7 Photocopy and submit a second copy of the front page to Quality Assurance for development of specifications and testing requirements.

5.8 Fill out the balance of the part number request form ensuring that all entries are accurate.

5.8.1 Check all entries for completeness and accuracy.

5.9 Place the original request form in the Part Number Request Log.

5.10 Determine and order the appropriate quantity of material as needed.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : Part Number Assignment

Procedure No. : PL-119

PART NUMBER ASSIGNMENT

PART NUMBER: _____

DESCRIPTION: _____

_____

PURCHASING U/M: _____

SHELF LIFE: _____

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure: Control of Inventoried Items

Procedure No.: PL-120

Revision Record	
Page	Date
1	
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1.0 PURPOSE

1.1 The purpose of this procedure is to describe the method of recording usage of inventoried items.

2.0 SCOPE

2.1 This procedure applies to any employee who removes an inventoried item for any purpose.

2.2 This procedure also applies to any deduction of items prior to their release, e.g., samples withdrawn for assay purposes.

3.0 APPLICABLE DOCUMENTS

3.1 Inventory Card Form

3.2 Part Number Assignment, PL-119

3.3 Batch Record

3.4 Shipping Notices

4.0 GENERAL

4.1 Follow all safety rules as they apply the te safe handling and use of any items.

4.2 By definition, inventoried items are those items assigned a part number as outlined in PL-119.

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By

STANDARD OPERATING PROCEDURE

Procedure : Control of Inventoried Items

Procedure No. : PL-120

4.3 Items are generally removed from inventory via an Inventory Transfer Form; as determined on the batch record; or via Shipping Notices.

4.4 Only Manufacturing employees are approved to remove any item from a released inventory.

4.5 Only Quality Assurance personnel are approved to remove items from a quarantined inventory, however, proper deductions must be made on the assigned inventory card.

4.6 See PL-121 for dispensing raw materials.

5.0 PROCEDURE

5.1 Prior to the removal of any inventoried items, locate the correct corresponding inventory card for that item.

NOTE: This also applies to deductions made by Quality Assurance prior to release of the item.

5.2 Locate the inventoried item.

5.3 Check that the part number and receiving numbers match the inventory card.

5.4 Check for the use before date (if present).

5.4.1 If past date, notify Quality Assurance and remove from the released area immediately.

5.5 Check quantity on hand of te requested part number.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Control of Inventoried Items

Procedure No.: PL-120

5.5.1 If item requested is not manufacturing specific, inform the manufacturing supervisor so a determination can be made as to whether the item can be spared from future manufacturing needs.

5.5.1.1 If approved, proceed to the next step. If not approved, inform requestor.

5.5.2 If quantity is short, and no other receiving number exists, inform requestor and supervisor.

5.6 Remove the requested amount of the item from inventory.

5.6.1 Items are requested via batch record bill of materials, Inventory Transfer Forms or Shipping Notices.

5.7 Document the removal on the inventory card, making proper deductions and initial and date the entry.

5.8 Return the inventory card to its proper location.

5.9 Transfer the materials to the indicated individual, location, or secured holding area.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Control of Inventoried Items

Procedure No.: PL-120

Card Number_____

Part Number_____ Receiving Number_____

Item Name_____

Vendor_____ Vendor Lot_____

P.O. Number_____ Quantity_____in_____Containers

Use Before_____ Storage Conditions_____ Inv. Loc._____

Date	Purpose of Use (Lot Number)	Container Number	Quantity Removed	Balance	Completed By	Checked By

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Control of Inventoried Items

Procedure No.: PL-120

INVENTORY TRANSFER FORM

NAME _____ DATE _____

REASON FOR TRANSFER _____

	Item Description	Part No.	Lot/Rec. No.	Amt. Required
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				
9.				
10.				
11.				
12.				
13.				
14.				
15.				

APPROVAL _____ DATE _____

TRANSFERRED BY _____ DATE _____

RECEIVED BY _____ DATE _____

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure: Dispensing Raw Materials, In-Process Materials or Packaging Components

Procedure No.: PL-121

Revision Record	
Page	Date

1.0 PURPOSE

1.1 To describe the procedure for dispensing released raw or in-process materials, or packaging components and the proper documentation associated with this activity.

2.0 SCOPE

2.1 This procedure applies to all personnel approved to dispense released materials.

3.0 APPLICABLE DOCUMENTS

3.1 Material Requisition Form

3.2 Safety Manual

4.0 GENERAL

4.1 Follow all safety policies as they apply to the safe handling and use of any chemical raw material (see Safety Manual).

4.2 Equipment Required:

4.2.1 Calibrated scales or balance.

4.2.2 Appropriate size beakers, flasks, cylinders, etc.

4.2.3 Assorted spatulas, pipettes

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By

STANDARD OPERATING PROCEDURE

Procedure: Dispensing Raw Materials, In-Process Materials or Packaging Components

Procedure No.: PL-121

5.4 Locate the raw materials to be weighed and bring to the area designated for dispensing.

5.4.1 If there is more than one receiving number of a raw material in inventory, the general rule is to use the oldest unexpired material first unless a specific lot to be dispensed is indicated on the request.

5.4.2 Check that the gross weight has been entered on the container. If not, take the gross weight and make the entry on the label on the container.

5.5 Inspect the container part number, receiving number and container number against the requisition or pick list to verify that they are correct.

5.6 Check that the material is released and has a green Quality Assurance release ticket attached and that the "Retest" date has not passed.

5.7 Weigh or measure each item independently.

Note 1: If dispensing per a request outside of manufacturing processing only one employee is required for the procedure.

Note 2: If dispensing (issuing) packaging components proceed to Step 5.9.

5.7.1 No more than one chemical raw material is to be weighed/ at a time in the area designated for dispensing.

5.7.2 Use appropriate clean scoops, spatulas, etc., for dispensing and clean containers for holding dispensed materials.

5.7.3 All weights (gross, tare and net weights) and measures are to be verified by each employee.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Dispensing Raw Materials, In-Process Materials or Packaging Components

Procedure No.: PL-121

MATERIAL REQUISITION FORM

DATE_____

REQUESTOR_____

MFG APPROVAL_____

FOR MANUFCTURING USE ONLY

REQ. NO.:

POSTED BY/DATE_____

	PART NO.	DESCRIPTION	AMOUNT	LOT/REC NO.	FROM WRHS/LOCATION	TO W.O./ ACCT. NO.	POSTED
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

RECEIVED BY/DATE_____

TRANSFERRED BY/DATE_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Equipment Cleaning and Use Log

Procedure No.: PL-122

4.5 Completed log books are returned for filing.

4.6 Any damaged log is submitted to manufacturing supervisor for a replacement.

5.0 PROCEDURE

5.1 Enter the control number in the space provided. This number is either the lot number or the cycle number of a sterilizing and/or depyrogenating process.

5.1.1 Enter N/A under control number if maintenance, cleaning, calibration or other similar function is performed.

5.2 Supervisor periodically reviews entries in the log for completeness and accuracy. Initial if entries are correct.

5.2.1 If entries are not satisfactory (i.e., documentation errors, cross-outs, blanks, etc.), contact the operator for implementation of corrective action.

5.3 Enter the date and time in the columns provided for each job performed.

5.4 Describe the function performed in the column labeled "Description".

5.4.1 Enter the lot name when equipment is used for manufacturing.

5.4.2 Enter "cleaning" when the entry is for cleaning the equipment per the specified S.O.P.

5.4.3 Describe briefly the maintenance performd for the equipment in this column.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Equipment Cleaning and Use Log

Procedure No.: PL-122

5.4.4 Describe any other job performed on the equipment (e.g., calibration, validation, etc.).

5.5 Describe the process in the column provided for "Process Description".

5.5.1 The process description consists of cycle parameters.

5.5.2 Enter N/A if the column is not used.

5.6 Enter the validation or S.O.P. number followed for the function described in 5.4.

5.6.1 Enter N/A if no S.O.P. or validated cycle is available.

5.7 Enter initials or signature for the entries made for each function or description to verify that it is performed (5.4).

5.7.1 Check that all entries are complete and accurate.

5.8 Sign the Equipment Clean Ticket for any equipment cleaned and attach to the equipment or to the room door.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : Equipment Cleaning and Use Log

Procedure No.: PL-122

EQUIPMENT CLEANING AND USE LOG

Equipment Name_____

Equipment Identification Number_____

Date Log Started_____

Date Log Ended_____

Control/ Lot No.	Date	Time	Description	Process Description	S.O.P./ Validation	Performed/ Used By	Verified By	Reviewed By

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Equipment Cleaning and Use Log

Procedure No. : PL-122

EQUIPMENT CLEAN TICKET

Previous Lot Name_____

Previous Lot Number_____

Equipment/Item Description:_____

_____

ID #_____

Cleaned By/Date_____

Lot Number_____

Lot Name_____

Date_____

Sterilization/Depyrogenation_____

_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Cleaning Procedures For Class 100 Hoods	**Revision Record** Page	Date
Procedure No. : PL-123	1	
	2	
	3	

1.0 PURPOSE

1.1 The purpose of this procedure is to describe the method of cleaning the laminar flow hoods located in the manufacturing areas.

2.0 SCOPE

2.1 This procedure applies to all employees who use the laminar flow hoods located in the controlled environment room of manufacturing.

2.2 The procedures apply to cleaning the interior of the hoods prior to and after any processes performed.

3.0 APPLICABLE DOCUMENTS

3.1 Equipment Clean Ticket
3.2 Equipment Cleaning and Use Log
3.3 Preparation of 70% Isopropyl Alcohol Solution, PL-125

4.0 GENERAL

4.1 Follow all safety policies as they apply to the use of any item required for this procedure.

4.2 Safety glasses and gloves are to be worn for this procedure, as well as the required apparel.

4.3 Solutions required:

- Sterile Water for Irrigation, USP
- 70% Isopropyl Alcohol Solution
- Staphene or other approved disinfectant

Approvals		**Date**			
Approved By	**Q.C.**		**Approved By**	**Mfg**	**Effective Date**
					Issued By____

STANDARD OPERATING PROCEDURE

Procedure: Cleaning Procedures For Class 100 Hoods

Procedure No.: PL-123

5.0 PROCEDURE

5.1 Prior to starting any activity using the laminar flow hood, the following cleaning procedure must be followed.

5.1.1 Remove all equipment from the hood.

5.1.2 Remove all instruments from the hood.

5.1.3 Wipe the interior of the hood and all surfaces (starting close to airflow air moving away) with a low-fibre-releasing wipe and sterile water for irrigation. Discard the wipe into a labeled trash receptacle.

5.1.4 Wipe the interior of the hood and all surfaces with 70% Isopropyl Alcohol (alternate Staphene) and a low-fibre-releasing wipe. Discard the wipe in a labeled trash receptacle.

5.1.5 Wipe/spray any equipment and/or instruments that will return to the hood with 70% Isopropyl Alcohol and a low-fibre-releasing wipe. Discard the wipe into a labeled trash receptacle.

5.1.6 Sign and date the Equipment Cleaning and Use Log for cleaning the hood. Be sure to indicate the SOP followed.

5.1.7 Run the hood for a minimum of 15 minutes prior to use.

5.2 Proceed with the process requiring the hood. Make proper entries into the Equipment Cleaning and Use Log for the process.

5.3 At the conclusion of the process, attach the clean ticket(s) to the batch record or notebook.

5.4 Clean the hood per steps 5.1.1-5.1.6.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Cleaning Procedures For Class 100 Hoods

Procedure No.: PL-123

EQUIPMENT CLEAN TICKET

Previous Lot Name_____

Previous Lot Number_____

Equipment/Item Description:_____

_____

ID #_____

Cleaned By/Date_____

Lot Number_____

Lot Name_____

Date_____

Sterilization/Depyrogenation_____

_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

	Revision Record	
Procedure : Guidelines for Personnel Using the Class 100 Hoods	**Page**	**Date**
Procedure No.: PL-124	1	
	2	
	3	

1.0 PURPOSE

To describe the practices employed for processes requiring a low particulate, non-contaminating technique (clean-room technique) when using the Class-100 Hoods.

2.0 SCOPE

This procedure applies to all trained manufacturing employees conducting processes requiring clean-room technique.

3.0 APPLICABLE DOCUMENTS

3.1 PL-126, Gowning Procedure for Processes Requiring Class 100 Status

3.2 PL-123, Cleaning Procedure for Class-100 Hoods

3.3 PL-127, Controlled Environment Daily Use Procedure

3.4 PL-125, Preparation of 70% Isopropyl Alcohol Solution

3.5 PL-126, Gowning Procedures for the Controlled Environment Area

4.0 GENERAL

4.1 Prior to using the class-100 hood for any process, verify the status by reviewing the Equipment Clean and Use Log.

4.2 Solutions required: 70% Isopropyl Alcohol Solution or Staphene, See Pl-125 and PL-127.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg	Effective Date
				Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Guidelines for Personnel Using the Class 100 Hoods

Procedure No.: PL-124

4.3 Any employee using the class-100 hoods to work must be in good health and physical condition. It is the responsibility of the employee to report to their immediate supervisor any personal illness, open lesion, or other condition which could have an adverse effect on the product. If the condition warrants it, the employee should be temporarily assigned to another project until the condition is approved or eliminated.

4.4 Follow all procedures for ingress/egress into the controlled environment area.

4.5 Movement of all personnel within the room containing the class-100 hood should be kept at a minimum and limited to only approved personnel.

5.0 PROCEDURE

5.1 Wear appropriate apparel according to PL-126.

5.2 Ensure the hood is clean by reviewing the Equipment Cleaning and Use Log and Equipment Clean Ticket.

5.3 Clean the hood per PL-123 and PL-127.

5.4 Place all equipment required for the process under the hood.

5.4.1 Do not stack equipment.

5.4.2 All equipment and materials must be cleaned and sterilized or depyrogenated as processing requires prior to placement under the hood.

5.4.2.1. External surfaces of equipment should be sprayed or wiped with 70% Isopropyl Alcohol or Staphene.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Guidelines for Personnel Usins the CLass 100 Hoods

Procedure No.: PL-124

5.4.3 Do not remove the covers from these items until ready for use so as to maintain the sterile or depyrogenated condition.

5.4.4 Do not use any item where the integrity of the protective wrap is questionable.

5.5 Never reach across an open sterile container with the arm or hand or another piece of equipment.

5.6 Rinse or spray gloves with a 70% Isopropyl Alcohol solution prior to commencing any activities within the hood.

5.6.1 Change gloves in the gowning room (per PL-126) whenever there is a tear. Always rinse with 70% Isopropyl Alcohol solution prior to continuing with activities.

5.6.2 If gloves become contaminated during a procedure, rinse the gloved hands in the 70% Isopropyl Alcohol solution.

5.7 Inform supervisor and Quality Assurance of any occurrence that could jeopardize the sterility of the process.

5.8 Upon completion of the process, clean the hood and equipment per specified SOPs.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

	Revision Record	
Procedure: Preparation of 70% Isopropyl Alcohol Solution	**Page**	**Date**
Procedure No.: PL-125	1 2	

1.0 PURPOSE

To describe the unit preparation of 70% Isopropyl Alcohol solutions to be used for equipment sanitation as indicated in equipment preparation standard operation procedures.

2.0 SCOPE

This procedure is to be followed by all trained manufacturing employees for the preparation of equipment cleaning solution.

3.0 APPLICABLE DOCUMENTS

3.1 Equipment Cleaning Solution Log

4.0 GENERAL

4.1 Follow all safety rules as they apply to the handling of any item or solution used during this procedure.

4.2 Equipment required:

- 1 L sterile receiver
- 0.2 um filter
- 1 L sterile graduated cylinder

4.3 Solutions required:

- Sterile Water for Irrigation, USP
- Isopropyl Alcohol, USP

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By

6000:

STANDARD OPERATING PROCEDURE

Procedure: Preparation of 70% Isopropyl Alcohol Solution

Procedure No.: PL-125

5.0 PROCEDURE

5.1 To prepare 1 L of solution measure 700 mL of the Isopropyl Alcohol into the 1 L sterile graduated cylinder.

5.2 Q.S. to 1 L with Sterile Water for Irrigation.

5.3 Filter solution through an isopropanol-resistant, sterile 0.2 um filter into a sterile, labeled receiver.

5.4 Fill out, sign, and date the Equipment Cleaning Solution Log.

5.5 Store solution in the receiver at room temperature no more than 30 days.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Gowning Procedures for Controlled Environment Area
Procedure No. : PL-126

Revision Record	
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1.0 PURPOSE

1.1 To minimize microbial particulate contamination exposure in designated clean work areas for designated processes from human sources and to provide personnel with proper protection while working in a controlled environment.

2.0 SCOPE

2.1 All personnel entering designated work areas are responsible for following this procedure and for monitoring compliance with this procedure or anyone entering a defined controlled environment area under their direction.

3.0 APPLICABLE DOCUMENTS

N/A

4.0 GENERAL

4.1 Only authorized employees, as designated by supervisor, are allowed to enter the controlled environment area.

4.2 Authorized employees with rspiratory symptoms or with open cuts or lesions are not to enter the aseptic areas without permission of their supervisor.

5.0 PROCEDURE

5.1 Wash hands thoroughly before entering the area.

5.2 Entering the gowning area and on nonsterile side of the dividing line:

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STANDARD OPERATING PROCEDURE

Procedure : Gowning Procedures for Controlled Environment Area

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5.2.1 Remove watches, bracelets, rings and other jewelry. Place a sterile face mask, clean shoe covers, gloves and clean lab coat on the nonsterile side of the line.

5.2.2 Put on face mask and clean gloves (note 5.2.5).

5.2.3 Put on shoe covers. Step over to "sterile" side of the line.

5.2.4 Remove clean lab coat and put it on. Use care to avoid floor contact and mimimize contact with the outer, clean side of the garment.

5.2.5 If assigned to handle finished devices for inspection or packaging wear sterile gloves. Put on the sterile gloves using the following method:

5.2.5.1 Open outside cover of the gloves by peeling at the indicated arrows and discarding the outer wrapping.

5.2.5.2 Set the inner wrapping on a clean surface and open the inner wrapping by pulling on the indicated edges. Do not touch area of gloves that is not cuffed.

5.2.5.3 Grasp the right glove in the left hand by the cuffed area only and slide over right hand.

5.2.5.4 Slide the right (gloved) hand under the cuff on the left glove and slide it over the left hand, pulling the cuff over the sleeve of the coverall.

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STANDARD OPERATING PROCEDURE

Procedure: Gowning Procedures for Controlled Environment Area

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5.2.5.5 Place the fingers of the left hand under the cuff of the right hand glove and pull it over the sleeves of the coverall.

5.2.5.6 Dispose of the inner wrapping by picking up the paper by the inside of the wrapping and throw it into a labeled trash receptacle.

5.2.5.7 Spray gloves with filtered 70% alcohol reagent (made with sterile water for irrigation).

5.2.6 Remove goggles from the cabinet and place over the eyes. Avoid touching the face or eyes and minimize goggle adjustment with gloved hands.

5.2.7 Proceed to the assigned processing area and task.

NOTE: Prior to starting any new operation, change gloves.

5.3 Changing sterile gloves:

5.3.1 Return to the gowning area.

5.3.2 Remove soiled or torn gloves and dispose of them in a controlled trash receptacle.

5.3.3 Put on a new pair of gloves per 5.2.5.

5.3.4 Proceed back to the aseptic hood.

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STANDARD OPERATING PROCEDURE

Procedure: Gowning Procedures for Controlled Environment Area

Procedure No.: PL-126

5.4 Leaving the processing area:

5.4.1 Remove goggles and place in cabinet.

5.4.2 Proceed to gowning area.

5.4.3 Discard mask and gloves in the container provided.

5.4.4 Remove garment and shoe covers and place in proper bins.

5.4.5 Exit controlled processing area.

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STANDARD OPERATING PROCEDURE

Procedure: Controlled Environment Daily Use Procedures

Procedure No.: PL-127

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1.0 PURPOSE

1.1 To establish the method to be followed in the preparation of Laminar Air Flow Hoods (LAF) and filling work area prior to production use.

NOTE: Laminar Flow Hoods Air circulating Systems are to be left on continuously. The light switch and fan are turned on and off by a single switch (for LAF prefilter changing only).

2.0 SCOPE

2.1 All personnel using controlled environment work areas.

3.0 APPLICABLE DOCUMENTS

3.1 PL-124, Guidelines for Personnel Using the Class 100 Hoods

3.2 PL-126, Gowning Procedures for the Controlled Environment Area

4.0 PROCEDURES

4.1 Preparation of filling station at beginning of shift.

4.1.1 Gown in the manner described in PL-126, Gowning Procedures for the Controlled Environment Area.

4.1.2 Check LAF unit to insure fan is running.

4.1.3 Using a clean sterilized towel soaked with Staphene solution or equivalent, disinfect the work area in this order:

4.1.3.1 Inside the hood; wipe down the top, sides and working surface.

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STANDARD OPERATING PROCEDURE

Procedure: Controlled Environment Daily Use Procedures

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4.1.3.2 Wipe down the outer sides, top and front of the unit.

4.1.3.3 Wipe down chairs and carts to be used.

4.1.3.4 Wipe the underneath side of the outer edge of hood work surface.

4.1.4 Obtain clean sterilized towel or wipe.

4.1.4.1 Wipe all nonsterile equipment with Staphene or spray with isopropyl alcohol before placing inside the work area.

4.1.4.2 Arrange equipment under Laminar Air Flow Hood to best minimize cross section in air fow.

4.2 Returning to work area during shift.

4.2.1 When returning to a station that has been unattended, put on a new pair of sterile gloves or spray gloves with 70% isopropyl alcohol.

4.2.2 Spray working surface of hood with 70% isopropyl alcohol.

4.3 Cleaning station at end of shift.

4.3.1 Remove all equipment from under hood. Wipe down work surface of LAF with 70% isopropyl alcohol.

4.3.2 Transfer all opened sterile equipment containers to be re-processed to "dirt cart". Return all unopened sterile equipment containers to storage shelfs.

4.3.3 Return nonsterile equipment to storage area or store on bottom shelf of cart. Stands are to be wiped with 70% isopropyl alcohol and stored under the laminar hood.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Controlled Environment Daily Use Procedures

Procedure No.: PL-127

4.3.4 Contact supervisor for instructions as to what to do with finished and unfinished units and remaining materials.

4.3.5 Wipe carts with 70% isopropyl alcohol.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Performing Air Pressured Differential Test

Procedure No.: PL-128

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1.0 PURPOSE

1.1 To describe the procedure to be followed to assure that the controlled environment room is maintaining a positive air pressure with relation to the non-controlled areas.

2.0 SCOPE

2.1 This procedure applies to the operation of the Controlled Environment Room.

3.0 APPLICABLE DOCUMENTS

3.1 Monitoring of Air Flow Velocity through Controlled Environment Room HEPA Filters, P1-132.

3.2 Certification of the Controlled Environment Area, P1-113.

4.0 GENERAL

4.1 This procedure must be performed each day to assure that the Controlled Environment Room has a positive air pressure with relation to the outside room areas.

4.2 This test shall be performd by the person designated to perform the Quality Assurance functions prior to use of this room.

4.3 This room shall not be used for processing unless positive pressure differential exists.

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STANDARD OPERATING PROCEDURE

Procedure: Performing Air Pressured Differential Test

Procedure No.: PL-128

5.0 PROCEDURE

5.1 Check that the air supply system to the controlled environment and outside rooms are turned on and functioning.

5.2 With the door tightly closed to the Controlled Environment Room, hold a piece of tissue against the bottom of this door and note whether the tissue is being blown in or out by the pressure differential.

5.3 If positive air pressure differential exists, the end of the tissue will be blown out.

5.4 If the proper air pressure differential does not exist, notify manufacturing that aseptic operations may not be conducted in this room until proper conditions are achieved.

5.5 Indicate on Page 1, Standard Product Formulation, by signing and dating that air pressure test has been performed and is positive (satisfactory) or (unsatisfactory.)

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Sampling of Incoming Purchased Components

Procedure No.: PL-129

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1.0 PURPOSE

To describe the sampling procedures for incoming purchased components.

2.0 SCOPE

This procedure applies to the sampling of all incoming purchased components used in the manufacture of a product for the purposes of release testing and retention. This procedure also applies to resampling of materials for retest purposes.

3.0 APPLICABLE DOCUMENTS

3.1 Appropriate specifications for purchased components

3.2 Sampling Testing Record

3.3 Quality Assurance Inspection/Testing Procedures, PL-130

3.4 Inventory Card

3.5 Sample Log Book

4.0 GENERAL

4.1 Product is defined as materials produced by or supplied to Plastafil and distributed under Plastafil labeling.

4.2 A purchased component is a substance used in the manufacture of any product.

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STANDARD OPERATING PROCEDURE

Procedure : Sampling of Incoming Purchased Components

Procedure No. : PL-129

4.3 Observe all special safety precautions or handling requirements as described in the item specification. When handling toxic compounds or biohazardous materials, conduct all manipulations in a biological safety cabinet or a ventilated chemical fume hood where appropriate. Otherwise, sample the container(s) in a well ventilated are designated for sampling incoming purchased components.

4.4 These procedures are performed by the individual designated to perform these quality assurance functions.

5.0 PROCEDURE

5.1 Upon receipt of purchased components, check each container or unit for the following:

5.1.1 Appropriate labeling which must include a description of contents, manufacturer's lot number, quantity, shelf life limitations, if applicable, and safety information. (Where the manufacturer's label bears an expiration date, this information must be recorded on the inventory card and Sampling Testing Record.

5.1.2 Check that the description of contents is in accordance with the inventory card for that item.

5.1.3 Check for container physical defects such as broken seals or any obvious contamination.

(Any descrepancies in the above may result in rejection of the material. Such materials shall be evaluated by Quality Assurance to determine disposition. This disposition may include partial lot acceptance, reinspection, or rejection. Rejected materials shall be labeled as "Rejected" and moved to a rejected materials area in quarantine for destruction or returned to the supplier.)

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STANDARD OPERATING PROCEDURE

Procedure: Sampling of Incoming Purchased Components

Procedure No.: PL-129

5.2 Refer to the appropriate specification form to determine the amount of material required for testing and retention.

5.3 For raw materials:

5.3.1 Observe special safety precautions or handling requirements as described in the item specification. Bring refrigerated powders to room temperature and thaw frozen materials before sampling to facilitate adequate mixing of the material before sampling.

5.3.2 In the case of multiple containers of the same manufacturer's lot, consult the Sampling Plan section of the item specification to determine the number of containers to sample. For liquids or solids that are homogeneous materials, samples from containers which were individually sampled should be combined in a single container and well mixed.

Materials that are suspensions should be sampled individually, and each sample from each container placed in a separate sample container. (Number the sample container to correspond with the individual number on the container from which it is sampled.)

5.3.3 Mix the contents of the container to be sampled by inverting or stirring.

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STANDARD OPERATING PROCEDURE

Procedure: Sampling of Incoming Purchased Components

Procedure No.: PL-129

5.3.4 If necessary to avoid contaminating the container contents, clean the outside of the container with 70% alcohol. Open the container in a manner which avoids contamination of the contents and so that it may be adequately resealed.

5.3.5 Use a separate clean dry glass or stainless sampling device for each sample taken. Use sterile sampling devices and sample containers for those materials requiring a Bacterial Content Test. Use sterile, depyrogenated sampling devices and sample containers for materials requiring a Bacterial Endotoxin Test or sterility test.

5.3.6 Transfer sample to a clean dry non-reactive sample container and seal to prevent contamination of the sample.

5.3.7 If chemicals or liquids are a mixture of substances or if liquids are a suspension, mix the contents as thoroughly as possible. If the lot consists of a single container, take three individual samples from different areas of the container. If multiple containers for the lot, sample as per 5.3.2. These samples are evaluated separately.

5.3.8 Reseal item container and record the quantity sampled, initials, and date sampled on the quarantine sticker of the sampled container. Record quantity sampled on the inventory card.

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STANDARD OPERATING PROCEDURE

Procedure: Sampling of Incoming Purchased Components

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5.3.9 Label sample with item name, part number, receiving or lot number, quantity sampled, date, and initials.

5.3.10 Record item name, part number, receiving or lot number, and initials in the sample log book. Also record the quantity sampled for testing/inspection purposes and the quantity sampled for retention, if required.

5.3.11 Complete Sampling Testing Record Form, and transport test sample for testing/inspection. Store the remaining sample in retention.

5.4 Check to see if supplier certification has accompanied the lot. If not, request supplier to provide the necessary certification.

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STANDARD OPERATING PROCEDURE

Procedure : Sampling of Incoming Purchased Components

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Sampling Testing Record

Material Sampled

Name:_____

Part No.:_____

Receiving No.:_____ Mfg. Lot No.:_____

Mfg. Exp. Date:_____

Cert. Supplied_____

Quantity Sampled:_____

Testing/Inspection

Procedures:_____

_____

_____

Results:_____

_____

_____

Lot Accepted ( ) Rejected ( )

Sampled By:_____ Date:_____

Released/Rejected By:_____ Date:_____
Quality Assurance

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Inspection/Testing Procedures

Procedure No.: PL-130

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1.0 PURPOSE

To describe the process for test assignment, inspection and testing procedures, and review and approval of test results.

2.0 SCOPE

This procedure applies to purchased components, finished components, packaging items, manufactured product, and sterilized final product. Quality Assurance is responsible for following this procedure.

3.0 APPLICABLE DOCUMENTS

3.1 Item Specifications

3.2 Sampling Testing Record

3.3 Sample Log Book

3.4 Q.A. Inspection/Testing Summary

3.5 Sampling of Incoming Purchased Components, PL-129

3.6 Manufactured Product Test Form

3.7 Quality Assurance Final Release Procedures, P1-131

4.0 GENERAL

4.1 Quality Assurance records for each lot of material inspected or tested are stored in a water resistant envelope. The envelopes are filed in chronological order by part number in the lot file. This file is a lockable, fireproof cabinet.

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Procedure: Quality Assurance Inspection/Testing Procedures

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4.2 In general, all tests are performed in duplicate or as specified in the individual test methods.

4.3 All inspections or tests indicated in the item specifications are performed by individuals designated to perform the Quality Assurance functions.

5.0 PROCEDURE

5.1 Test Assignments

5.1.1 Transfer the sample to the designed area for inspection and testing.

5.1.2 Enter sample in the Sample Log Book.

5.1.3 Notify individual qualified to perform the inspection or test that sample is available and requires inspection or testing.

5.2 Quality Assurance Inspection/Testing

5.2.1 Consult item specification for required procedures.

5.2.2 Perform procedure as required using specified methods.

5.2.3 Record the following information in the appropriate record.

- Part number and lot number
- Quantity tested
- Test or inspection method used and its edition number
- All data secured during the test

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Procedure: Quality Assurance Inspection/Testing Procedures

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- Calculations
- Signature of the person doing the test or inspection and date performed.

5.2.4 If test or inspection does not meet specification, perform the following:

5.2.4.1 Review method and all calculations to to assure test was performd correctly.

5.2.4.2 Verify all equipment used is within calibration period and functioning properly.

5.2.4.3 Verify test reagents, if used, were prepared correctly and are within assigned expiration periods. Observe test reagents for detectable contamination or physical changes.

5.2.4.4 Verify correct sample was inspected or tested. Observe sample for detectable contamination or physical changes.

5.2.5 Standardize or calibrate equipment and reagents as necessary to correct the problem.

5.2.6 Request a new sample of material if sample is the suspected source. Repeat assay or inspection with the new sample.

5.2.7 Record the suspected problem and correction in the appropriate test report form.

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STANDARD OPERATING PROCEDURE

Procedure: Qualtiy Assurance Inspection/Testing Procedures

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5.2.8 Review results with the manufacturing supervisor and the President if results of inspection or testing do not meet specifications or requirements.

5.2.9 Report all final results on the appropriate test result forms.

5.3 Document Review By Quality Assurance

5.3.1 Review all results and accompanying documents for accuracy and completeness.

5.3.2 Compare results to the Item Specification to determine whether the material meets or does not meet specification.

5.3.2.1 For in-process or miscellaneous samples, compare test results to the expected results.

5.3.2.2 Maintain copies of the test results and the original Test Request Form for files.

5.3.3 Complete QA Inspection/Testing Summary, indicating disposition of material.

5.3.3.1 If the material does not meet item specifications, notify the President.

5.3.4 Review the summary form and test results for accuracy and completeness. Verify review and disposition on Quality Assurance Release Summary.

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Inspection/Testing Procedures

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MANUFACTURED PRODUCT TEST FORM

Date: _____

SAMPLE IDENTIFICATION

Description: _____

Part No. or Step No.: _____ Lot No.: _____

Quantity Sampled: _____ Sampled By: _____

Date Sampled: _____

Inspection/Test	Method	Results	Performed By	Date

Remarks: _____

Results Reviewed By: _____ Date: _____

Meets Specifications: ( ) Yes ( ) No

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

Procedure No.: PL-131

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1.0 PURPOSE

To describe the review process of all pertinent manufacturing and Quality Assurance inspection and test records prior to the release of an individual batch of a sterilized final product. This review establishes that: all required manufacturing steps have been completed as stipulated, all specifications for in-process manufacturing processes and check-points have been met and that all specifications for Quality Assurance final release testing have been met.

2.0 SCOPE

Each final product batch is subject to this review process prior to its release for distribution.

3.0 APPLICABLE DOCUMENTS

3.1 Applicable Production Batch Record

3.2 Product Specifications

3.3 Sterilized Product Specifications

3.4 Packaging Record

3.5 QA Inspection/Testing Summary

3.6 Final Product Disposition

3.7 QA Review of Manufacturing Batch Record

3.8 Quality Review Board Action

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Approved By	Q.C.		Approved By	Mfg	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure : Quality Assurance Final Release Procedures

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4.0 GENERAL

4.1 Product batch is defined as a specific quantity of product intended to have uniform composition and quality. A batch is manufactured according to a single manufacturing order and batch record during the same cycle of manufacture and at essentially the same time.

4.2 Quality Assurance tests and specification release requirements are predicated on the production batch being reviewed having been made under the designed conditions. Deviations whether planned or unplanned may result in the necessity to perform additional and/or different testing than would be the case for "standard" conditions. Hence the importance of this pre-release review.

4.3 This review and subsequent release or rejection is performed by the individual designated to perform these Quality Assurance functions.

5.0 PROCEDURE

5.1 Compile, review, and approve all manufacturing documents pertaining to the batch under review.

Documents should include:

5.1.1 Cleaning, sterilization/depyrogenation records and chart recordings for equipment and containers used in the manufacture of the batch.

5.1.2 Batch records pertaining to the following:

1. Formulation of solutions used in manufacturing product.

2. Cleaning records for product where applicable.

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3. Packaging of the product into final product containers.

4. Terminal sterilization results and records from contractor.

5. Inspection records of the final product.

6. Labeling and packaging records.

5.2 Review the above documentation for compliance with established written procedures and the following:

5.2.1 Completeness of the batch record. Check that all entries are accurate and each manufacturing step has been signed and verified, that all steps have been completed satisfactorily and in the order prescribed.

5.2.2 Sterilization/depyrogenation cycles were conducted under approved cycle parameters and the chart recordings indicate that the cycle meets the approved acceptance criteria.

5.2.3 Equipment used in manufacturing was properly cleaned, prepared and was within calibration during manufacture of the product.

5.2.4 Entries for components listed on the batch records are complete. Part numbers and receiving or lot numbers are accurate.

5.2.5 Calculations are done correctly.

5.2.6 Yields are within acceptable range.

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STANDARD OPERATING PROCEDURE

Procedure : Quality Assurance Final Release Procedures

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5.3 Record any critical deviations from standard procedures for review by the Quality Review Board. Make a recommendation whether inspections or testing other than the normal specification release testing is appropriate prior to batch release.

5.4 If the review process finds the documentation to be satisfactory, sign and date the batch record.

5.5 Summarize results of environmental monitoring and indicate whether results are within acceptable limits.

5.6 Compile and review all in-process and final release testing and summarize the results indicating whether the product meets or does not meet the specifications defined for that particular product.

5.6.1 Record final release test results on Final Product Release Form and indicate whether the final product meets or does not meet the specifications.

5.6.2 Record any deviations from the in-process or release specifications and submit it to the Quality Review Board.

5.7 Request that the Quality Review Board review unexplained discrepancies, failure of a process to meet the specified parameters or failure of a component or batch to meet any of its approved specifications. Document the review and make recommendations as to disposition of the batch based on investigation findings.

5.8 The President shall review the recommendation of the Quality Review Board members and determine whether to accept the recommendation in accordance with the Quality Review Board Procedure.

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STANDARD OPERATING PROCEDURE

Procedure : Quality Assurance Final Release Procedures

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5.9 Upon completion of the review process, the Quality Assurance designee shall approve and sign the Final Product Disposition Form.

5.10 Complete batch record files are retained by Quality Assurance indefinitely.

5.11 Release lots of product which meet requirements for distribution.

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STANDARD OPERATING PROCEDURE

Procedure : Quality Assurance Final Release Procedures

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PACKAGING ORDER

PRODUCT NAME AND SIZE	LOT NO.	ORDER QUANTITY	LABELED	ORDER NUMBER
			Yes / No	

COMPONENTS AND CODE NUMBERS	UNIT USAGE	NUMBER SUPPLIED	NUMBER USED	SAMPLES	NUMBER DESTROYED	NUMBER RETURNED

ORDER INSTRUCTIONS	LABELING COMPONENTS	LABELED LOT NUMBER	EXP. DATE

DATE(S) PROCESSED / DATE COMPLETED	SAMPLING INSTRUCTIONS	LOT ID CODE	VISUAL VERIFICATION BY AND DATE
	RETENTION:	CODE _____	CHECKED AND VERIFIED by _____ / /

SUPERVISORS COMMENTS / OBSERVATIONS	AREA CHECKED PRIOR TO START-UP AND FREE OF OTHER COMPONENTS. _____ / /	FINISHED COUNT

ORDER CHECKED BY _____ ACCOUNTABILITY CHECKED _____ CONTENTS APPROVED: _____

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

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Quality Assurance Review of
Manufacturing Batch Record Documentation

Manufacturing Batch Record	Form #	Date of Form	Reviewed By	Approved	Not Approved	Comments
Formulation						
Manufacture						
Cleaning						

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

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Quality Assurance Review of
Manufacturing Batch Record Documentation

Manufacturing Batch Record	Form #	Date of Form	Reviewed By	Approved	Not Approved	Comments
Inspection						
Labeling & Packaging						

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

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Quality Assurance Review of
Manufacturing Batch Record Documentation

Manufacturing Batch Record	Form #	Date of Form	Reviewed By	Approved	Not Approved	Comments
Environmental Monitoring Summary						
Sterilization Records						
QA Release Requirements						
Product Specifications						
Sterilized Product Specifications						

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

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QA Inspection/Testing Summary

ATTACH ALL TEST REPORTS

Date Tested_____

Part Number_____ Specification Edition_____

Item Name_____ Sterilized ( ) Yes ( ) No

Lot Size_____ in_____ Containers Lot No._____

Number Inspected/Tested_____

Inspection/Test	Method	Specification	Passes/Fails

Remarks_____

Performed By_____ Date_____

Reviewed By_____ Date_____

Material Meets Specification: ( ) Yes ( ) No

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STANDARD OPERATING PROCEDURE

Procedure: Quality Assurance Final Release Procedures

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FINAL PRODUCT DISPOSITION

Product Name:_____ Part Number:_____

Batch Number:_____

Batch Size:_____

☐ Release as Finished Goods

☐ Hold For Disposition

☐ Rejected

_____ _____

Quality Assurance Date

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Monitoring of Air Flow Velocity Through Controlled Environment Room HEPA Filters

Procedure No.: PL-132

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1.0 PURPOSE

1.1 To check for proper air flow across the HEPA filter face and to certify that the unit is working within acceptable limits.

2.0 SCOPE

2.1 This procedure applies to the HEPA filters located in the controlled environment area.

3.0 APPLICABLE DOCUMENTS

3.1 Performing Air Pressure Differential Test, PL-128

3.2 Certification of the Controlled Environment Area, P1-113

3.3 Incoming Room Air Flow Velocity Report

4.0 GENERAL

4.1 These tests are normally performed by outside contractors but may be performd inhouse under the direction of Quality Assurance.

4.2 These tests should be performed at one year plus or minus one month intervals.

4.3 The high efficiency absolute filters are capable of maintaining an atmosphere essentially free of airborne particles. A large volume of air is moved uniformly through those filters. The filters require replacement when a faulty or ruptured filter is discovered or when the filters become loaded such that air flow is reduced below the acceptable minimum or varies more than permitted.

Approvals		Date			
Approved By	**Q.C.**		**Approved By**	**Mfg**	**Effective Date**
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STANDARD OPERATING PROCEDURE

Procedure : Monitoring of Air flow Velocity Through Controlled Environment Room HEPA Filters
Procedure No. : PL-132

5.0 PROCEDURE

5.1 Testing

5.1.1 Equipment

5.1.1.1 The instructions given in this section are for a Shortridge Flowhood Model CF 80 which measures the air flow through an Alnoc Velometer. Readings from 50 to 2000 CFM can be taken through the Flowhood. The Velometer uses an averaging manifold to sense the air flow total pressure and static pressure at 16 location points.

(Note: Other units for monitoring airflow may be used which are comparable to the Shortridge unit provided they operate in the same manner and give the same readings.)

5.1.1.2 The Flowhood can be used for direct air flow measurements at supply or exhaust diffusers. A range selector switch allows readings on each of three Velometer scales in either CFM (range 50-2000) or litres per second (range 50-1000).

5.1.1.3 Flow Sensing Grid

The flow sensing grid in this unit is relatively delicate and can be damaged if subjected to physical abuse, excessive stress or jarring. If broken, it cannot be repaired. Maximum temperatures should not exceed 130°F for extended periods or 150°F for five minutes.

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5.1.1.4 Springs

The diamond shaped springs that gently support the grid should never be removed or tampered with. The springs allow for some degree or deformation out of square of the aluminum base without resultant damage to the sensing grid.

5.1.1.5 Spider

The spider (the aluminum rod structure that supports the top) must be stored folded with the ends of each pair of legs inserted into the top and middle holes of the two rear base corner tubes and with the head next to the selector switch in front. The four spider spring rods must be swung out to the side to avoid applying pressure to the grid.

5.1.1.6 Fabric Tops

The fabric tops will last longer if washed periodically in cool water with a mild detergent. Excessive dirt build-up should be avoided.

5.1.1.7 Static Build-up

The most common cause of static build-up is low relative humidity, but it also can be associated with clean room garments. The Velometer is coated with an anti-static solution. If it will not hold a zero setting or gives erratic readings, respray it wtih G.E. Cat. No. 50-177001AAAA1 Anti-Static Solution.

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5.2 Operation

5.2.1 Remove the Flowhood base which houses the Velometer, from the carrying case, being careful not to jar it.

5.2.2 Select the appropriate cloth top (depending on filter size) and place over top edges.

5.2.3 Insert legs of the spider assembly into top and middle holes located in four corners of the base.

5.2.4 Pull the cloth top to upright position.

5.2.5 Insert four support dowels onto the spider assembly. For 2' x 2' frame, insert the support dowel end pins into each corner bracket. For 2' x 4' frame, insert end pins into the inner set of locator cups (labeled on frame).

5.2.6 Attach the handle assembly to bracket on front of Flowhood.

5.3 Test Procedure

5.3.1 Place Flowhood over each air diffuser to be tested, making sure that the foam rubber edges of top are firmly against edges of diffuser.

5.3.2 Turn selector switch to appropriate range position, either incoming (arrow down), or exhaust (arrow up). Start in lowest range (0-500 CFM). If the reading goes off scale clockwise, then move selector switch to higher range. If it is known that the air speed is within the span of a higher range, the selector switch may be set in that range at once.

5.3.3 Take reading in CFM, which is printed in black on the lower scale of each range on the Velometer. The reading is an average of the air flow through 16 points on the sensor grid.

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5.3.4 Record the reading obtained on the Incoming Room Air Flow Velocity report.

5.3.5 When finished with measurement(s), turn the selector switch to the OFF position.

5.3.6 Disassemble the Flowhood and return to storage case.

5.3.7 Calculate number of room air changes from reading(s) obtained.

5.3.7.1 Multiply reading obtained in CFM by 60 to determine ft^3/hr volume. If the room has more than one diffuser, add the reading together.

5.3.8 Calculate the volume of the room in cubic feet.

5.3.9 Divide the hourly volume of air by the room volume to obtain the number of air changes per hour.

5.3.10 The minimum number of air changes per hour for the controlled environment area is NLT 20/hr.

5.3.11 Compare air flow velocity and number of air changes with original qualification data (if available). This comparison is one factor used to determine when a filter should be replaced.

5.4 Frequency of Testing

5.4.1 Each HEPA filter for incoming room air is to be tested NLT once/year. However, if at any time, Air Pressure Differential Test indicates a problem, air flow velocity testing will be performed.

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5.5 Recording Test Results

5.5.1 The test results are to be recorded on air flow velocity data report. Information to be recorded for each test is:

Date
Diffuser location
Filter size
Date of filter installation (if known)
Test results
Number of room air changes
Comments
Signature of person performing test

5.5.2 In the case of a satisfactory test, the original is placed in a three-ring binder entitled HEPA Filter Data, maintained by Quality Assurance.

5.5.3 In the case of an unsatisfactory test of any filter, the filter must be changed. The supervisor shall be notified of test failures and should issue a work order for replacement of the filter(s). This information is recorded on the original test form which is kept in the HEPA Filter Data notebook. New filters are installed according to manufacturer's instructions and checked for leaks by the Air Flow Velocity Test.

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Procedure: Quality Review Board

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1.0 PURPOSE

To establish a mechanism whereby certain key personnel will review and evaluate information concerning a failure of an individual lot or lots to meet all current specification criteria, deviations from procedures which could affect the quality of a lot or any other significant condition which could impact on the suitability of a lot or material. The purpose of such a review is to assure that the appropriate expertise participates and provides input into the decision process, to determine when additional tests or investigations, if any, are necessary in determining disposition, to initiate whatever corrective actions may be necessary, and to evaluate the suitability of such instituted corrective actions.

2.0 SCOPE

2.1 All lots of products produced which do not meet one or more current specifications, criteria. In addition, those procedural deviations and/or conditions which could impact on the quality or suitability of a lot or lots which should be reviewed by the Board to determine the disposition of the lot or material.

2.2 The Quality Review Board shall consist of the President, who shall act as Chairman, the individual responsible for manufacturing, the individual designated to perform the Quality Assurance function and such other expertise appropriate to properly review and determine disposition of the issue to be reviewed.

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3.0 APPLICABLE DOCUMENTS

3.1 Quality Review Board Report

3.2 Corrective Action Log

3.3 Corrective Action Request

3.4 Product/Process Incident Report

3.5 Customer Complaint, PL-153

3.6 Failure Investigation, PL-157

4.0 GENERAL

4.1 In general purchased components, packaging supplies, and labeling which do not meet specification requirements shall be dispositioned by Quality Assurance.

4.2 Lots of products the cause for whose failure to meet one or more specific criteria is obvious or where the nature of such a failure provides no basis for a decision other than reject or rework may be dispositioned by Quality Assurance without Quality Review Board input.

4.3 Quality Assurance may present any quality-related issue to the Quality Review Board for advice and consent.

4.4 Any employee may present a quality related issue to the Quality Review Board for review.

4.5 Where a decision to approve or release a lot is reached, all members who make up the review board must concur in that recommendation for Quality Assurance to so approve or release the lot.

4.6 Normally this board will meet as a body to review only the more significant issues. However, any member may request a joint meeting.

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4.7 Quality Assurance is responsible for performing all functions of this procedure unless other individuals or groups are specifically indicated.

5.0 PROCEDURE

5.1 Quality Assurance obtains or receives information or test results for a lot which indicate that:

5.1.1 One or more specifications criteria have not been met and this finding has been confirmed by retest or reinspection; or

5.1.2 A significant deviation has occurred in the method of manufacturing, filling, storage, or handling which can or could impact on the quality or suitability of a lot or material; or

5.1.3 A condition is confirmed or is suspect which can or could impact on the quality or suitability of a lot or material; or

5.1.4 A significant quantity of material has been returned which has been outside of Plastafil control with the intent for return to inventory; or

5.1.5 Any other situation that may involve a lot or product which warrants a review by the Quality Review Board.

5.2 Quality Assurance personnel reviews the information and/or test results and decides that the matter should be presented to the Quality Review Board for advice, a recommendation or consent to the proposed disposition. (If the issue is suspected to involve other than the lot(s) initially identified, this information along with a list of suspect lots or other products is included in the information to be presented to the Quality Review Board.)

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5.3 Quality Assurance prepares a Quality Review Board Report listing all the pertinent information and forwards a copy of this form together with all test results and other informtion concerning the issue to the appropriate board members.

5.4 Each board member reviews the information for the purpose of recommending such additional testing or evaluation, if any, concerning the issue as each may believe to be necessary to more fully evaluate the issue. Further, the member may recommend additional individual(s) to be consulted whose expertise should be utilized to most fully evalute the issue.

5.5 Each board member evaluates all information and makes a recommendation concerning the disposition of the lot or material, signing and dating the form to attest to this recommendation. Where corrective action is suggested or recommended, each so indicates on the form and attach any new information upon which this recommendation is made.

5.6 The President reviews the recommendations of the individual board members and determines whether a meeting of all members is necessary or appropriate to discuss and resolve divergent recommendations.

5.7 Quality Assurance proceeds to execute the recommendation for release, filing a copy of these forms together with all obtained data with the individual lot records.

5.8 Quality Assurance proceeds to initiate rework or rejection of the subject material unless the recommendation for release or approval is unanimous.

5.9 Initiates Request for Corrective Action Form when corrective action is recommended by Quality Assurance or other Board Members.

5.10 Enters the date that the corrective action was requested and the date a response was required from the group responsible for initiating the corrective action into a Corrective Action Log. Indicates also a review date to assess effectiveness of the recommended corrective action.

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5.11 Institutes additional routine tests and/or inspections as may be recommended by the Quality Review Board, revising the appropriate specification accordingly.

5.12 Follows up to assure that corrective action has been effected and reports the completion of the corrective action to the Quality Review Board. Provides an assessment of the effectiveness of the corrective action. Documents this in a full report.

5.13 The President reviews report of corrective action effectiveness and makes a recommendation to Quality Assurance concerning any additional steps to be taken to provide a final resolution in the subject issuse.

5.14 Quality Assurance reviews any additional board recommendation and initiates whatever action may be appropriate.

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QRBR #_____

QUALITY REVIEW BOARD REPORT

I. Preliminary Information:

Product	Lot No.	Problem:( )1st Occurrence( )General( )Random( )Continuous

Referred to QRB By:	Date	Manufacturing Area:	To President — Date

Problem Statement:

Observations — Causes of Problem if Known:

II. QRB Discussion:

Date QRB	Quality Assurance	Manufacturing	President(Chairman)

Others Attending:

Notes by Chairman (Attach Appropriate Reports)

III. QRB ACTION:
Disposition:

IV. Corrective Action: (Indicate Responsible Person)

Approvals:_____ _____ _____
Quality Assurance Manufacturing President (Chairman)

Disposition Completed By:_____ Date:_____

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1.0 PURPOSE

To describe the procedures followed for initial training, retraining and the qualification of Quality Assurance and manufacturing personnel to perform specific procedures.

2.0 SCOPE

This procedure applies to all Quality Assurance and manufacturing personnel.

3.0 APPLICABLE DOCUMENTS

3.1 Training Record

3.2 Qualification Record

3.3 Position Responsibilities (Job Descriptions)

4.0 GENERAL

4.1 Personnel employed or assigned to manufacturing or Quality Assurance are selected based on educational and experience guidelines to assure that each has a suitable background for the tasks to which each will be assigned.

4.2 Each new hire is given an orientation session including safety requirements.

4.3 Each employee receives training in general and specific procedures and in cGMP's which apply to his/her duties. This training, together with all retraining, is documented on Training Record. This training may consist, in whole or in part, of either in-house or outside training.

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Procedure: Plastafil Training Procedures

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4.4 Each new hire or employee who has not been previously qualified initially performs a new procedure with, or under the supervision of, an experienced individual with a review by the supervisor to insure that the individual understands and performs the procedure properly.

4.5 As each procedure has been mastered to the satisfaction of his/her supervisor, the supervisor notates on the Qualification Record Form that he/she is qualified to perform the procedures.

5.0 PROCEDURE

5.1 It is the responsibility of the President to assure that only personnel with suitable educational background and experience are employed to perform quality assurance or manufacturing tasks.

5.2 It is the responsibility of the President or designated alternate to assure that each person receives the necessary training to perform his/her task and is kept current with scheduled retraining as appropriate; but, in no case shall retraining exceed one year from the date of the last documented training.

5.3 Assign employees to work with or under the supervision of an experienced person to assure that the new employee understands and can satisfactorily perform each new procedure.

5.4 Monitor the progress of the employee and determine by both observations and discussions with the supervisor that the employee is qualified to perform that procedure.

5.5 Indicates that the employee is qualified for that procedure by indicating on the Qualification Record. Maintains these records current and files them in the Qualification Record file.

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5.6 Assures that only those individuals who are qualified for specific procedures are assigned to perform them.

5.7 Monitor the progress of each person to assure by both observation and discussion that each is qualified to perform the procedures to which he/she will be assigned.

5.8 Follows procedures 5.5 and 5.6 with respect to qualified personnel.

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TRAINING RECORD

The following employees have received training in the following:

Employees:

_____ _____ _____

_____ _____ _____

_____ _____ _____

_____ _____ _____

_____ _____ _____

_____ Corporation Policies and Procedures

_____ Manufacturing Methods/Procedures

_____ Good Manufacturing Practices

_____ Quality Assurance Procedures

_____ Other_____

Comments or Notes:

_____

_____

_____

_____

_____

Trainer or Supervisor_____

Date_____

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QUALIFICATION RECORD

EMPLOYEE:_____ HIRE DATE:_____

DEGREE:_____

PRESENT TITLE:_____

PROMOTED TO:_____ DATE:_____

PROMOTED TO:_____ DATE:_____

QUALIFIED TO PERFORM	APPROVED BY	DATE

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STANDARD OPERATING PROCEDURE

Procedure : Validation Review Board	**Revision Record** Page	Date
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1.0 PURPOSE

To define the function and make-up of the Validation Review Board.

2.0 SCOPE

The validation of all appropriate processes and procedures for the manufacture and control of Plastafil products.

3.0 APPLICABLE DOCUMENTS

3.1 Certification of Manufacturing Systems, Processes and Equipment, PL-111

3.2 Certification Document

4.0 GENERAL

4.1 This Board is made up of the same personnel who constitute the Quality Review Board, i.e., the President as Chairman, Manufacturing representative, Quality Assurance representative and such other expertise as may be appropriate for the matter being reviewed.

4.2 The Board meets at the request of any member when there is a matter or issue requiring Board review.

5.0 PROCEDURE

5.1 Reviews protocols and the acceptance criteria set forth and evaluates whether these protocols meet the guidelines set forth by the FDA for process validations.

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5.1.1 Makes recommendatiosn ot improve or correct protocols which are found to be unsatisfactory.

5.2 Reviews data collected to assure that the previously approved acceptance criteria have been met and that the validation package is complete.

5.3 Evaluates any discrepancies encountered during validated procedures and what action should be taken to rectify a problem.

5.4 Reviews proposed changes in procedures, equipment and processes to evaluate their possible impact on the validated status of a process and how this change could be best validated.

5.5 Evaluate new products and how they will be impacted by presently validated systems and whether new validations are required.

5.6 Issues final certification of a process when the review establishes that such should be certified.

5.7 Makes recommendations for those processes which can not be certified without additional data, changes, etc.

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Certification Document

This is to certify that the _____

System No._____ operates within the limits specified

In Validation Protocol _____

Edition No._____.

Review of this certification is due _____.

_____ _____
Quality Assurance Date

_____ _____
Manufacturing Date

_____ _____
President Date

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STANDARD OPERATING PROCEDURE

Procedure: Certification of Ovens

Procedure No.: PL-136

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1.0 PURPOSE

To describe the procedures for certifying ovens used in those manufacturing or quality assurance operations which require the heating of a component or item at a specified temperature range.

2.0 SCOPE

This procedure applies to all ovens used in manufacturing operations and Quality Assurance release testing. Manufacturing and Quality Assurance personnel are responsible for following the procedures set forth in this protocol.

3.0 PRINCIPLE

An operational qualification is conducted and is comprised of calibration of temperature controlling and recording RTDs and a temperature distribution study conducted on the empty oven for a specified period of time. A performance qualification is comprised of a temperature distribution study conducted on the oven while it contains a known volume of material or while under normal conditions of use.

4.0 APPLICABLE DOCUMENTS

4.1 Certification of Manufacturing System, Processes and Equipment, PL-111

4.2 Contractor's Calibration Procedure

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5.0 SAFETY PRECAUTIONS

Ovens and temperature recorders are electrically powered. Observe the usual safety precautions for Electrical Safety.

6.0 INTERFERENCES

Not Applicable

7.0 LIMITATIONS

Not Applicable

8.0 MATERIALS AND EQUIPMENT

8.1 Oven to be Certified

8.2 Chart Recorder, Model No.

8.3 Temperature Monitoring System (Supplied by Contractor)

8.4 Instruments Calibration Block (Supplied by Contractor)

9.0 REAGENTS

Not Applicable

10.0 PROCEDURE

10.1 The Contractor shall calibrate thermocouples according to the Contractor's SOP. (Calibrate at 0°C and at the desired oven temperature set point. Check calibration at two temperatures ± 15°C of the temperature set point. Thermocouples that are not within ± 0.2°C of the NBS traceable reference shold be repaired or replaced.)

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10.2 The Contractor shall calibrate recording and controlling RTDs at the temperatures specified in 10.1 against an NBS traceable reference.

10.3 Position the appropriate number of the calibrated thermocouples throughout the empty chamber so that all areas of the chamber are represented. Locate one of the thermocouples adjacent to the controlling RTD.

10.4 Indicate placement of the thermocouples on a schematic diagram of the oven chamber.

10.5 Adjust temperature controller to the desired temperature set point. Allow 1-2 hours for the oven temperature to equilabrate.

10.6 Label circular chart for chart recorder with date, operator's initials and run number.

10.7 Program monitor to record temperature data at 15-minute intervals.

10.8 Record thermocouple and RTD temperatures for 48 hours.

10.9 On completion of the above, check the calibration of the thermocouples at the temperatures specified in 10.1.

10.10 Place a known mass of material in a container similar to that used for material to be heated into the oven along with any other equipment normally used according to current manufacturing or quality assurance procedures.

10.11 Place one thermocouple in the center of the mass and position appropriate other thermocouples throughout the chamber so all areas are represented. Locate one of the thermocouples adjacent to the controlling RTD.

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10.12 Indicate placement of thermocouples, RTDs, and the materials on a schematic diagram of the oven chamber. Record date, operator initials, and run number on circular chart.

10.13 Record thermocouple and RTD temperature at 15-minute intervals for 48 hours.

10.14 On completion of 10.13, check the calibration of the thermocouples at the temperatures specified in 10.1.

11.0 DATA ANALYSIS

11.1 On the conclusion of each study, compile all recording charts and thermocouple data.

11.2 Determine the statistical average of all thermocouple recordings during incubation for the empty chamber and loaded chamber studies.

11.3 Determine the "hot" and "cold" spots in the chamber by averaging the temperature data during the heating period for each individual thermocouple.

11.4 The acceptability of each study is determined based on the following criteria:

11.4.1 Not more than one thermocouple may malfunction during the heating period.

11.4.2 Temperature uniformity is considered acceptable if thermocouple and RTD recordings are within ± 5°C during the hearing period.

11.4.3 Thermocouples should be within ± 0.2°C of the NBS traceable reference for the calibration check at the completion of each study.

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12.0 RECORDING AND REPORTING OF DATA

12.1 Prepare a validation report which summarizes the average temperature in the chamber and the "hot" and "cold" spots in the chamber for each study.

12.2 Indicate whether each study met the required acceptance criteria.

12.3 Describe any problems that were encountered during conducting these studies and what actions were taken to correct them.

12.4 Specify the placement of the recording RTD during use of the oven for subsequent use based on the temperature variations within the chamber.

12.5 Bind all chart recordings and thermocouple data in a permanent folder along with the report, obtain a Validation Report number and submit the report to the Validation Review Board for review and approval.

12.6 Upon review of the above, if the Validation Review Board finds that the documentation meets the acceptance criteria, Manufacturing or Quality Assurance Department verify the approval by signature.

12.7 Maintain all documentation indefinitely in the Validation file for the oven.

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STANDARD OPERATING PROCEDURE

Procedure : Operation of the Impulse Heat Sealer

Procedure No. : PL-137

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1.0 PURPOSE

To describe the operation of the impulse heat sealer.

2.0 SCOPE

This procedure is to be used for all manufacturing applications of the heat sealer. These applications are, but not limited to, heat sealing of foil/poly laminate pouches and paper/poly laminate pouches.

3.0 APPLICABLE DOCUMENTS

3.1 Service Manual for the impulse heat sealer.

4.0 GENERAL

4.1 This heat sealer is a device for heat sealing or welding layers of thermoplastic film.

4.2 Follow all safety policies as they apply to using electrical equipment. Care should be taken not to catch foreign material between the sealing jaws. The operator is cautioned against placing hands near moving machine parts.

4.3 During actuation the heater bar is clamped and heated.

4.4 The DWELL setting should be numerically as close to the HEAT dial setting as production requirements allow. For extended periods of operation, the DWELL setting should not be less than two (2) scale divisions below the HEAT setting.

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Procedure : Operation of the Impulse Heat Sealer

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4.5 See the Service Manual for maintenance and adjustments.

4.6 Principle of Operation

Operation of the heat sealer is based on a process in which the thermoplastic films are:

4.6.1 Gripped by a pair of jaws.

4.6.2 Heated to their welding temperature by a short powerful heat impulse.

4.6.3 Allowed to cool while still under pressure between the jaws.

4.7 Description

To best understand the operation of this machine, it should be considered in three major parts:

(1) The Sealing Jaw Assembly,
(2) Jaw Closing Assembly, and,
(3) Impulse Generator and its controls.

4.7.1 The Sealing Jaw Assembly

The Sealing Jaw Assembly is comprised of two jaws, one of which is the stationary Heater Bar and, the other, the movable Pressure Bar. The Heat Impulse is roduced in the Heater Bar. The Pressure Bar (moving jaw) is surfaced with a resilient strip and, together with the Heater Bar, holds the film firmly in place during the sealing cycle.

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4.7.2 The Jaw Closing Assembly

The jaws are closed by a mechanical linkage. This linkage serves as a force multiplier which exerts a very small force when the jaws are open and applies the sealing force only after the jaws are closed, thus minimizing possible injury to the operator.

4.7.3 The Impulse Generator and its Controls

The Heat Timer Circuit is employed for controlling the flow of current from a step-down transformer through the heater element. When the sealing jaws are closed, the films are under pressure, thus starting the Heat and Dwell cycle. This cycle is automatically terminated after a time interval whose length is determined by the adjustment of Heat and Dwell.

5.0 PROCEDURE

5.1 Plug foot switch into 2 prong socket.

5.2 Plug line cord into 115 V, 60Hz AC power supply.

5.3 Turn ON/OFF switch "ON".

5.4 Turn Heat and Dwell dials to predetermined setting.

5.4.1 Place film between jaws and press these closed and allow to remain there for about 2 seconds during which time the film will heat and cool.

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Procedure : Operation of the Impulse Heat Sealer

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5.4.2 Examine the seal. A watery clear glaze indicates that there is insufficient heat penetrating the film. A visual indication of a satisfactory seal is a dull grey line. In addition, a satisfactory seal can be determined by pulling the sealed surfaces of samples apart. A satisfactory seal when sealing film to paper is obtained when, on pulling the surfaces apart, paper fibers are noted on the film portion. For foil film seals, a satisfactory seal is present when film tear is observed when the two layers are pulled apart.

5.4.3 Increase both the HEAT dial and the DWELL dial one division at a time until a satisfactory seal is produced. If the seals appear melted or shriveled, increase the DWELL dial only. The optimum setting of the HEAT dial is the lowest setting that produces a satisfactory seal.

5.4.4 With continuous use, the Heater jaw temperature will become slightly elevated due to residual heat. This pre-heated state may require a higher Dwell setting to produce cooled seals when the jaws open.

5.4.5 The maximum output of the sealer or shortest time cycle per seal is obtained by adjusting the two dials to the lowest setting which will produce a satisfactory seal and not exceed the design limits of the machine.

5.5 Place a test film between jaws and press to close. The jaw will close and remain there for a consistent time period dependent on dwell setting.

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Procedure: Operation of the Impulse Heat Sealer

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5.6 Repeat sealing at least 5 times to pre-heat jaws so that no further adjustments need to be made. Discard films used for testing. Repeat this testing whenever the sealer is not used for extended periods of time (greater than 15 minutes).

5.7 Proceed to seal accordingly. Notify supervisor of any unusual observations or sealing malfunctions.

5.8 At the completion of the operation turn equipment off and unplug from AC power source.

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STANDARD OPERATING PROCEDURE

Procedure: Internal Auditing

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1.0 PURPOSE

To describe those procedures to be followed to internally audit and monitor the various manufacturing and quality assurance operations performed at Plastafil facilities.

2.0 SCOPE

2.1 All operations including but not limited to receiving, component storage, manufacturing, filling, labeling, finished item, packaging, storage, Quality Assurance and distribution of approved products are subject to these auditing and monitoring procedures.

2.2 These monitoring and auditing functions will be performed by personnel not responsible for functions being audited, however, outside consultants may perform these functions.

3.0 APPLICABLE DOCUMENTS

3.1 Internal Systems Review Check List

3.2 Internal Process Review Report

3.3 Product/Process Incident Report

3.4 Quality Assurance Release Check List

Approvals		Date			
Approved By	Q.A.		Approved By	Mfg	Effective Date
					Issued By

STANDARD OPERATING PROCEDURE

Procedure: Internal Auditing

Procedure No.: PL-138

4.0 GENERAL

4.1 A systems audit is defined as a review of the overall compliance by personnel performing all those operations defined in 2.0 to those approved current systems and procedures and to current Good Manufacturing Practice (cGMP) which may apply and govern the specific operation. These systems audits are conducted at a minimum of once per calendar year. These audits are documented using the Internal Systems Review Check List.

4.2 An internal process review is defined as an intensive review of an individual major manufacturing process to assess effectiveness. These reviews are conducted at appropriate intervals; however, during a 12-month period all major processes shall be reviewed at least once. These reviews are documented using the Internal Process Review Report.

4.3 Product/process investigations are performed as the result of quality problems or potential quality problems such as lot failures, processor equipment problems, product stability issues, customer complaints or as the result of findings from routine audits or inspctions. These investigations are documented.

4.4 All manufacturing lot records are audited by Quality Assurance prior to release to assure completeness and correctness, and to determine that no deviations occurred during the manufacturing processes which may require a change in the qualty assurance sampling, inspection and testing requirements prior to release.

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4.5 Copies of all systems audits and copies of reports of significant deviations or conditions detected during process reviews, product/process investigations, or lot record reviews are provided to top management. Copies of all reports are provided to Quality Assurance and manufacturing.

4.6 Where findings implicate or potentially implicate other lots or products beyond those being evaluated, Quality Assurance shall institute such action that may be necessary or appropriate to prevent the distribution of such material until the investigation establishes that such material is satisfactory for distribution.

4.7 Copies of these internal audit or investigation reports shall not be shown to regulatory inspectors or to other third parties without the approval of the President.

5.0. PROCEDURE

5.1 Systems Audit and Review

5.1.1 Personnel performing the audit shall prepare a schedule for performing the complete systems review to assure that such reviews are conducted at least one per year.

5.1.2 These reviews shall be conducted using a Check List as the basis for this review. Where findings dictate, appropriate deviations may be made from the check list form to more fully evaluate the observations.

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5.1.3 These systems audits should normally be conducted following the complete process beginning with the purchase of components through the storage and distribution of released lots.

5.1.4 Significant findings or deviations observed during this review shall be promptly reported to the appropriate personnel for prompt corrective action. Where questions concerning lot quality or suitability are observed, Quality Assurance shall be notified so that appropriate actions can be initiated.

5.1.5 All findings shall be documented, reported and retained.

5.1.6 Where follow-up reviews are considered necessary or appropriate, these shall be scheduled and performed to assure that needed correction(s) have been performed. These follow-up reviews shall be documented.

5.1.7 Copies of reports shall be retained in a systems review file in the audit file for at least seven years.

5.2 Internal Process Reviews

5.2.1 Personnel performing the audit shall prepare and schedule these process reviews to assure that each major process is reviewed at least once per year.

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5.2.2 These reviews shall be conducted using the appropriate Standard Operating Procedures as the basis for the review. Where appropriate, special samplings or other evaluations may be initiated to better assess the effectiveness the process as it is actually being performed.

5.2.3 Significant findings or deviations observed shall be promptly reported as per 5.1.4.

5.2.4 All findings shall be documented and reported.

5.2.5 When follow-up reviews are considered necessary or appropriate these shall be scheduled and performed to assure that the needed corrections have been performed. These follow-ups shall be documented.

5.2.6 Copies of these reports shall be retained for at least seven years.

5.3 Product/Process Investigation

5.3.1 Quality Assurance shall conduct these investigations.

5.3.2 These investigations may be initiated for the reasons indicated under 4.4 or for any other reason where a real or potential quality-related problem is suspected.

5.3.3 Significant findings or observations shall be promptly reported as per 5.1.4

5.3.4 All findings shall be documented and reported.

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5.3.5 Where follow-up investigations are considered necessary or appropriate these shall be scheduled and performed to assure that needed corrections have been performed. Such follow-up investigations shall be documented.

5.3.6 Reports of these investigations shall be provided to management and copies retained.

5.4 Manufacturing Lot Records Audit

5.4.1 These lot records reviews shall be conducted by Quality Assurance prior to lot release.

5.4.2 The purpose of these reviews is to assure that all records are complete and correct and that no conditions or deviations occurred during the various manufacturing operations.

5.4.3 Quality Assurance personnel shall investigate all significant deviations from the approved Standard Operating Procedures and determine whether additional inspections and/or testing or other steps should be initiated to properly evaluate the lot prior to release.

5.4.4 All deviations shall be reported to the appropriate manufacturing supervisor to effect actions to prevent recurrence.

5.4.5 Significant observations may result in the initiation of a process review or a product/ process investigation where appropriate/

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Procedure : Internal Auditing

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5.4.6 The manufacturing lot records review shall be documented using the Quality Assurance Release Check List. These shall be filed in the lot folder.

5.5 Reports of major deviations or conditions observed during any of the several audits or reviews shall be acted on promptly to assure that necessary and appropriate actions are initiated.

5.6 Where procedure changes, additional equipment, or training is necessary to correct the situation and/or to prevent recurrence, such action shall be promptly initiated.

Effective Date

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Internal Systems Review Checklist

Review Initiated: _____

Auditor(s): _____ _____

Rating	Interpretation	
3	Excellent	Item/Area/System/Knowledge is superior.
2	Adequate	Item/Area/System/Knowledge meets basic minimum requirements.
1	Poor	Item/Area/System/Knowledge is weak and not up to acceptable standards.
0	Unsatisfactory	Item/Area/System/Knowledge is missing or of such nature to warrant serious quality concerns.

3 2 1 0

I. Receiving Procedures

1. Is the receiving area clean and orderly?
2. Do receiving personnel inspect incoming shipments for requirements specified on the purchase order and item specification sheet?
3. Are receiving logs up to date?
4. Are appropriate SOPs readily accessable and current?

II. Quarantine Procedures

1. Is the area restricted to authorized personnel?
2. Is the area clean and orderly?
3. Are all materials stored off the floor and in a manner to prevent contamination, damage, or mixups?
4. Are all materials properly labeled with item number, lot, or receiving number and "Quarantine"?
5. Are inventory records maintained for every item in quarantine and is the inventory properly adjusted after sampling.
6. Are containers appropriately labeled after sampling?

II. **Quarantine Procedures** (continued)

7. Is the material sampling log up to date?

8. Are appropriate SOPs reaily accessable and current?

III. **Manufacturing Materials - Storage and Handling**

1. Is the area clean and orderly?

2. Is access to stockrooms and materials storage restricted to authorized personnel?

3. Are all materials stored off the floor and in a manner to prevent contamination, damage, or mixups?

4. Are all materials properly labeled?

5. Is there an inventory/accountability system which will provide traceability to a finished product?

6. Is there a system to provide for the use of oldest materials first?

7. Are appropriate SOPs readily accessable and current?

IV. **Production**

1. Is the area clean and orderly? Are cleaning procedures and schedules followed and is cleaning documented?

2. Are production employees suitably attired for the area in which they are working?

3. Are cleaning and routine maintenance procedures established and followed for production equipment and is this documented?

4. Is equipment requiring calibration within current calibration? Is the expiration date for the calibration clearly visible.

5. Are equipment and room usage logs maintained?

6. Are sterilized/depyrogenated items clearly labeled and stored to prevent contamination and mixup with nonsterile equipment?

IV. Production (continued)

7. Are sterilization/depyrogenation logs maintained? Do current procedures reflect documented validated procedures?

8. Are filter integrity tests performed on filters used to sterilize solution before and after filtration?

9. Are personnel adequately gowned and trained in aseptic processing techniques?

10. Is the area monitored for microbial contamination during aseptic processing?

11. Do batch records reflect the following:

    a. Each step in processing is signed and dated by the individual performing the operation.

    b. Critical measuring, combining, or monitoring steps are independently checked, dated, and signed by a second individual.

    c. The name and weight or measure of each ingredient is recorded.

    d. A complete list of components is provided.

    e. Identity of equipment used is recorded along with documentation of cleaning.

    f. Any calculations are clearly recorded.

    g. Theoretical yields are recorded at appropriate phases of production along with minimum and maximum percentages at which an investigation is necessary.

    h. Each step is clearly stated and includes special precautions if necessary.

    i. There are provisions for in-process samples at appropriate stages of manufacture.

    j. There are time limitations for holding of in-process items. Actual time intervals are recorded.

IV. Production (continued)

12. Are batch records kept at work area during operations?

13. Are batch records or changes to batch records approved prior to initiating processing?

14. Are SOPs readily accessable to employees performing operations?

15. Are directions followed on Batch Records and SOPs?

16. Are sterilization processes validated?

17. have all process stages of manufacture which have the potential for causing variability of in-process and final product been validated?

18. Are support systems such as water system validated?

19. Are current procedures in accordance with the validations?

20. Is there a distinct area provided for labeling operations?

21. Are procedures established for pre-clearance of the area prior to labeling or packaging operations to prevent mixups.

22. Are labels checked for proper part number, lot number, and expiration date prior to label application?

23. Is the part number and lot number of the material to be labeled verified with those specified on the batch record.

24. Is a copy of the label affixed to the batch record?

25. Are there restrictions on authority for access to labels?

26. Is there an established program for the training of production personnel in CGMPs and specific SOPs? Is this training documented?

V. Packaging, Shipping, and Distribution

1. Is the finished goods area restricted to authorized personnel?

2. Is the area clean and orderly? Are lots sufficiently segregated to prevent mixup?

3. Is there documentation that specifies the final product configuration?

4. Is this configuration verified prior to shipment?

VI. Quality ASSURANCE

1. Are Quality ASSUR. facilities clean, neat, and orderly?

2. Are personnel properly attired for work within the are?

3. Are purchased components, intermediate materials, packaging, and labeling materials sampled and tested according to the appropriate item specification prior to release to manufacturing?

4. Do specifications specify the sampling procedure and quantity? Are these specifications followed?

5. Are SOPs readily available which adequately describe test procedures?

6. Are test results documented by the individual performing thes test? Does a second individual review the test results and document the review by signature?

7. Is laboratory equipment within current calibration? Is the recalibration due on date clearly marked on the equipment? Are there provisions for a recalibration schedule?

8. Are laboratory reagents properly identified and labeled with expiration dates and safety precautions?

9. Are reserve samples maintained for raw materials used in finished product?

VI. Quality

10. Are reserve samples matintained for finished product?

11. Is a log maintained of test samples and reserve samples?

12. Is a log maintained of QA tests completed?

13. Are records of inspection and test results maintained?

14. Are batch records reviewed prior to release of product?

15. Is there an established program for the training of Quality Control personnel in CGMPs and specific SOPs. Is this training documented?

VII. Facility Engineering

1. Are preventative maintenance procedures established for HVAC equipment, boilers, and water systems and vacuum systems?

2. Is there an equipment file which documents the installation and maintenance history for each item of equipment?

3. Is there a history of equipment calibrations maintained and a schedule for future calibrations? Is equipment identified to reflect the calibration date and recalibration due date?

4. Are there procedures to assure proper sanitation of the facility and pest control?

5. Are the building exterior and grounds maintained?

6. Are adequate washing facilities with hot and cold water, soap, clean toilets, and towels or driers provided?

7. Are adequate waste containers provided for all areas with an adequate system for disposal collection?

Audit Summary

Rating Results

Number of excellent observations: _____

Number of adequate observations: _____

Number of poor observations: _____

Number of unsatisfactory observations: _____

Total number of observations: _____

Items receiving rating of 1 or 0 require further comment:

Comments: _____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Review Completed: _____

_____ _____

Auditor Date

_____ _____

Quality Assurance Date

STANDARD OPERATING PROCEDURE

Procedure : Calibration of Balances

Procedure No. : PL-139

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1.0 PURPOSE

To provide a procedure for routine calibration of the balances used by Manufacturing and Quality Assurance.

2.0 SCOPE

This procedure is used for routine calibration of balance. Quality Assurance is responsible for the calibration of these balances.

All results from both the calibration and calibration checks will be entered into a designated notebook or log report. Quality Assurance will document results. Quality Assurance personnel are responsible for the maintenance of the calibration records and ensuring that the balances are calibrated according to this SOP.

All balances will, in addition, be calibrated by an outside contractor every six months plus or minus one month.

3.0 APPLICABLE DOCUMENTS

3.1 Operating Instructions –
3.2 Operating Instructions –
3.3 Operating Instructions –
3.4 Operating Instructions –
3.5 Calibration Report
3.6 Calibration Programs, PL-106
3.7 Calibration Logs

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Calibration of Balances

Procedure No. : PL-139

4.0 GENERAL

4.1 Safety Precautions

Observe usual laboratory precautions.

4.2 References

4.2.1 Statistical Validation of Balance.

4.2.2 Statistical Validation of Balance.

4.2.3 Statistical Validation of Balance.

4.2.4 Operation of the

4.3 Interferences

4.3.1 Vibration, dirt, particles from previous weighing and air movement interfere with the weighing accuracy.

4.3.2 Skin oils will corrode calibration weights; wear cotton gloves or use forceps when handling weights.

4.3.3 If a balance is moved from one location to another, it will need to be calibrated and checked with external weights before use.

4.4 Limitations

4.4.1 The individual sensitivity of each balance.

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STANDARD OPERATING PROCEDURE

Procedure : Calibration of Balances

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4.5 Materials and Equipment

4.5.1 Laboratory Balances

4.5.1.1
4.5.1.2
4.5.1.3
4.5.1.4

4.5.2 ASTM Class 1 balance weights (are built in).

4.5.3 Class S weights (1 mg - 100 g)

4.5.4 Class S weights (100 g - 1000g)

4.5.5 Class S weights (2000 g)

5.0 PROCEDURE

5.1 Balances are to be calibrated prior to their initial use for each day of operation. They are also to be checked at the low and high end of their weighing range using external class S weights.

5.1.1 Assure balance has been connected to the power supply for at least 60 minutes.

5.1.2 Remove all objects from pan, assure pan is clean.

5.1.3 Verify that the balance is level by checking the bubble indicator in the weighing chamber.

5.1.4 Protect weighing pan from air drafts.

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STANDARD OPERATING PROCEDURE

Procedure : Calibration of Balances

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5.1.5 Set the balance to the calibration mode.

5.1.6 Calibrate in accordance with the manufacturer's instructions.

5.1.7 Enter results in the calibration log.

5.1.8 If balance is found to be out of calibration at any weight, complete Calibration Report and follow procedures indicated in Calbration Programs, PL-106.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Calibration of Balances

Procedure No. : PL-139

Appendix I. Tolerances for New Weights in Sets. From USP XXI

[41] WEIGHTS AND BALANCES

Pharmacopeial tests and assays require the use of balances that vary in capacity, sensitivity, and reproducibility. The accuracy needed for a weighing dictates the type of balance and the class of weights required for that weighing. Where substances are to be "accurately weighed", the weighing is to be performed so as to limit the error to not more than 0.1%. For example, a quantity of 50 mgs is to be weighed so that the error does not exceed 50 ug. A balance should be chosen such that the value of three times the standard deviation of the reproducibility of the instrument, divided by the amount to be weighed, does not exceed 0.001.

Tolerances for New Weights in Sets

Denomination g	Class M Individual ug	Class M Group ug	Class S Individual ug	Class S Group ug	Class S-1 Individual ug	Class P Individual ug
100	200		250		1000	2000
50	250		120		600	1200
30	150		74	154	450	900
20	100		74	154	320	700
10	50		74	154	250	500
5	34	65	54	105	180	360
3	34	65	54	105	150	300
2	34	65	54	105	130	260
1	34	65	54	105	100	200
mg						
500	5.4	10.5	25	55	80	160
300	5.4	10.5	25	55	70	140
200	5.4	10.5	25	55	60	120
100	5.4	10.5	25	55	50	100
50	5.4	10.5	14	34	42	85
30	5.4	10.5	14	34	38	75
20	5.4	10.5	14	34	35	70
10	5.4	10.5	14	34	30	60
5	5.4	10.5	14	34	28	55
3	5.4	10.5	14	34	26	52
2	5.4	10.5	14	34	25	50
1	5.4	10.5	14	34	25	50

Effective Date

Issued By

STANDARD OPERATING PROCEDURE - VALIDATION

Procedure: Validation of Manufacturing Procedures	**Revision Record** Page	Date
Procedure No.: PL-140	1	
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1.0 PURPOSE

To describe the procedures for validating a particular manufacturing process used to produce product. The intent of this validation is to demonstrate that the manufacturing process in question can consistently produce a product that meets specifications.

2.0 SCOPE

This procedure applies to products and sterilized final products manufactured in part or solely by Plastafil which become part of an approved marketable final product. Manufacturing and Quality Assurance personnel are responsible for following this procedure.

3.0 PRINCIPLE

3.1 Prior to approval and marketing of a final product it must be demonstrated that major processes utilized in manufacturing this product can consistently produce material that meets specification. This is demonstrated by manufacturing at least three lots using the same manufacturing procedure and demonstrating uniformity by means of normal Quality Assurance testing. Efforts will be made during the manufacture of these lots to assure that, where practical, the limits of acceptability will be probed to assure that normal expected variation will result in acceptable and uniform product. After this, the batch records and Qualtiy Assurance test documents will be reviewed to determine the consistency of the manufacturing process.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By_____

3.2 If any major changes are made to the process after the original validation is completed, the new process resulting from these changes must be revalidated according to this protocol. The validation of this new process must be completed before material produced by it can be marketed. The Validation Review Board will determine if a change to an existing validated process constitutes a major change.

3.3 If necessary this protocol can also be used for retrospective process validations. This would consist of reviewing batch records and accompanying Quality Assurance test documentation of at least three previously completed lots where no major subsequent changes have been made and determining the consistency of the process used. The Validation Review Board will determine if a retrospective validation of a certain process is warranted.

3.4 Ideally, different lots of active ingredients should be used for each lot which is part of the validation to assure that all expected variables are covered during validation.

4.0 APPLICABLE DOCUMENTS

4.1 Batch Records for the process to be validated.

4.2 In-process test reports for each lot.

4.3 Final Quality Assurance test reports and Final Product Disposition.

4.4 Validation reports for test methods where applicable.

STANDARD OPERATING PROCEDURE - VALIDATION

Procedure: Validation of Manufacturing Procedures

Procedure No.: PL-140

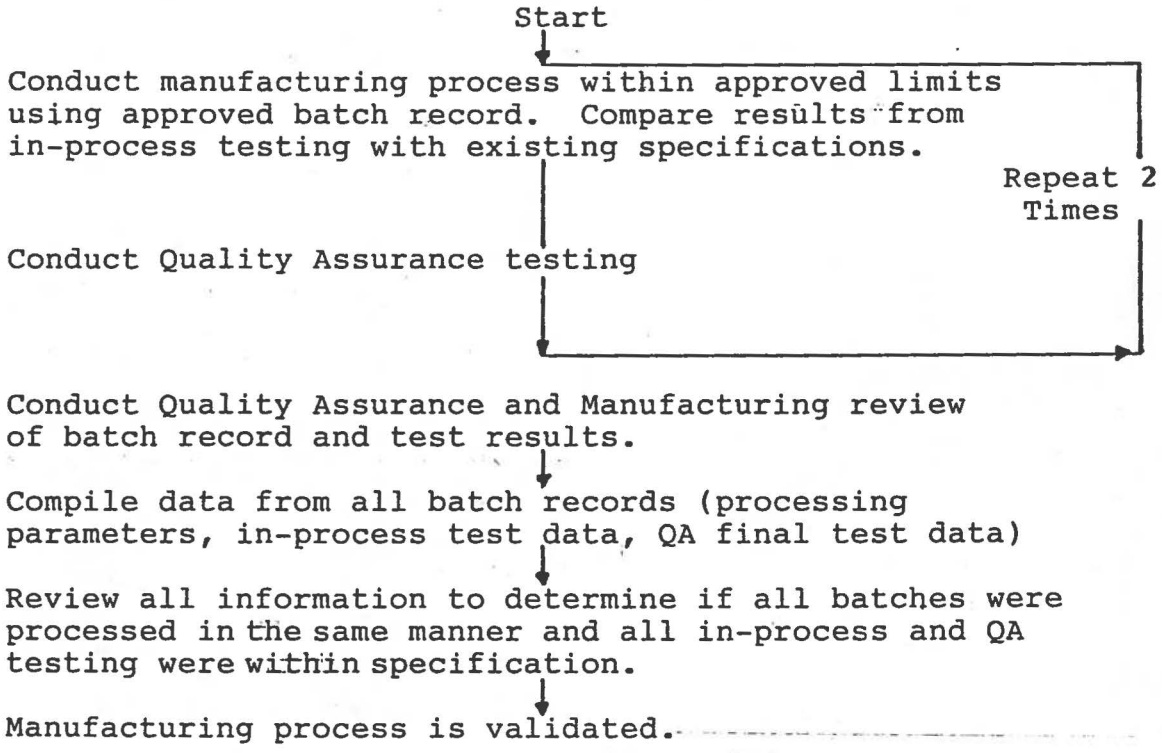
5.0 SAFETY PRECAUTIONS

All safety precautions described in the batch records, and SOP's used and the Material Safety Data Sheets.

6.0 MATERIALS AND EQUIPMENT

Materials and equipment specified in the batch records used.

7.0 FLOW DIAGRAM



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STANDARD OPERATING PROCEDURE - VALIDATION

Procedure : Validation of Manufacturing Procedures

Procedure No. : PL-140

8.0 PROCEDURE

8.1 Conduct process to be validated.

8.2 Submit material and batch record to QA for testing and review.

8.3 Repeat steps 8.1 and 8.2 at least two more times (a total of three lots of material produced).

8.4 Compile processing parameter data and test data (both QA and in-process) from the lots conducted.

8.5 Review processing parameter data and test data to determine if the process used was consistent and produced material that met specifications.

9.0 DATA ANALYSIS AND ACCEPTABILITY

In order for a process to be considered validated the lots produced must meet the following criteria:

9.1 All lots must be sequentially produced without failure attributable to the process.

9.2 Final batch record review on all lots produced is approved by Quality Assurance and Manufacturing.

9.3 The processing parameters compiled from the batch records must show that each lot was manufactured within the acceptable ranges as defined in the batch record.

9.4 The in-process tests conducted during processing must meet acceptance criteria.

9.5 The final Quality Assurance tests conducted on the material must meet specifications.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Revising, Rewriting or Deleting SOPs

Procedure No.: PL-141

Revision Record	
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1.0 PURPOSE

To describe the procedures used to revise, rewrite, or delete an existing SOP and the control of these procedures.

2.0 SCOPE

This procedure is followed without deviation by all personnel involved with rewrites, revisions, or deleting of procedures.

3.0 APPLICABLE DOCUMENTS

3.1 SOP Request
3.2 SOP Form
3.3 Writing SOPs, PL-109
3.4 Document Change Order
3.5 Document Control, PL-151

4.0 GENERAL

4.1 It is the responsibility of personnel performing the document control function to control all SOPs to ensure that all persons authorized to have these current editions of any procedure.

4.2 SOPs become effective after the indicated effective date.

5.0 PROCEDURE

5.1 Persons desiring to recommend revision or rewriting shall fill out SOP Request Form and submit to Document Control.

Note: If the SOP is to be deleted, explain reason and submit form to Document Control.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By___

STANDARD OPERATING PROCEDURE

Procedure: Revising, Rewriting or Deleting SOPs

Procedure No.: PL-141

5.2 The Document Control person shall review request form for

5.2.1 Sign request form and file with the master copy of the SOP.

5.2.2 Send copies to the requestor.

5.3 Revise, rewrite the procedure. Refer to procedure P1-109. Fill out the Document Change Order Form.

5.4 Submit the revised SOP and the Form to Document Control for typing of the final draft. The Document Control person shall:

5.4.1 Type the final draft and route for final approval signatures.

Note: Stamp new effective date on the first page of the SOP and indicate effective date and sign on the lower right hand corner of effected page of the SOP master.

5.4.1.1 File master.

5.4.2 Route copies of the revised, approved SOP to only those individuals that appear on the distribution list.

5.4.3 Obtain all old editions of the SOP or deleted SOP when issuing revisions.

5.4.4 Retain the master copy of the old edition of the SOP or the deleted SOP in a scured area.

5.4.5 Destroy the copies of the old edition of the SOP

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Revising, Rewriting or Deleting SOPs

Procedure No.: PL-141

S.O.P. REQUEST FORM NO.

Document Name and Number_____

Title_____

_____ Edition No._____

Reason for Request /__/ Revision

/__/ Rewrite

/__/ Other: Explain_____

Requested By_____ Date_____

Released By_____ Date_____

(Must be released by Document Control)

Effective Date
Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Revisig, Rewriting or Deleting SOPs

Procedure No.: PL-141

DOCUMENT CHANGE ORDER

Document Title_____

Document No._____ Product No._____ Edition Date of Document_____

____Major Revision ____Minor Revision ____New Document ____Deletion

Step No(s).	Describe Document Change (continue on back if necessary)

Reason for Change
(continue on back if necessary)

Originator_____ Date_____

Approvals:
Manufacturing_____ Date_____

Quality Assurance_____ Date_____

New Edition Date_____

Document Replaced in Applicable Departments By

_____ Date_____

Effective Date

Issued By_____

600Q÷

STANDARD OPERATING PROCEDURE

Procedure: Revising A Batch Record or Specifications Master
Procedure No.: PL-142

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1.0 PURPOSE

To describe the approved method for revising a Specification or Batch Record Master.

2.0 SCOPE

This procedure applies to any responsible employee who has determined the need for revising a batch record master or specifications.

3.0 APPLICABLE DOCUMENTS

3.1 Document Change Order Specification or Batch Record
3.2 Batch Record/Specifications Request Form
3.3 Document Control, PL-151

4.0 GENERAL

4.1 A manufacturing batch record master is the document from which copies are made for manufacturing use. It is the original signed document secured by document control.

4.2 A Specifications is a document which defines the criteria for evaluating and approving a component or product.

4.3 This SOP pertains to batch records which have had an effective date assigned.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By

STANDARD OPERATING PROCEDURE

Procedure : Revising a Batch Record or Specifications Master

Procedure No. : PL-142

5.0 PROCEDURE

5.1 The requestor shall obtain and complete a request form and document Change Order Form when the need to revise a Manufacturing Batch Record Master or Specification has been determined.

5.2 Follow SOPs P1-102, P1-109, P1-141 as appropriate with regard to the document change order procedure.

5.3 Upon final typing, document control shall insert new edition date and sign the new edition in the appropriate location.

5.4 Route a copy of the approved edition to those persons authorized to have such issues.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : Revising a Batch Record or Specifications Master

Procedure No.: PL-142

DOCUMENT CHANGE ORDER SPECIFICATIONS OR BATCH RECORD

Document Title_____

Document No._____ Product/Index No._____ Edition Date of Doc._____

____Major Revision ____Minor Revision ____New Document ____Deletion

Describe Proposed Change
(continue on back if necessary)

_____

_____

_____

_____

Reason for Change
(continue on back if necessary)

_____

_____

_____

_____

Originator_____ Date_____

Approvals:
Manufacturing_____ Date_____

Quality Assurance_____ Date_____

New Edition Date_____

Document Replaced in Applicable Departments By

_____ Date_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure : Revising a Batch Record or Specifications Master

Procedure No.: PL-142

BATCH RECORD/SPECIFICATIONS REQUEST FORM

Document (Batch Record)(Specifications)_____

Product Number_____

Title_____

_____Edition No._____

Reason for Request /__/ Revision

/__/ Issuing for Production

/__/ Other: Explain_____

Requested By_____ Date_____

Released By_____ Date_____

(Must be released by Document Control)

Effective Date
Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Insect and Rodent Control

Procedure No.: PL-143

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1.0 PURPOSE

To specify those procedures and materials necessary to prevent the contamination of equipment components, product containers, closures, packaging, labeling materials or product by insects or rodents.

2.0 SCOPE

This procedure applies to all Plastafil facilities and buildings where components, intermediates and manufacturing supplies, labeling and products are manufactured, handled or stored.

3.0 APPLICABLE DOCUMENTS

3.1 Cleaning and Sanitation Procedures, Pl-144

3.2 Federal Insecticide, Fungicide and Rodenticide Act (7 USC 135).

3.3 List of Approved Insecticides, Rodenticides, Fungicides and mechanical traps.

4.0 GENERAL

4.1 No substance shall be used as an insecticide or a rodenticide unless it has been registered and is used in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (7 USC 135).

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
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Procedure: Insect and Rodent Control

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4.2 No substance shall be used unless it is approved by Quality Assurance. Quality Assurance shall maintain data concerning the registration of the product(s), ingredients, warnings and proper use of these materials and shall retain copies of certification for each routine use of these materials within the facilities.

4.3 Routine insect and rodent control procedures will be performed by an approved outside contractor. Contractor's personnel shall comply at all times with Plastafil safety, cleaning, gowning and sanitation procedures while performing their service.

4.4 These services shall be performed at the Plastafil facilities.

4.5 Unless otherwise indicated these procedures are performed and followed by Quality Assurance.

5.0 PROCEDURE

5.1 Quality Assurance shall select and approve a qualified commercial pest control company or companies to perform these contracted services.

5.2 Consulting with the approved contractor(s), establishes those approved insecticides, rodenticides, fungicides and mechanical devices which shall be approved for use.

5.3 Establishes an initial schedule for routine control and monitoring of the program to determine whether more frequent treatments are appropriate. Accompanies the contractor's representative during performance of services.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Insect and Rodent Control

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5.4 An appropriate contractor performs services as per the following:

5.4.1 Plastafil Facilities

5.4.1.1 Outside perimeter spraying with a product containing Diazinon at a concentration of 0.5% on a monthly basis.

5.4.1.2 Crack and crevice spraying with either a product containing Pyrethins 0.3%, Technical Piperonyl Butoxide 2.2%, N-Octyl Bicycloheptene Dicarboximide 1.209% or Pyrethins 0.5% Technical Piperonyl Butoxide 1.0% 3.36% and Petroleum distillates N-Octyl Bicycloheptene Dicarboximide 1.0% and Refined Petroleum Oil 8% on a monthly basis.

5.4.1.3 Placement and monitoring of mechanical rodent traps on a monthly basis (Quality Assurance to monitor weekly).

5.4.1.4 Other areas as required based on observations. Use only for products defined in 5.4.1.2 for spraying.

5.4.1.5 Should flying insects be observed in warehouse and non-manufacturing areas, in approved product containing 0.5% Pyrethrins, 1% Technical Piperonyl Butoxide, 1% N-Octyl Bicycloheptene Dicarboximide and 8% Refined Petroleum Distillates as the only active ingredients may be used.

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STANDARD OPERATING PROCEDURE

Procedure : Insect and Rodent Control

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5.5 Provides a certification to Plastafil after each monthly treatment indicating what materials were used and inspection results.

5.6 Any employee observing insects or rodents in any area of the facilities shall promptly report the observation to Quality Assurance.

5.7 Quality Assurance shall contact the contractor and request prompt action to control the insects or rodents observed by employees. If the observation was made in an area presently serviced, Quality Assurance shall increase frequency of treatment. If the observation was made in an area not routinely treated, Quality Assurance shall add that area to the treatment schedule.

5.8 Files and maintains contractor certifications, retaining them for at least 3 years.

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STANDARD OPERATING PROCEDURE

Procedure: Insect and Rodent Control

Procedure No.: PL-143

APPROVED CHEMICALS AND DEVICES FOR INSECT AND RODENT CONTROL

I. Approved Contractor

A. Approved Chemicals for Insect Control

1. For outside perimeter spraying:

2. Airborne Insect Control

Active Ingredients:

3. Crack and Crevice Spraying

Active Ingredients:

4. Mechanical Traps

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STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

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1.0 PURPOSE

To describe the basic cleaning and sanitation procedures for the manufacturing facility.

2.0 SCOPE

2.1 The following cleaning and sanitation procedures apply during general manufacturing facility operation. They are considered a minimum and may be superseded by more specific and detailed cleaning and sanitation procedures where deemed necessary by a particular procedure or process.

2.2 These procedures are to be followed by all Plastafil and contracted employees designated for cleaning duties for all manufacturing areas, including the warehouse shipping and receiving areas.

3.0 APPLICABLE DOCUMENTS

3.1 Equipment Cleaning and Use Log

3.2 Equipment Clean Ticket

3.3 Manufacturing Cleaning Form

3.4 Insect and Rodent Control, PL-143

3.5 Cleaning Procedures for Class 100 Hoods, PL-124

3.6 Controlled Environment Daily Use Procedures, PL-127

3.7 Gowning Procedures for Controlled Enviroment Area, PL-126

Approvals		Date			
Approved By	**Q.C.**		**Approved By**	**Mfg**	**Effective Date**
					Issued By

STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

4.0 GENERAL

4.1 Different areas of the manufacturing facility require varying degrees of cleanliness as dictated by precise cleaning procedures. This procedure only covers general cleaning. Procedures specific to a process are to be performed by the responsible manufacturing employee.

4.2 By definition, daily means any day that manufacturing activities take place. Weekly means any week that manufacturing activities take place.

4.3 Manufacturing supervisors are responsible to monitor cleaning and prevent any unsatisfactory conditions due to poor cleaning practices.

4.4 For cleaning procedures of the controlled environment areas refer to PL-124 and PL-127.

4.5 Refer to PL-143 for pest control of the manufacturing facility.

4.6 Refer to PL-126 when entering Controlled Environment Area to perform cleaning procedures.

5.0 PROCEDURE

5.1 General Area

The following services are to be performed on a daily basis by designated cleaning personnel:

5.1.1 Empty all normal waste containers. Replace any liners as needed. Empty other containers, boxes, etc., marked by occupant to be thrown away.

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STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

5.1.2 Sweep uncarpeted floors. Wipe or damp-mop any spillage.

Note: Do not sweep manufacturing processing area floors.

5.1.3 Clean and sanitize drinking fountains.

5.1.4 Clean all toilets, toilet seats, urinals, mirrors, door knobs, and sinks with approved germicides.

5.1.5 Refill towel, tissue, hand soap, sanitary napkin, and seat cover dispensers in the restrooms.

5.1.6 Wet-mop the restroom floors with a germicide solution.

5.1.7 Change tacky mats entering controlled environment areas.

The following services are to be performed on a weekly basis:

5.1.8 Dust all shelves, desks and counter tops.

5.1.9 Thoroughly vacuum carpets, including edges and under furniture.

5.1.10 Make all entries and initial these entries in the logs or cleaning forms where provided.

5.1.10.1 Manufacturing Cleaning Forms are to be obtained from supervisor.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

5.1.10.2 Initial the form for each activity completed. At the end of the month, submit the form to the supervisor for review.

5.1.11 Supervisor reviews the Manufacturing Cleaning Form to ensure that all activities performed are being recorded.

5.1.11.1 If documentation is missing or questionable, contact the operator to discuss corrective action and subsequent documentation.

5.1.12 Sign the bottom of the form when complete and file for future reference. Retain files for at least three years.

5.2 The Controlled Environment Area

5.2.1 Follow procedure PL-126 for gowning prior to entering the Controlled Environment Area.

5.2.2 On a weekly basis wet-mop the area using a solution of approved germicide.

5.2.3 Wipe down walls, hood exteriors and all stationary equipment using an approved germiced.

5.2.4 Proceed as directed in paragraphs 5.1.10-5.1.12.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Cleaning and Sanitation Procedures

Procedure No. : PL-144

EQUIPMENT CLEAN TICKET

Previous Lot Name_____

Previous Lot Number_____

Equipment/Item Description:

_____

ID # _____

Cleaned By/Date_____

Checked By/Date_____

Verified By/Date_____

Lot Number_____

Lot Name_____

Date_____

Sterilization/Depyrogenation Graph #

_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

MANUFACTURING CLEANING FORM -- GENERAL

Areas Covered _____ Month/Year _____

FUNCTION	DAY OF THE MONTH																													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
DAILY																															
Empty Trash																															
Sweep Floors																															
Sanitize Drinking Fountains																															
Clean & Sanitize Restrooms																															
Refill Dispensers																															
Wet-mop Restroom Floors																															
WEEKLY																															
Vacuum Carpets																															
Dust all shelves, desks & counter-tops																															

Reviewed By: _____ Date: _____

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

Procedure No.: PL-144

MANUFACTURING CLEANING FORM -- CONTROLLED AREA

Month/Year_____

Week 1 ____Floor ____Walls ____Hoods ____Equipment

Week 2 ____Floor ____Walls ____Hoods ____Equipment

Week 3 ____Floor ____Walls ____Hoods ____Equipment

Week 4 ____Floor ____Walls ____Hoods ____Equipment

Week 5 ____Floor ____Walls ____Hoods ____Equipment

Reviewed By_____Date_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Cleaning and Sanitation Procedures

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EQUIPMENT CLEANING AND USE LOG

Equipment Name_____

Equipment Identification Number_____

Date Log Started_____

Date Log Ended_____

Effective Date
Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Eating, Drinking and Smoking Policy

Procedure No.: PL-145

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1.0 PURPOSE

To describe Policy concerning eating, drinking and smoking in manufacturing areas.

2.0 SCOPE

This procedure will be followed in the laboratory and in all manufacturing areas by all employees.

3.0 APPLICABLE DOCUMENTS

Plastafil Safety Policy

4.0 GENERAL

4.1 All employees, contractors and visitors are responsible for following this procedure.

4.2 Eating is defined as consumption of food items. This would also include the chewing of gum and the dissolving of hard candy in the mouth.

5.0 PROCEDURE

5.1 Eating and Drinking.

5.1.1 The consumption of food and/or beverages is not permitted in areas where product or raw materials are stored or manufactured. Consumption is limited to offices or other specifically designated areas.

Approvals		Date			
Approved By	**Q.C.**		**Approved By**	**Mfg**	**Effective Date**
					Issued By

STANDARD OPERATING PROCEDURE

Procedure : Eating, Drinking and Smoking Policy

Procedure No. : PL-145

5.1.2 The storage of food and/or beverages is limited to those areas provided. Under no circumstances will these items be stored in manufacturing or warehousing areas.

5.2 Smoking

5.2.1 Smoking is not permitted in the laboratory, manufacturing or storage areas at any time.

5.2.2 Smoking is permitted only in offices or other specifically designated areas.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure: Sterilizing by Radiation

Procedure No.: PL-146

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1.0 PURPOSE

The purpose of this procedure is to establish the systems and controls for preparing, shipping, and sampling labeled and packaged product to be sterilized.

2.0 SCOPE

All products to be sterilized by radiation.

3.0 APPLICABLE DOCUMENTS

3.1 Shipping Order Form

3.2 Labeling and Packaging of Product, PL-149

3.3 Warehousing and Shipping Procedures, PL-150

3.4 Sterilized Final Product Specifications

3.5 Quarantine Procedures or Incoming Materials, PL-103

3.6 Quality Assurance Final Release Procedures, PL-131

4.0 GENERAL

4.1 These procedures are to be performed by Quality Assurance unless otherwise indicated.

4.2 Product to be sterilized must be sent only to approved contract sterilizers with an approved agreement. This agreement states the manner for controlling and sterilizing the individual products.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By____

STANDARD OPERATING PROCEDURE

Procedure : Sterilizing By Radiation

Procedure No. : PL-146

5.0 PROCEDURE

5.1 The product to be sterilized will have been labeled, packaged and packed into cartons specified in the Packaging Order by manufacturing personnel.

5.2 After completion of the packaging operation, the cartons of labeled product will be delivered to Quality Assurance together with the completed packaging documents.

5.3 Quality Assurance shall inspect packaged items and review Packaging Order for completeness and correctness.

5.4 Quality Assurance shall place five spore strips of 10^6 Bacillus pumilus previously sealed individually into specially distinctly labeled sealed paper/film pouches into each carton.

5.4.1 The location of each strip shall be determined as a result of dose mapping the carton so as to assure that low and high radiation locations will be monitored.

5.5 The cartons shall be sealed and the lot sent to the contract sterilizer together with the sterilization instructions.

5.6 The lot shall be received by the contractor who shall include dosimeters with each carton positioned at locations found by dose mapping to be appropriate to monitor the process.

5.6.1 Results of dosimeter testing shall be returned to Plastafil with the radiated lot.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Sterilizing By Radiation

Procedure No.: PL-146

5.7 On return from the contractor, the lot shall be placed into quarantine for inspection and sampling by Quality Assurance.

5.8 Quality Assurance shall inspect the cartons to determine that the tell tale sticker has turned from orange to red.

5.9 Quality Assurance shall remove all the pouches containing the spore strips and send them to the contract laboratory for sterility testing and samples for pyrogen test are also to be taken and sent to a contract laboratory.

5.10 The lot shall remain in quarantine until all specifications have been met and the lot is released for shipping.

5.11 After release, transfer to the warehouse location.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Approved Detergents, Germicides and Antiseptic Solutions

Procedure No.: PL-147

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1.0 PURPOSE

1.1 The purpose of this procedure is to establish a list of approved detergents, germicides and antiseptic solutions used for various manufacturing processes.

2.0 SCOPE

2.1 This procedure applies to all personnel engaged in activities requiring manufacturing approved solutions.

3.0 APPLICABLE DOCUMENTS

3.1 Plastafil Safety Policy

3.2 Cleaning and Sanitation Procedures, Pl-144

4.0 GENERAL

4.1 Follow all directions indicated on each container for proper dilution and use.

4.2 Follow all safety rules indicated on each container as well as all Plastafil safety regulations, as they apply to the use of any of the approved solutions.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Approved Detergents, Germicides and Antisetic Solutions

Procedure No.: PL:147

5.0 PROCEDURE

5.1 All manufacturing employees or contracted personnel.

5.1.1 Use the following approved detergents and cleaning agents for cleaning equipment:

- SS-660 Special Clean Room Detergent -- Liberty Industries
- Cidex™ Industrial Disinfecting Solution Concentrate
- Liqui-Nox™

5.1.2 Use the following approved Germicides for cleaning the controlled environment area:

- Staphene
- 70% Isopropyl Alcohol Solution

5.1.3 Use the following approved antiseptic solutions for washing hands and forearms:

- Alcare® Clean Room Hand Germicidal
- Acu-Dyne™ Skin Cleanser
- 70% Isopropyl Alcohol Solution

5.1.4 Upon opening a new container of cleaning solution, enter date opened and initials on the container using indelible ink.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Preventative Maintenance Program

Procedure No.: PL-148

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1.0 PURPOSE

To describe the general procedures for a preventative maintenance program.

2.0 SCOPE

All manufacturing and quality assurance equipment requiring preventative maintenance.

3.0 APPLICABLE DOCUMENTS

3.1 General Calibration Program Requirements, PL-105
3.2 Calibration Programs, PL-106
3.3 Equipment Installation Report
3.4 Preventative Maintenance Form
3.5 Service/History Report
3.6 Work Order
3.7 Scheduling File
3.8 Maintenance Procedures for the Specific Items

4.0 GENERAL

4.1 A specific procedure is required for each item requiring preventative maintenance which describes what procedures and inspections are necessary and the frequency of such preventative maintenance.

4.2 All records are retained in an equipment history file.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By

STANDARD OPERATING PROCEDURE

Procedure : Preventative Maintenance Program

Procedure No. : PL-148

4.3 All work required to repair an instrument or equipment must be documented on a work order.

4.4 Preventative maintenance is the responsibility of Manufacturing. The performance of this work may be performed by outside contractors who perform these services under the supervision of Manufacturing.

4.5 Quality Assurance shall audit this program to assure that it is being performd as required.

4.6 Each item has its own file. The file contains the Service/History Reports, equipment SOP's, Preventative Maintenance Forms, Work Orders and all other relevant records.

5.0 PROCEDURE

5.1 All equipment is assigned an equipment identification number. This information is maintained in a file listing all equipment by number.

5.2 A master list of equipment and required intervals for maintenance is maintained. This shall be used to schedule the required service.

5.3 Manufacturing and/or Quality Assurance personnel shall inspect each piece of equipment before scheduling service to assure it is operating correctly within operational parameters. If it is, then service can be scheduled, if not, an evaluation must be made as to what action must be taken. Both the preservice inspection and actions taken, if any, must be documented.

5.4 Preventative maintenance is documented on the Preventative Maintenance Form. Upon completion this record is filed in the specific file for the individual item.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure : Preventative Maintenance Program

Procedure No.: PL-148

5.5 If the item is found to require service, it should not be used for manufacturing or quality assurance until it has been serviced or repaired.

5.6 After servicing or repair, the equipment must be evaluated to assure that it is operating within its operational parameters. This evaluation shall be documented.

5.7 Equipment which can not be returned to proper operational status shall not be used for manufacturing or quality assurance. Such must be replaced with an item which can and does perform within the required operational parameters.

5.8 Quality Assurance shall audit the performance and effectiveness of this program. This audit shall be performed at least annually and documented.

Effective Date

Issued By_____

PREVENTATIVE MAINTENANCE FORM

Equipment Name_____ Location_____

Model No._____ Serial No._____ Equip. No._____

Items To Be Checked	Frequency	Pass/Fail

Performed By_____ Date Completed_____

SERVICE/HISTORY REPORT

ENGINEERING

REPORT NO.

/ / MFG / / QA | Page of

EQUIPMENT NO.

SERVICE REQUESTED

CONTACT NAME | PHONE NUMBER | DATE

SERVICE REQUESTED (PLEASE BE SPECIFIC)

EQUIPMENT

DESCRIPTION

LOCATION | TAG NO.

MANUFACTURER | MODEL NO. | SERIAL NO.

SERVICE PERFORMED

ACTION TAKEN

	DATE	HOURS	SERVICE COMPLETED / /Yes / / No

SERVICED BY

PRINT NAME | SIGNATURE | DATE

Other

ADDRESS | PHONE NUMBER

PRINT NAME | SIGNATURE | DATE

ATTACH APPLICABLE INSTALLATION DOCUMENTATION, CERTIFICATIONS, WARRANTIES, ETC.

STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No.: PL-149

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1.0 PURPOSE

The purpose of this procedure is to describe the preparation and process of labeling and packaging of all salable products.

2.0 SCOPE

This procedure applies to any product for salable use only and is to be followed by all approved, trained manufacturing personnel.

3.0 APPLICABLE DOCUMENTS

3.1 Control of Inventoried Items, PL-120

3.2 Inventory Transfer Form

3.3 Labeling Accountability Form

3.4 Packaging Order

3.5 Warehousing and Shipping Procedures, PL-150

4.0 GENERAL

4.1 Follow all safety procedures as they apply to the safe use and handling of any item to be labeled and packaged.

4.2 These procedures are to be performed by manufacturing personnel unless otherwise indicated.

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Approved By	Q.C.		Approved By	Mfg	Effective Date

STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No.: PL-149

5.0 PROCEDURE

5.1 Label Imprinting

5.1.1 Obtain the appropriate labels for the material to be labeled via the Inventory Transfer Form.

5.1.2 Obtain a Label Accountability Form from Document Control.

5.1.3 Enter the appropriate information on the form including the assigned lot number and the quantity from stock.

5.1.3.1 Obtain the lot number for the material to be labeled from the manufacturing supervisor.

5.1.4 Imprint the lot number on the label per current procedures.

5.1.5 Enter the quantity of labels imprinted and the amount destroyed during the imprinting process.

5.1.6 Sign and date the form after all other entries are complete and have another employee verify the entries with initials and date.

5.1.7 Affix a sample of the completed label (with lot number) on the form.

5.1.8 Place the labels in a closed container and store until approved.

5.1.9 Send the form to Quality Assurance for proof-reading and approval.

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STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No. : PL-149

5.2 Labeling and Packaging

5.2.1 Obtain the items to be labeled using the Inventory Transfer Form.

5.2.1.1 The items to be labeled must already be released by Quality Assurance.

5.2.2 Transfer the items to be labeled and the approved labels to the Controlled Environment Area for the labeling and packaging operations.

5.2.2.1 The labeling and packaging process must take place in a segregated area with no other labeling operations taking place.

5.2.2.2 Personnel handling products to be packaged shall wear sterile gloves.

5.2.3 The supervisor shall assure that this order is labeled and packaged in accordance with the Packaging Order.

5.2.3.1 Only those components specified for this order shall be present in the segregated area.

5.2.3.2 Check and verify the identity and count of all components and supplies.

5.2.4 Select a Toggle and place into the Paper/Foil pouch; select a Bollard and a Pin, place the Pin into the hole in the Bollard head snugly and place into the pouch. Select a Carbon Fiber Implant, carefully coil into a tight coil and insert into the pouch.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No.: PL-149

5.2.5 Smooth the open end of pouch and seal in accordance with PL-137.

5.2.5.1 Select and seal a dummy pouch containing an empty vial for volume at the beginning, middle and end of the packaging and submit to Quality Assurance for seal integrity testing.

5.2.6 Affix a product label to the center of the pouch.

5.2.7 Affix a Tell Tale radiation sticker label to the same side of the pouch as the product label.

5.2.8 Place the sealed pouch into a Paper/Film pouch, smooth the open end of the pouch and seal in accordance with PL-137.

5.2.8.1 The foil pouch must be inserted into the outer pouch so that the product label shows through the film side of the Paper/Film pouch.

5.2.9 Place the sealed pouch in the carton, label the carton with the carton label and affix a Tell Tale radiation sticker on the carton. Provide to Quality Assurance for placing the spore strips in and sealing.

5.2.10 Complete, sign and date the Packaging Order and have anther employee verify entries with initials and date.

5.2.10.1 Submit the form to the Manufacturing suprvisor for review.

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STANDARD OPERATING PROCEDURE

Procedure : Labeling and Packaging of Product

Procedure No. : PL-149

5.2.11 The supervisor shall review the accountability form and sign and date if approved. Notify the manufacturing employee to transfer materials to Quality Assurance Quarantine.

5.2.12 The supervisor shall destroy all unused labels after they are accounted for.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No.: PL-149

Labeling Accountability Form

Date_____

Quantity from Stock_____
(a)

Label Part Number_____ Revision Number_____

Batch Name/Strength_____

Assigned Lot Number_____Assigned Expiration Date_____

Quantity Imprinted_____+_____=_____
(Destroyed during Imprinting) (b)

Count Checked By/Date_____Verified By/Date_____

Attach Label Here

Quality Assurance Approval/Date_____

Quantity Used_____+_____+_____=_____
(Attached to Product) (Destroyed during Processing) (Samples Removed) (c)

Number Unused_____
(d)

Variance (a-(b+c+d)) = _____

If not equal to zero, explain:_____

Form Completed By/Date_____Checked By/Date_____
Reviewed By/Date (Supervisor)_____
Unused Labels Destroyed By/Date_____
Checked By/Date_____

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Labeling and Packaging of Product

Procedure No.: PL-149

INVENTORY TRANSFER FORM

NAME _____ DATE _____

DEPARTMENT _____

REASON FOR TRANSFER _____

	Item Description	Part No.	Lot/Rec. No.	Amount Required
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

MANUFACTURING APPROVAL _____ DATE _____
Supervisor

TRANSFERRED BY _____ DATE _____

RECEIVED BY _____ DATE _____

Effective Date

Issued By _____

STANDARD OPERATING PROCEDURE

Procedure : Labeling and Packaging of Product

Procedure No. : PL-149

PACKAGING ORDER

PRODUCT NAME AND SIZE	LOT NO.	ORDER QUANTITY	LABELED	ORDER NUMBER
			Yes / No	

COMPONENTS AND CODE NUMBERS	UNIT USAGE	NUMBER SUPPLIED	NUMBER USED	SAMPLES	NUMBER DESTROYED	NUMBER RETURNED

ORDER INSTRUCTIONS	LABELING COMPONENTS	LABELED LOT NUMBER	EXP. DATE

DATE(S) PROCESSED / DATE COMPLETED	SAMPLING INSTRUCTIONS	LOT ID CODE	VISUAL VERIFICATION BY AND DATE
	RETENTION:	CODE _____	CHECKED AND VERIFIED by _____ / /

SUPERVISORS COMMENTS / OBSERVATIONS	AREA CHECKED PRIOR TO START-UP AND FREE OF OTHER COMPONENTS. _____ / /	FINISHED COUNT

ORDER CHECKED BY | ACCOUNTABILITY CHECKED | CONTENTS APPROVED

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Warehousing and Shipping Procedures

Procedure No.: PL-150

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1.0 PURPOSE

To establish the methods for warehousing and shipping released materials.

2.0 SCOPE

This procedure applies to those warehousing and shipping activities at Plastafil.

3.0 APPLICABLE DOCUMENTS

3.1 Freight Bill
3.2 Airbill
3.3 Shipping Notice
3.4 Quality Assurance Final Release Procedures, PL-131
3.5 Requisition
3.6 Inventory Cards
3.7 Shipping Log Book

4.0 GENERAL

4.1 These procedures are performed by Manufacturing personnel responsible for warehousing and shipping.

4.2 Follow all safety rules as they apply to the handling, storage and shipping of products.

4.3 All materials must be stored under the conditions indicated on this labeling.

Approvals		Date			
Approved By	Q.C.		Approved By	Mfg	Effective Date
					Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Warehousing and Shipping Procedures

Procedure No.: PL-150

5.0 PROCEDURE

5.1 Warehousing

5.1.1 The warehouse area is divided into two storage locations, Released Goods and Quarantine. Only Quality Assurance personnel shall be authorized to move material into or out of Quarantine.

5.1.2 Released materials transferred from Quarantine to the released goods area shall be accompanied by a properly prepared Inventory Card listing the name, lot number and quantity of the item.

5.1.3 Warehouse personnel shall check the material and the inventory card for correctness and count before placing the item into storage.

5.1.4 All released materials shall be stored in appropriate storage locations.

5.1.4.1 Components, supplies and released goods shall be stored in separate locations segregated by lot numbers.

5.1.5 Materials shall be issued out of storage only against an approved requisition or shipping order. The inventory card shall be adjusted to reflect the new count.

5.1.6 When materials are to be supplied to fill internal requisitions or for shipping, where possible these shall be made using single lots.

5.1.7 Unless otherwise stated in the requisition or order, the oldest lots shall be supplied first.

STANDARD OPERATING PROCEDURE

Procedure : Warehousing and Shipping Procedures

Procedure No. : PL-150

5.2 Shipping

5.2.1 A properly authorized Shipping Order shall be prepared listing all the necessary information such as customer, address, item to be shipped, packaging information, quantity and lot number.

5.2.2 The shipping supervisor or designee shall verify that the shipping order is properly prepared.

5.2.3 Check the quantities and descriptions of the material listed with the physical material for shipment. Notify the requestor of any deviations.

5.2.4 Select and prepare the material for shipment using the appropriate packaging document(s) or batch record.

Note: Use the information provided on the shipping order request to fill out the packaging document(s).

5.2.5 Inform the requestor if the shipment cannot be made by the requested date.

5.2.5.1 Advise the requestor of the revised shipment date and wait for an approval before continuing.

5.2.6 Add routing data on the packaging document.

5.2.7 Prepare an airbill or freight bill as appropriate with the pertinent information.

5.2.8 Schedule the carrier to pick up the shipment.

Effective Date

Issued By

STANDARD OPERATING PROCEDURE

Procedure : Warehousing and Shipping Procedures

Procedure No. : PL-150

5.2.9 Log the shipment information in the Shipping Log Book, giving each shipment a sequential number.

5.2.10 File all packaging documents in shipping. Send one copy to Finance and retain one for the packing list.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Warehousing and Shipping Procedures

Procedure No.: PL-150

No._____

SHIPPING ORDER FORM

SHIP

TO:

SOLD

TO:

ate	Requisition No.	Date Promised Customer

Qty	Unit Meas	Name Description, Lot #

Suggested Method of Shipping	Prepay	Collect	Charge Shipping To

Shipment Authorized By:

Shipping Information

Date Shipped_____ How Shipped_____

Freight Bill/Airbill No._____

cc: Finance
Shipping
Packing List

Effective Date

Issued By_____

6000+

STANDARD OPERATING PROCEDURE

Procedure: Warehousing and Shipping Procedures

Procedure No.: PL-150

No._____

SHIPPING NOTICE

Ship To:

Name

Street

City

Attention

Quantity	Description

Hazardous / /Yes / /No
Reason for Shipment:

Suggested Method Of Shipment:	Prepay	Collect	Approx Value	Charge Shipping To
Will Material be Returned / /Yes / /No	Shipment Authorized By		Ship By (Date)	

Shipping Information

Date Shipped_____ How Shipped_____

Airbill No._____

cc: Finance
Requestor
Shipping
Packing List

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Document Control

Procedure No.: PL-151

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1.0 PURPOSE

To describe the procedures for document control.

2.0 SCOPE

This procedure applies to the control of all documents, procedures, test methods and drawings which concern the manufacture or quality assurance for products and processes.

3.0 APPLICABLE DOCUMENTS

3.1 Revising, Rewriting or Deleting SOPs, PL-141
3.2 Revising a Batch Record or Specifications Master, PL-142
3.3 Document Change Order
3.4 Writing SOPs, PL-109
3.5 Document Change Order Specification or Batch Record
3.6 Batch Record/Specifications Record Request Form
3.7 SOP Request
3.8 SOP Form
3.9 Record Retention, PL-156

4.0 GENERAL

4.1 Written procedures, engineering drawings, specifications, and test methods serve as a written referral for future operations, thereby reducing errors and omissions by providing a standard protocol.

4.2 Written procedures provide a training medium to assure that all affected understand what is required and how functions are to be performed. It is therefore of prime importance that only the most recent issue and that only is in the possession of those required to perform the procedure defined.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
				Issued By

STANDARD OPERATING PROCEDURE

Procedure: Document Control

Procedure No.: PL-151

4.3 All documents become effective on and after the indicated effective date.

4.4 It is the responsibility of the person performing the document control function defined under Scope to ensure that all persons authorized to have specific documents have the most current version and that all superceded issues are retrieved.

4.5 Superceded document masters are retained in accordance with Record Retention, PL-156. Copies of superceded masters are destroyed after they are accounted for.

5.0 PROCEDURE

5.1 Any individual recognizing the need for a new procedure or new engineering drawings may request or initiate it.

5.2 Procedures should be written in active voice.

5.3 Engineering drawings should be made in accordance with standard engineering drawing practices.

5.4 Specifications, test or inspection methods should be initiated by Quality Assurance using accepted practices. Official compendia should be used as a source for specifications and methods where these exist.

5.5 Rough drafts should be forwarded to Document Control for typing and assigning a control number.

5.6 All procedures shall be followed which are listed under 3.0, Applicable Documents.

5.7 After the final version has been prepared in accordance with the applicable procedures, this shall be routed by Document Control for final approval signatures.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Document Control

Procedure No.: PL-151

5.8 Once all approvals have been obtained, Document Control shall assign an effective date, shall stamp the original "Master Copy", and shall make the appropriate number of copies and stamp these copies "Controlled Copy". Document Control shall maintain the master on file.

5.9 Document Control shall maintain a list of all persons receiving one of the controlled copies.

5.10 No copies shall be made of a controlled copy.

5.11 Revised or Deleted Documents, Drawings, Specifications, Test Methods, etc.

5.11.1 Document Control shall obtain and account for all superceded issues or deleted issues when issuing the revisions.

5.11.2 Document Control shall retain the superceded or deleted master in a separate file. These shall be retained in accordance with the procedures for Record Retention.

5.11.3 All retrieved controlled copies of the revised or deleted masters shall be destroyed by Document Control.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Manufacture and Packaging of Product and Accessory Items

Procedure No.: PL-152

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1.0 PURPOSE

To describe the procedures to be followed to manufacture and package the product and accessory items.

2.0 SCOPE

2.1 This procedure applies to all aspects of the manufacture of the Carbon Fiber Implant, Coated Carbon Fiber Bundles for Molding, Bollard, Pin, and Toggle.

2.2 This procedure applies to the packaging of the Packaged Implant Set.

3.0 APPLICABLE DOCUMENTS

3.1 Standard Production Formulation, Carbon Fiber Implant
3.2 Standard Production Formulation, Coated Carbon Fiber Bundles for Molding
3.3 Standard Production Formulation, Bollard
3.4 Standard Production Formulation, Pin
3.5 Standard Production Formulation, Toggle
3.6 Labeling and Packaging of Product, PL-149
3.7 Document Control, PL-151

4.0 GENERAL

4.1 This procedure is performed by the personnel responsible for the manufacturing and packaging functions unless otherwise indicated.

4.2 Personnel responsible for the document control function is the custodian of the masters and issues the true working copies of the master documents so indicated.

Approvals		Date		
Approved By	Q.C.		Approved By Mfg.	Effective Dat
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STANDARD OPERATING PROCEDURE

Procedure: Manufacture and Packaging of Product and Accessory Items

Procedure No.: PL-152

5.0 PROCEDURE

5.1 The manufacturing supervisor or alternate shall schedule the manufacture or packaging of each item in accordance with the master schedule issued or otherwise provided by the President.

5.2 Prior to the scheduled date, the manufacturing supervisor or alternate shall determine that all necessary components are available and released by Quality Assurance for the item to be made or packaged. He/she shall also assure that the intended area is cleaned and suitable for the scheduled use and free of components of previous lot.

5.3 The manufacturing supervisor or alternate shall obtain a copy of the master Standard Production Formulation or Packaging Record, as appropriate from Document Control. Document Control shall assign the next sequential lot and identify the copy with this assigned number.

5.4 On receipt of the Formulation or Packaging Record, the supervisor or alternate shall obtain and stage the released components in the intended area and check these for quantities and lot numbers to assure that sufficient quantities of the required items are present. (See Dispensing Raw Materials).

5.5 After performing the above checks, the supervisor or alternate shall supervise the manufacture or packaging, as appropriate, of the lot following the steps indicated in the document in the exact order indicated, recording the quantities and lot numbers of components so used as they are used.

5.6 No deviations shall be made from the instructions without approval from the President. If a deviation is approved, such shall be specifically hand written on the instructions and Quality Assurance Notified.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Manufacture and Packaging of Product and Accessory Items

Procedure No.: PL-152

5.7 The supervisor or alternate shall assure that the required samples are taken during the operation as required.

5.8 At the completion of the operations, the supervisor or alternate shall determine the quantity made or packaged; make an accountability of components used vs. completed items; place satisfactory units into suitable containers which will provide the proper protection; label these with quantity, product and lot number and place them in the designated storage area(s). Defects, excess labels and unused components shall be checked and the quantities determined. These shall be accounted for, properly identified, and given to Quality Assurance for proper disposition. (Raw materials and labels once removed from an original container shall not be returned to the original container.)

5.9 The supervisor or alternate shall see that all entries have been made on these manufacturing or packaging Documents and that the yield is within acceptable limits. If the yield is outside the acceptable limits, he/she shall notify Quality Assurance and jointly review and attempt to resolve the difference.

5.10 The supervisor or alternate shall endorse and date these documents attesting that the operation was performed as required (listing in detail any deviations made) and indicating any observations made during the operation which may be unusual or different from the norm. These completed documents shall be forwarded to Quality Assurance with samples taken from the lot.

5.11 The supervisor or alternate shall assure that the area is cleaned and that all components and/or labels are removed before the area is next scheduled to be used.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Customer Complaints

Procedure No.: PL-153

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1.0 PURPOSE

This procedure describes the procedures necessary for documentation and handling of customer complaints.

2.0 SCOPE

This procedure applies to all statements of dissatisfaction made to the company by users of their products.

3.0 APPLICABLE DOCUMENTS

3.1 Customer Complaint Form
3.2 Returned Goods Procedure, PL-110
3.3 Product Recall, Field Correction and Withdrawal, PL-114
3.4 Quality Review Board, PL-133
3.5 Failure Reporting, PL-154
3.6 Regulatory Inspection Procedures, PL-155
3.7 Failure Investigation, PL-157

4.0 GENERAL

4.1 A complete file shall be maintained of all customer complaints by Quality Assurance, who shall be responsible for the evaluation, processing and investigation of all customer complaints. This file shall contain a complete record of the complaint, investigation, and a copy of the response. This information shall only be shown to third parties in accordance with Regulatory Inspection Procedures, PL-155.

4.2 All complaints pertaining to injury, death or hazard to safety shall be maintained in a separate file.

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Approved By	Q.C.		Approved By Mfg.	Effective Dat
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STANDARD OPERATING PROCEDURE

Procedure: Customer Complaints

Procedure No.: PL-153

4.3 All customer complaints shall be evaluated to determine whether the incident is to be forwarded to the Quality Review Board or to the Recall/Field Correction Review Board as appropriate.

5.0 PROCEDURE

5.1 All complaints, whether oral or written, shall be recorded on the customer complaint form by Quality Assurance or other Plastafil personnel receiving the complaint.

5.2 Any complaint involving the possible failure of a product to meet the performance specifications shall be investigated. The investigator may include a record check of the product in question, evaluation of samples retained by the customer, evaluation of retained samples, or a general review of processing practices.

5.3 Whenever an investigation is deemed not to be necessary, the record shall include that fact and the name of the individual making that determination.

5.4 Whenever a complaint is received or information made available that reasonably suggests a product may have caused or contributed to a death or serious injury or has malfunctioned and may cause or contribute to a death or serious injury should the malfunction recur, a report shall be submitted to the FDA. A telephone report is required to be made to FDA as soon as possible, but in no case later than 5 calendar days from the date of the initial report, followed by a written report. A written report must be submitted with 15 working days after notification that the product may have caused or contributed to a death or serious injury.

5.4.1 This report shall be sent to Device Monitoring Branch (HFZ-343), F.D.A., 8757 Georgia Ave., Silver Spring, MD 20910 (Telephone number 301-427-8100).

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Customer Complaints

Procedure No.: PL-153

5.4.2 This report shall include as a minimum the following information:

5.4.2.1 The identity of the device and lot number.

5.4.2.2 The manufacturer.

5.4.2.3 The name, address and telephone number of the person making the report.

5.4.2.4 Description of the event which occurred.

5.4.2.5 The name and address of the individual submitting the information regarding the event.

5.4.2.6 A statement whether or not additional information will be provided.

5.5 Upon timely completion of the investigation and evaluation of the complaint, Quality Assurance shall make a recommendation concerning whether the complaint shall be brought before either the Quality Review Board or the Recall/Field Correction Review Board, as appropriate. Quality Assurance shall take the appropriate actions and initiate follow-up.

5.6 Quality Assurance or other individual at the direction of the President shall prepare and issue a response to the person making the complaint in a timely manner.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Customer Complaints

Procedure No.: PL-153

CUSTOMER COMPLAINT FORM

Customer Name:_____ Tel. no.:_____
Address: _____
_____
_____

Person Receiving Complaint: _____ Date:_____
Time:_____
Product: _____ Lot No(s).:_____
_____
_____

Complaint (attach additional sheet if necessary):
_____
_____
_____
_____

Is Product Being Retained: ___Yes (If yes, list authorization no.)_____
___No
_____

Investigation (attach additional sheet if necessary):_____
_____
_____
_____
_____
_____

Actions To Be Taken (attach additional sheet if necessary):_____
_____
_____
_____

By:_____ Date:_____

Priority: Urgent _____ Routine _____
Report to Customer by: _____ Date:_____
Follow-up by Quality Assurance by:_____ Date:_____
Received by:_____ Date:_____

cc: President _____ Sales/Marketing_____
Manufacturing_____ Finance_____

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Failure Reporting

Procedure No.: PL-154

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1.0 PURPOSE

To describe and define the procedures to report complaints, malfunctions, or defect situations which have or may cause death or serious injury.

2.0 SCOPE

This procedure applies to all product malfunctions detected by or reported to Plastafil.

3.0 APPLICABLE DOCUMENTS

3.1 Customer Complaint, PL-153
3.2 Failure Investigation, PL-157

4.0 GENERAL

4.1 Definition - Malfunction. "The failure of a device to meet any of its performance specifications or otherwise perform as expected. All claims on labeling are considered specifications. Any or all claims may be considered binding."

4.2 Definition - Serious Injury. A serious injury is one that is:

4.2.1 Life threatening.

4.2.2 Results in permanent injury.

4.2.3 Requires a surgical intervention.

4.2.4 Unanticipated temporary impairment or damage in a body function or body.

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Approved By	Q.C.		Approved By Mfg.	Effective Dat
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STANDARD OPERATING PROCEDURE

Procedure: Failure Reporting

Procedure No.: PL-154

5.0 PROCEDURE

5.1 When Plastafil becomes aware of any information that establishes that one of its marketed products may have caused or contributed to a death or serious injury or has manfunctioned and that the device or any other device marketed by Plastafil would be likely to cause or contribute to a recurrence then:

5.1.1 A report is to be generated and sent to FDA within five calendar days of first report of such information.

5.2 Reports may come from customers, literature, internal sources, or any other source.

5.3 When a report concerning death or serious injury is received, Plastafil shall report to FDA by:

5.3.1 Telephone as soon as possible, but no later than five calendar days of the initial report.

5.3.2 A written report must be submitted to FDA within fifteen working days of initial receipt.

5.4 If a malfunction occurs in a device and it can be reasonably assumed that the malfunction could recur and cause a serious injury or death, Plastafil must report the situation within fifteen calendar days of receiving this information. This report should be telephoned and followed in writing within these fifteen days.

5.5 Telephone and written reports must contain:

5.5.1 The brand name, common or unusual name, model, catalog or other I.D. number and the lot number.

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STANDARD OPERATING PROCEDURE

Procedure: Failure Reporting

Procedure No.: PL-154

5.5.2 Manufacturer's name.

5.5.3 Name, address and telephone number of person making the report to FDA.

5.5.4 Describe the event and the number of such events. (If the report is a literature citation the article must be included with the written report.)

5.5.5 Name and address of person reporting the incident to Plastafil.

5.5.6 Indicate whether additional information will be submitted and when.

5.5.7 Is this event occurring more frequently than the labeling on the device states?

5.6 A report must be made each time an event occurs.

5.7 A report must be submitted even if the incident is due to improper use by the customer.

5.8 Only one report is required if the same incident is reported to Plastafil by a number of sources.

5.9 No report is required if:

5.9.1 Plastafil determines that the report is erroneous.

5.9.2 The device was not a Plastafil device.

5.9.3 Plastafil labeling describes the possibility of this type of death or serious injury.

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STANDARD OPERATING PROCEDURE

Procedure: Failure Reporting

Procedure No.: PL-154

5.9.4 Plastafil labeling describes the malfunction.

5.9.5 The malfunction is occurring at or below the frequency stated in product labeling or if no stated frequency, at or below the frequency or severity that is expected or is usual for this device.

5.9.6 The malfunction does not require remedial action for other devices than that in which the malfunction occurred.

5.9.7 FDA advises in writing that reports are not required.

5.10 FDA may require additional information and they will request this in writing and specify a due date.

5.11 All reports to FDA are potentially releasable under the Freedom of Information Act, therefore no trade secret, confidential or financial information should be disclosed in any report.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Regulatory Inspection Procedures

Procedure No.: PL-155

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1.0 PURPOSE

To define the Plastafil policy with respect to federal and state regulatory inspections and those procedures to be followed during such inspections.

2.0 SCOPE

This policy and these procedures apply to all regulatory agency inspections.

3.0 APPLICABLE DOCUMENTS

3.1 Food, Drug and Cosmetic Act, as amended
3.2 EPA regulations
3.3 D.O.T. regulations
3.4 FDA regulations

4.0 GENERAL

4.1 Regulatory agencies, both federal and state, are authorized by legislation to inspect facilities to assure that regulations are being adhered to. FDA regulators have the additional responsibility to assure that medical devices are being made under proper conditions and with adequate controls to protect the public health.

4.2 Regulatory investigators are required to identify themselves and to provide a notice of inspection.

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Approved By	Q.C.		Approved By Mfg.	Effective Date
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STANDARD OPERATING PROCEDURE

Procedure: Regulatory Inspection Procedures

Procedure No.: PL-155

4.3 Inspections may be made for any of the following reasons:

4.3.1 Routine scheduled inspections.

4.3.2 Survey inspections.

4.3.3 Complaint follow-up inspections.

4.3.4 Product Defect Report follow-up inspections.

4.3.5 Adverse Reaction follow-up inspections.

4.3.6 Recall inspections.

4.3.7 Establishment licenses.

4.3.8 New product inspections.

4.4 Plastafil Policy

4.4.1 It is our policy that all employees be courteous and cooperative with all regulatory inspectors and will extend to providing the information, documents, and samples which the investigator is entitled to see under the authority of the enabling legislation.

4.5 Inspection Coordinator

4.5.1 The Inspection Coordinator is that individual authorized by the President to accompany a regulatory investigator at all times while he/she is at Plastafil, to provide the information requested which falls within the authority of the investigator, to provide a report to the President concerning the inspection and to draft a formal response to the agency concerning any deficiencies observed during the inspection.

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STANDARD OPERATING PROCEDURE

Procedure: Regulatory Inspection Procedures

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4.5.2 The following individuals may serve as Inspection Coordinators:

4.5.2.1 The President.

4.5.2.2 Quality Assurance personnel.

4.5.2.3 Manufacturing supervisor.

4.6 Regulatory inspections are made only during regular working hours.

5.0 PROCEDURE

5.1 The following procedures shall be followed when a regulatory inspector arrives:

5.1.1 The receptionist shall immediately notify the President. If absent, the receptionist shall in turn notify as an alternate the Quality Assurance personnel and manufacturing supervisor.

5.1.2 The President or alternate shall appoint an Inspection Coordinator.

5.1.3 The Inspection Coordinator shall meet the investigator, check his/her credentials, and ask for the written notice of inspection.

5.1.4 The investigator should be escorted into a neutral room such as the conference room where the investigator can work.

5.1.5 The purpose of the inspection should be discussed and an agenda prepared for the inspection. This agenda will serve to organize the inspection and to schedule discussions with specific personnel.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Regulatory Inspection Procedures

Procedure No.: PL-155

5.1.6 The Inspection Coordinator shall accompany the investigator at all times. The Coordinator shall take detailed notes of the inspection including:

- Investigator(s) name
- Times, Dates
- Details of inspection
- Observations by investigator
- Suggestions and comments by investigator
- Lot numbers of samples taken
- Duplicates of copies of documents taken
- Questions asked and answers given

5.1.7 At the end of the inspection, the Coordinator shall arrange for an exit interview with the investigator(s) and key Plastafil personnel to review and discuss observations and deficiencies, if any, observed. The investigator may during this meeting present a written report if his/her observations warrant such a written report. No documents or other items shall be signed by any Plastafil personnel even if requested by the investigator.

5.1.8 The Inspection Coordinator shall prepare a written report concerning the inspection, attaching copies of all documents and labeling taken by the investigator.

5.1.9 The Inspection Coordinator shall prepare a draft response to the written report submitted by the investigator for approval by the President. Where appropriate, this response should be reviewed by outside legal counsel before sending it to the agency.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Record Retention

Procedure No.: PL-156

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1.0 PURPOSE

To establish minimum retention periods for important records and documents and to discourage the retention of inappropriate and unnecessary records.

2.0 SCOPE

All important records and documents by Plastafil.

3.0 APPLICABLE DOCUMENTS

See the listing under Section 5.0 of this procedure.

4.0 GENERAL

4.1 Only the current calendar year's manufacturing and control records shall be maintained in a working file readily available for reference.

4.2 Previous years' records shall be stored in separate fire-resistant files or stored off-site. Microfilm copies of these may be retained in lieu of actual records off-side for space savings.

4.3 A copy or a microfilm copy shall be maintained off-site for all important specifications, Quality Assurance procedures and specifications, research data and manufacturing procedures as a back-up in case these are destroyed at Plastafil.

4.4 Non-Plastafil employees shall not be shown important records without approval of the President.

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STANDARD OPERATING PROCEDURE

Procedure: Record Retention

Procedure No.: PL-156

4.5 Finance shall be responsible for implementing these procedures.

4.6 At least once per year, each file shall be checked and documents and records discarded which have been retained beyond the indicated retention period. Consult the President if in doubt concerning the retention of any document.

5.0 PROCEDURE

5.1 The following is the recommended retention period for documents:

5.1.1 Manufacturing Records

5.1.1.1 Manufacturing and process files - Permanent.
5.1.1.2 Engineering drawings and Procedure masters - Permanent.
5.1.1.3 Receiving records - 3 years.
5.1.1.4 Shipping records - 7 years.
5.1.1.5 Inventory records - 3 years.
5.1.1.6 Packaging records - 7 years.
5.1.1.7 Purchase requisitions and records - 4 years.

5.1.2 Personnel Records

5.1.2.1 Personnel records - 5 years after termination.
5.1.2.2 Training records - 5 years after termination.
5.1.2.3 Accident and medical records - Permanent.

5.1.3 Quality Assurance

5.1.3.1 Component records - 5 years.
5.1.3.2 Inspection/Testing records - 7 years.
5.1.3.3 Lot history file - 7 years.
5.1.3.4 Superceded or deleted manuals, component and product specifications - Permanant.

Effective Date

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STANDARD OPERATING PROCEDURE

Procedure: Record Retention

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5.1.3.5 Correspondence - Until obsolete.
5.1.3.6 Vendor certifications - 7 years.
5.1.3.7 Dates of self-inspection audits, contractor audits and audit follow-ups - 7 years.
5.1.3.8 Actual audit reports - Until the deficiencies have been corrected.
5.1.3.9 Product complaints - Permanent.
5.1.3.10 Warranty claims - 3 years.
5.1.3.11 Material safety data sheets - Permanent.
5.1.3.12 Label text masters - 7 years.

5.1.4 EPA Records

5.1.4.1 EPA and DOT manuals - Permanent.
5.1.4.2 Training records - Permanent.
5.1.4.3 Hazardous waste manifest copies - Permanent.
5.1.4.4 Receipts from waste disposal contractors - Permanent.

5.1.5 General Office Records

5.1.5.1 Financial records - 7 years.
5.1.5.2 Accounts receivable and payable records - 4 years.
5.1.5.3 Federal and state tax records - 7 years.
5.1.5.4 Social Security tax payments - 7 years.
5.1.5.5 Employee payroll records - 5 years.
5.1.5.6 Sales tax records - 5 years.
5.1.5.7 Correspondence - Until no longer needed.
5.1.5.8 Sales records - 7 years.
5.1.5.9 Sales brochures - Permanent.

Effective Date

Issued By_____

STANDARD OPERATING PROCEDURE

Procedure: Failure Investigation

Procedure No.: PL-157

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1.0 PURPOSE

To describe the procedures, methods and responsibilities for initiating investigations and reporting failures and for specifying the actions to correct the problem.

2.0 SCOPE

All failures, both internal and those reported for released lots in distribution.

3.0 APPLICABLE DOCUMENTS

3.1 Failure Report.
3.2 Product Recall, Field Correction and Withdrawal, PL-114.
3.3 Customer Complaint, PL-153.
3.4 Failure Reporting, PL-154.

4.0 GENERAL

4.1 These procedures are to be performed by those personnel indicated in each section.

4.2 Reports for lots in distribution shall be investigated promptly and the results reported to the Recall Board.

4.3 A failure is defined as a completed unit or accessory item which fails to meet its performance specifications.

5.0 PROCEDURE

5.1 Internal Failures - Product/Lots not in distribution

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STANDARD OPERATING PROCEDURE

Procedure: Failure Investigation

Procedure No.: PL-157

5.1.1 The person detecting a failure defined under 4.3 above shall prepare a failure report. This failure report shall utilize a format appropriate to the incident reported. This report shall be promptly given to Quality Assurance together with the failed unit(s).

5.1.2 Quality Assurance shall review the failure and consult with others as appropriate to assess the cause.

5.1.2.1 Quality Assurance shall make an assessment as to whether this is an isolated unit or if there is cause to believe additional units of the same lot, other lots or other products may be involved.

5.1.2.2 Quality Assurance shall conduct an investigation to assess the implications of this failure, quarantine all lots in-house, contain the failed component or unit until the cause and ramifications of the failure are understood. This investigation shall be documented.

5.1.2.3 Quality Assurance may request others to perform such testing as may be appropriate to identify the cause and to obtain a solution.

5.1.3 Quality Assurance shall present the results of the investigation and test results to the Quality Review Board for a recommendation. The conclusions and recommendations made shall be documented.

5.1.3.1 If the Board believes that the failure may involve products already in distribution, the Board will take the appropriate action in accordance with the procedures in 3.2 above.

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STANDARD OPERATING PROCEDURE

Procedure: Failure Investigation

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5.1.4 Quality Assurance shall implement the recommendations of the Quality Review Board. These actions shall be documented and Quality Assurance shall see to the proper disposition of materials involved.

5.1.5 Quality Assurance shall assure that all reports required under Failure Reporting, PL-154 are made, if required.

5.2 External Failures - Product/Lot in distribution

5.2.1 Reports of failure, whether written or verbal, shall be documented in accordance with Customer Complaints, PL-153.

5.2.2 Quality Assurance shall promptly conduct an investigation and request samples for testing and verification. This investigation shall be documented.

5.2.2.1 This investigation shall also assess if the failure reported could extend to other products and/or lots either in distribution or not in distribution.

5.2.2.2 Quality Assurance shall request others perform such testing as may be appropriate to identify the cause and to obtain the solution.

5.2.3 Quality Assurance shall present the results of the investigation and test results to the Quality Review Board for a recommendation. The conclusions and recommendations shall be documented.

5.2.3.1 If the recommendation of the Board is to recall or make a field correction, this recommendation shall be presented to the Recall/Field Correction Review Board.

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STANDARD OPERATING PROCEDURE

Procedure: Failure Investigation

Procedure No.: PL-157

5.2.3.2 If no action with respect to material(s) in distribution is recommended, the conclusions and rationale shall be documented and signed by the Chairman of the Board.

5.2.4 Quality Assurance shall implement the recommendations of the Quality Review Board with respect to materials within Plastafil control.

5.2.5 For Recalls and Field Corrections, Quality Assurance shall monitor these field activities and see to the proper disposition of returned materials in accordance with 3.2.

5.2.6 Quality Assurance shall assure that all reports required in accordance with Failure Reporting, PL-154 are made, if required.

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PROTOTYPE OPERATIONAL QUALIFICATION PROCEDURE

STANDARD OPERATING PRCCEDURE - VALIDATION

Procedure : Operational Qualification of a Mettler AE163 Analytical Balance

Procedure No.: PL-V1

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1.0 PURPOSE

This procedure is designed to determine the precision, accuracy and sensitivity of a Mettler Balance Model AE163. Weighing is a nonspecific measurement of mass; therefore, no test for specificity will be performed.

2.0 PRINCIPLE

2.1 The Mettler AE163 analytical balance has a range of 162 g, covered by two weighing ranges:

1) 30 g to 0.01 mg
2) 160 g to 0.1 mg

To test the upper and lower limits of each weighing range, measurements must be taken of low, medium and high values. The following representative values were chosen:

	Weighing Range	
	30 g	160 g
Low	1 mg	1 mg
Medium	1 g	1 g
High	30 g	160 g

3.0 SCOPE

This procedure will qualify the operation of the Mettler AE163 analytical balance used in the performance of Quality Assurance test methods. Validation is the responsibility of Quality Assurance.

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STANDARD OPERATING PROCEDURE - VALIDATION

Procedure : Operational Qualification of a Mettler AE163 Analytical Balance
Procedure No. : PL-V1

4.0 REFERENCES AND APPLICABLE DOCUMENTS

4.1 Operating Instructions for Mettler AE163, Publication Number ME-701936. Mettler Instruments, 1985.

4.2 United States Pharmacopeia XXI.

4.3 Calibration of Balances, Pl-139.

5.0 SAFETY PRECAUTIONS

Observe usual laboratory precautions.

6.0 INTERFERENCES

6.1 Perform all weighings with the balance doors closed.

6.2 Record weight readings when the green stability indicator light goes off.

6.3 Locate balance on level, vibration-free surface.

6.4 Handle weights with forceps or gloved hands.

7.0 LIMITATIONS

The Mettler AE163 analytical balance is capable of weighing from 0.01 mg to 162 g.

8.0 MATERIALS AND EQUIPMENT

8.1 Mettler AE163 analytical electronic balance.

8.2 NBS Class S weights, 1 mg to 100 g. Troemner Number 1625.

9.0 REAGENTS

Not applicable.

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STANDARD OPERATING PROCEDURE - VALIDATION

Procedure: Operational Qualification of a Mettler AE163 Analytical Balance
Procedure No.: PL-V1

10.0 PROCEDURE

10.1 Precision and accuracy are determined in each weighing range. The precision of a balance is the extent to which the instrument replicates its results when making consecutive measurements on the same unit of mass. Indications of the scatter of these measurements are the standard deviation and coefficient of variation of the measurements. The accuracy of a balance is the extent to which the mean of a series of measurements made by the instrument on a single unit of mass differs from the true value of that unit.

10.1.1 Calibrate the balance per PL-139.

10.1.2 Make thirty measurements using a 1 g Class S balance weight, zeroing the balance between each measurement. Record the readings.

10.1.3 Make thirty measurements using 30 g Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.1.4 Enter the 160 g weighing range.

10.1.5 Repeat Steps 10.1.2 and 10.1.3.

10.1.6 Make thirty measurements using 160 g Class S balance weights, zeroing the balance between measuremens. Record the readings.

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STANDARD OPERATING PROCEDURE - VALIDATION

Procedure: Operational Qualification of a Mettler AE163 Analytical Balance
Procedure No.: PL-V1

10.0 PROCEDURE

10.1 Precision and accuracy are determined in each weighing range. The precision of a balance is the extent to which the instrument replicates its results when making consecutive measurements on the same unit of mass. Indications of the scatter of these measurements are the standard deviation and coefficient of variation of the measurements. The accuracy of a balance is the extent to which the mean of a series of measurements made by the instrument on a single unit of mass differs from the true value of that unit.

10.1.1 Calibrate the balance per PL-139.

10.1.2 Make thirty measurements using a 1 g Class S balance weight, zeroing the balance between each measurement. Record the readings.

10.1.3 Make thirty measurements using 30 g Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.1.4 Enter the 160 g weighing range.

10.1.5 Repeat Steps 10.1.2 and 10.1.3 .

10.1.6 Make thirty measurements using 160 g Class S balance weights, zeroing the balance between measuremens. Record the readings.

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Procedure: Operational Qualification of a Mettler AE163 Analytical Balance
Procedure No.: PL-V1

10.2 The sensitivity of a balance is the smallest difference between units of mass which leads to a measurable difference in response. Sensitivity will be determined by taking measurements in 1 mg increments about the low and high ends of each weighing range. One mid-range measurement (1 g) will also be taken.

10.2.1 Calibrate the balance according to PL-139.

10.2.2 Make five measurements using a 1 mg Class S balance weight, zeroing the balance between each measurement. Record the value when the stability indicator goes off.

10.2.3 Make five measurements using a 2 mg Class S balance weight, zeroing the balance between each measurement. Record the readings.

10.2.4 Make five measurements using 30 g Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.2.5 Make five measurements using 30 g and 1 mg Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.2.6 Make five measurements using 30 g and 2 mg Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.2.7 Enter the 160 g weighing range.

10.2.8 Repeat steps 10.2.2 through 10.2.3.

10.2.9 Make five measurements using 160 g Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.2.10 Make five measurements using 160 g and 1 mg Class S balance weights, zeroing the balance between each measurement. Record the readings.

10.2.11 Make five measurements using 160 g and 2 mg Class S balance weights, zeroing the balance between each measurement. Record the readings.

11.0 DATA ANALYSIS

11.1 To determine the precision of the balance, use statistical software capable of calculating the standard deviation and the coefficient of variation. Calculate 95% confidence intervals. Compare these values to the tolerances described in the USP XXI: Weights and Balances (Appendix I).

11.2 Evaluate accuracy by calculating the bias of the measurements of each weight.

11.3 Evaluate sensitivity by calculating the t-statistic and compare to a critical value obtained from Dunnet's t-table.

12.0 RECORDING AND REPORTING DATA

12.1 The data generated in this operational qualification are recorded in the laboratory notebook of the individual performing the procedure or in a laboratory notebook reserved for Quality Assurance process validation.

Procedure: Operational Qualification of a Mettler AE163 Analytical Balance
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12.2 Data are entered from the laboratory notebooks into the computer for statistical analysis.

12.3 The operational qualification, tabular data, data analysis, conclusions and summary are compiled in a validation task report.

Calibration and Revalidation Schedule

1. The Mettler AE163 is calibrated daily using the internal calibration protocol described in SOP Index Number PL-139. The calibration log is dated and signed by the technologist performing the calibration.

2. The calibration is checked weekly using Class S weights.

3. The Mettler AE163 is revalidated annually ± thirty days.

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Procedure : Operational Qualification of a Mettler AE163 Analytical Balance

Procedure No. : PL-V1

⟨41⟩ WEIGHTS AND BALANCES

Pharmacopeial tests and assays require the use of balances that vary in capacity, sensitivity, and reproducibility. The accuracy needed for a weighing dictates the type of balance and the class of weights required for that weighing. Where substances are to be "accurately weighed," the weighing is to be performed so as to limit the error to not more than 0.1%. For example, a quantity of 50 mg is to be weighed so that the error does not exceed 50 μg. A balance should be chosen such that the value of three times the standard deviation of the reproducibility of the instrument, divided by the amount to be weighed, does not exceed 0.001.

Tolerances for New Weights in Sets

Denomination g	Class M		Class S		Class S-1	Class P
	Individual μg	Group μg	Individual μg	Group μg	Individual μg	Individual μg
100	500		250		1000	2000
50	250		120		600	1200
30	150		74	154	450	900
20	100		74	"	350	700
10	50		74	"	250	500
5	34	65	54	105	180	360
3	34	"	54	"	150	300
2	34	"	54	"	130	260
1	34	"	54	"	100	200
mg						
500	5.4	10.5	25	55	80	160
300	5.4	"	25	"	70	140
200	5.4	"	25	"	60	120
100	5.4	"	25	"	50	100
50	5.4	10.5	14	34	42	85
30	5.4	"	14	"	38	75
20	5.4	"	14	"	35	70
10	5.4	"	14	"	30	60
5	5.4	10.5	14	34	28	55
3	5.4	"	14	"	26	52
2	5.4	"	14	"	25	50
1	5.4	"	14	"	25	50

NOTE—Not more than one-third of Class S-1 weights are in error by more than one-half of the tabulated tolerances.

A weight classification should be chosen so as to limit the error to 0.1%. This generally means that Class P weights can be used for quantities greater than 100 mg, Class S-1 for quantities greater than 50 mg, Class S for quantities greater than 20 mg, and Class M for quantities greater than 10 mg. Quantities of less than 10 mg may be weighed on balances having appropriate reproducibilities and designed to afford electrical or optical methods for accurately subdividing a 10-mg, full-scale range, after calibration with a 10-mg. Class M weight.

The tolerances shown in the accompanying table are for new or newly adjusted weights. For weights that have been in use, the tolerances are somewhat larger, as follows:

Class M: 100-, 200-, 300-, and 500-mg denominations—10.5 μg; and 20.0 μg for the group.

Class S: 100-mg and heavier denominations—Twice the values shown in the accompanying table (for individual and group).

Class S-1: Same as shown in the accompanying table.

Class P: For all weights—Twice the values shown in the accompanying table.

Weights should be calibrated periodically, preferably against an absolute standard weight.

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3. ENVIRONMENTAL ASSESSMENT

3. ENVIRONMENTAL ASSESSMENT

Plastafil considers that the manufacture of the items indicated in this PMA is likely to have a minimal impact on the environment. Only a small quantity of solvent will be used amounting to an estimate of 1 liter per week. The small quantities of carbon/polysulfone dust that will be generated during finishing will be collected and not put into the air.

All waste materials, packaging materials and defects with the exception of solvent can be safely incinerated or disposed of in a sanitary landfill. Solvent will be disposed of using a licensed contractor in accordance with EPA regulations.

Packaging materials and unused implants can be safely disposed of in licensed sanitary landfills or incinerated in accordance with local codes.