LIST OF PROPOSED PRODUCTS ALONG WITH PRODUCTION CAPACITY

SR. NO.	NAME OF PRODUCT	QUANTITY (TPA)
1.	Betamethasone Sodium Phosphate	1.5
2.	Betamethasone Dipropionate	1.5
3.	Betamethasone Valerate	1.2
4.	Beclomethasone Dipropionate	1.2
5.	Clobetasol Propionate	1.8
6.	Dexamethasone Sodium Phosphate	1.5
7.	Methyl Prednisolone	1.2
8.	Prednisolone Acetate	0.8
9.	Deflazacort	1.2
10.	Methylcobalamin	1.2
11.	Prednisolone Sodium Phosphate	1.2
12.	Budesonide	0.7
	Total	**15**

M.K. DRUGS

F-10 INDUSTRIAL FOCAL POINT

DERABASSI – 140507 DISTRICT MOHALI (PUNJAB)

INDIA

MANUFACTURING PROCESS OF BETAMETHASONE SODIUM PHOSPHATE

IP/ BP/ USP

Raw Material : -

1. Betamethasone (Base)
2. Pyro Phosphoryl Chloride
3. T.H.F.
4. Chloroform
5. Isopropyl Alcohol
6. Acetone
7. Caustic Flakes (LR)
8. Activated Carbon
9. Hyflow Supercell
10. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charging of T.H.F.
3. Charging of Betamethasone (Base)
4. Cool it up to -5^0 C
5. Add. Of Pyro Phosphoryl Chloride
6. Stirring
7. Rx / mass quenched in ice + water
8. Stirring
9. Charge Rx / mass in glass flask
10. Heating
11. Recover T.H.F. / concentration U /Vacuum
12. Stirring
13. Filtration
14. Washing with D.M. Water
15. Drying
16. Cleaning and checking in Glass flask
17. Charging of Thinner
18. Add. B.H.P.
19. Heating
20. Stirring

MANUFACTURING PROCESS OF BETAMETHASONE SODIUM PHOSPHATE

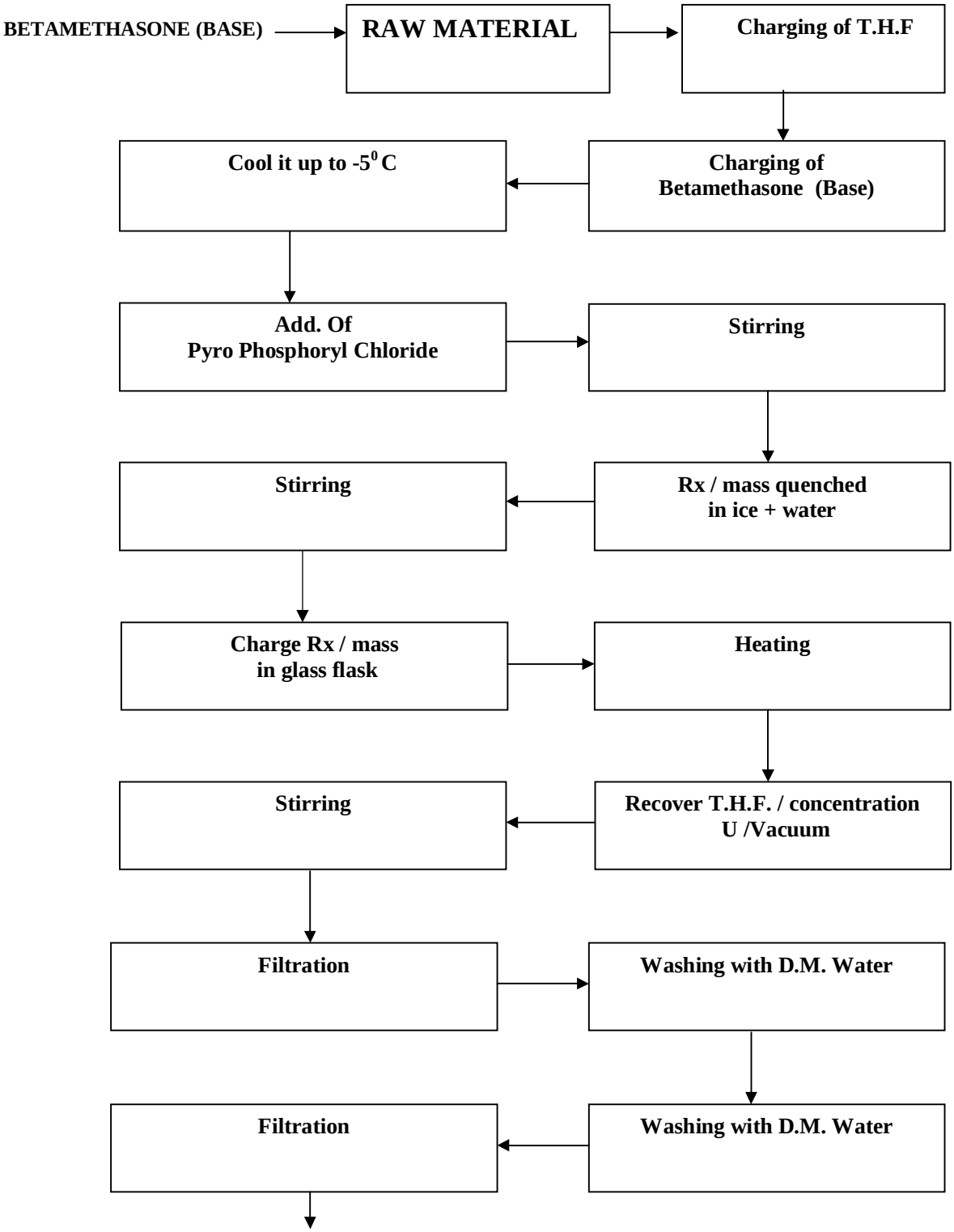
IP/ BP/ USP

21. Add. Activated Carbon
22. Stirring
23. Filtration over hyflowbed
24. Collect filtrate in glass flask
25. Add. of NaOH
26. Stirr and add Isopropyl Alcohol
27. Add. of Acetone
28. Stirring
29. Filtration and wash with acetone
30. Drying
31. Final Quality Control sampling to be done for complete analysis.
32. Packed in specified containers with proper label

FLOW CHART OF BETAMETHASONE SODIUM PHOSPHATE

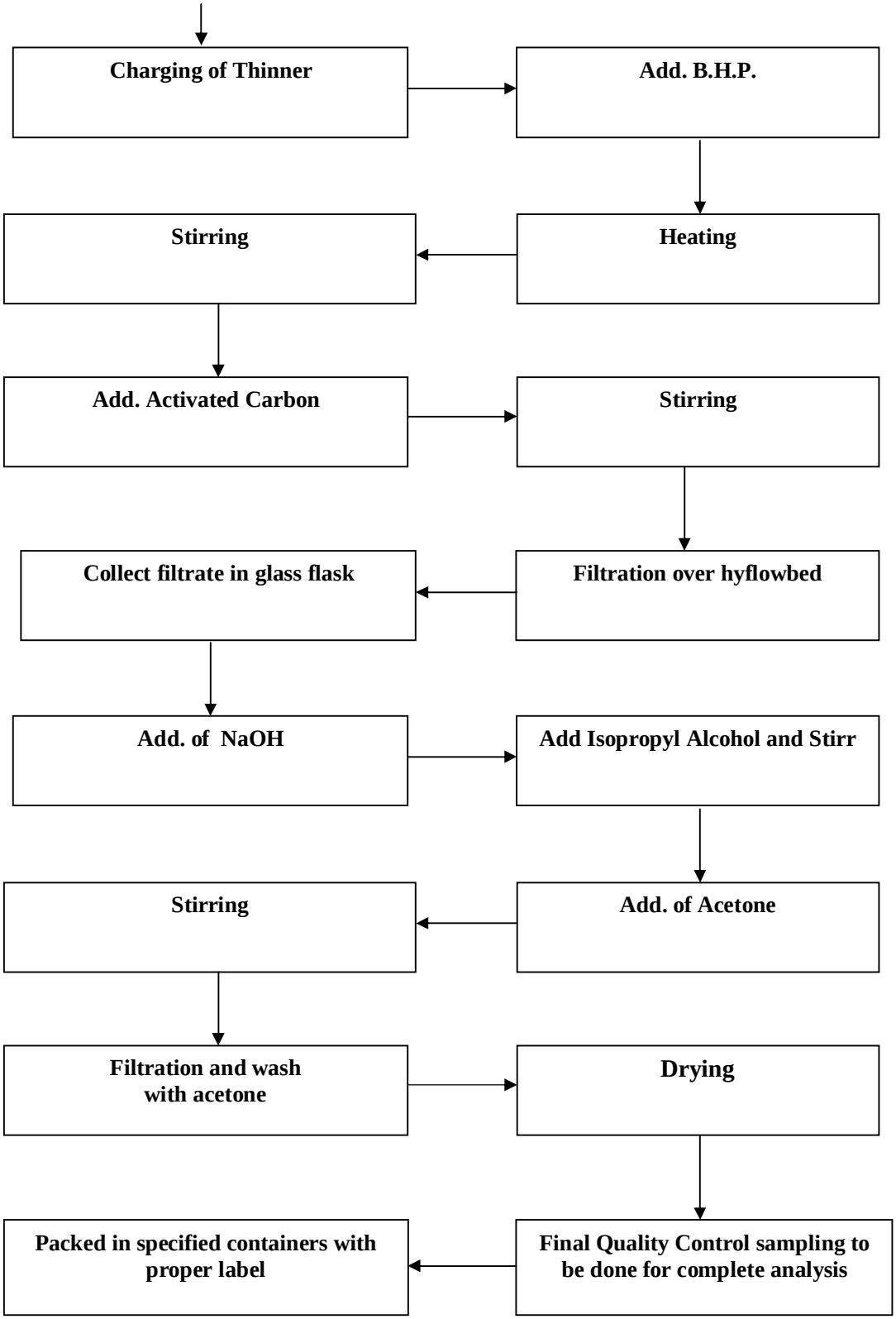
IP/ BP/ USP

FLOW CHART



FLOW CHART OF BETAMETHASONE SODIUM PHOSPHATE

IP/ BP/ USP



MANUFACTURING PROCESS OF BETAMETHASONE DIPROPIONATE

IP/BP/ USP

Raw Material : -

1. Betamethasone (Base)
2. Methylene Chloride
3. Tri Ethyl Ortho Propionate
4. Para Toluene Sulphonic Acid
5. Ethyl Acetate
6. Acetone
7. Orthophosphoric Acid
8. Pyridine
9. Propionic Anhydride
10. Activated Carbon
11. Hyflow Supercell
12. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charging of Methylene Chloride
3. Charging of Betamethasone (Base)
4. Heat to Reflux and then add Tri Ethyl Ortho Propionate
5. Distill out Methylene Chloride
6. Addn. of Para Toluene Sulphonic Acid
7. Addn. of Ethyl Acetate and Acetone
8. Reflux the Rx. Mixture at 55 ºC
9. Cool the Rx. Mixture at 25 ºC
10. Then add Orthophosphoric Acid
11. And the Rx. Mixture at 25 ºC
12. Filtration & Washing with
13. Charging of Acetone
14. Rx / Mass Quinch in D.M. Water
15. Filtration and Washing with D.M. Water
16. Drying, In process testing (B.M.P.)
17. Charging of Pyridine
18. Charging of B.M.P. (Dry) & cooling
19. Addn. of Propionic Anhydride.

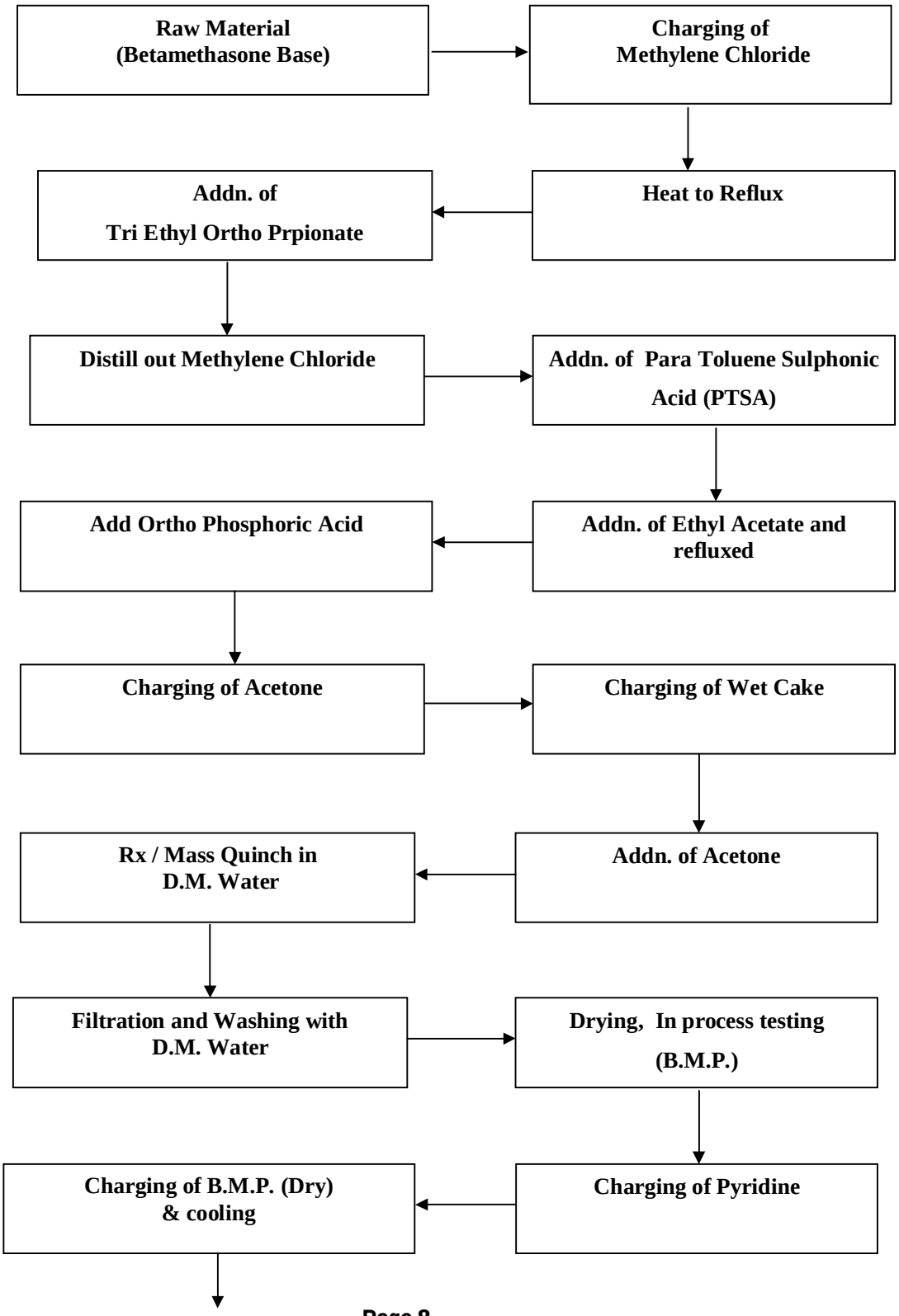
MANUFACTURING PROCESS OF BETAMETHASONE DIPROPIONATE

IP/BP/ USP

20. Add. D.M. Water
21. Stirring
22. Filtration and washing with DM water.
23. Drying , In process testing (BDP Crude)
24. Charging of Acetone
25. Charging of BDP Crude
26. Add Activated Carbon and filter it over hyflowbed
27. Cooling
28. Rx / Mass Quinch in D.M. Water
29. Filtration & washing with D.M. Water
30. Drying , In Process Testing (Betamethasone Dipropionate)
31. Milling
32. Final Quality Control sampling to be done for complete analysis
33. Release the material after obtaining the results from Quality Control
34. Packed in specified containers with proper label.

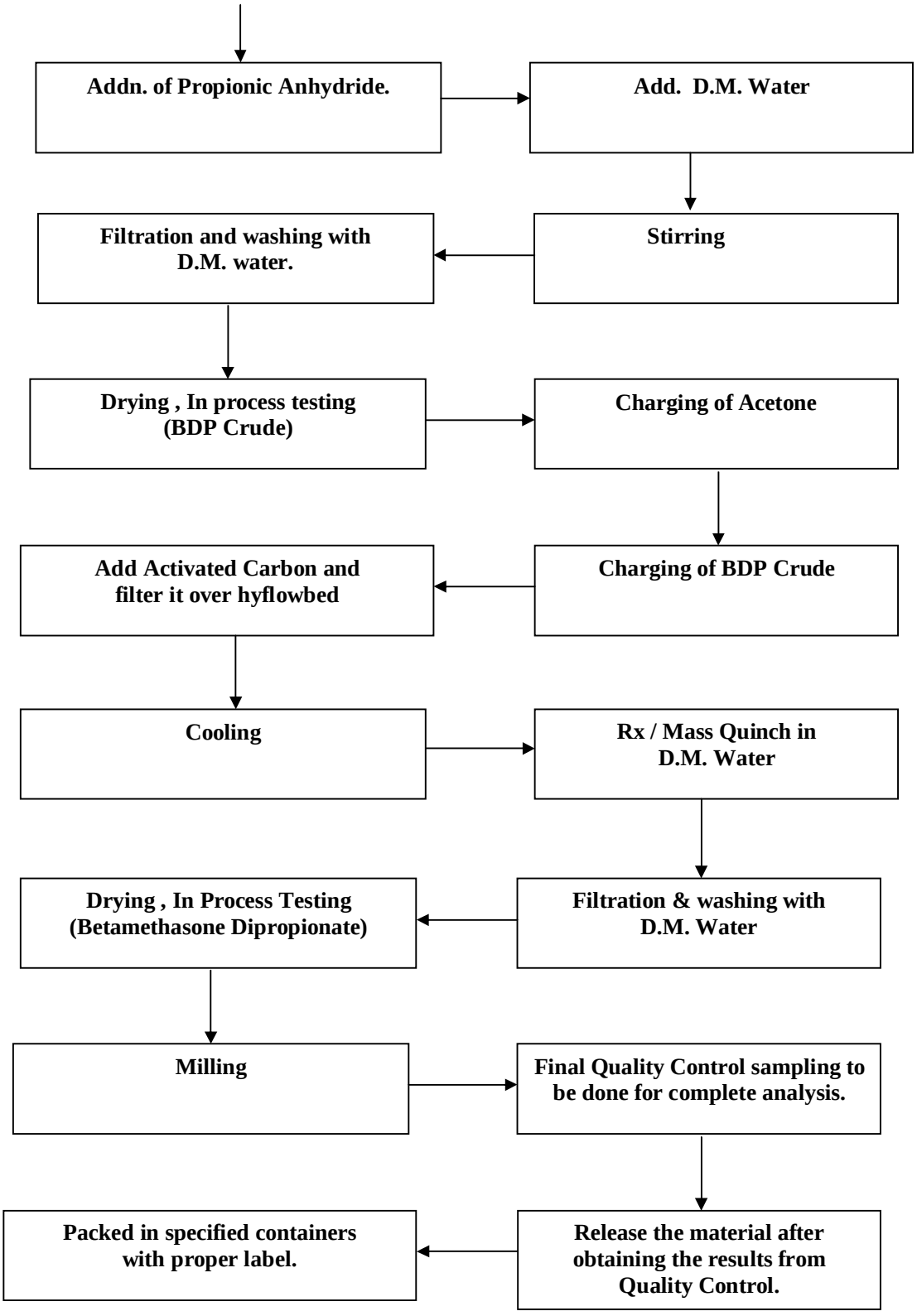
FLOW CHART OF BETAMETHASONE DIPROPIONATE

IP /BP/ USP



FLOW CHART OF BETAMETHASONE DIPROPIONATE

IP /BP/ USP



MANUFACTURING PROCESS OF BETAMETHASONE VALERATE

IP/BP/ USP

Raw Material : -

1. Betamethasone (Base)
2. Methylene Chloride
3. T.M.O.V.
4. Para Toluene Sulphonic Acid
5. Ethyl Acetate
7. Acetone
8. Orthophosphoric Acid
9. Activated Carbon
10. Hyflow Supercell
11. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charging of Methylene Chloride
3. Charging Of Betamethasone (Base)
4. Heat to Reflux
5. Addn. of T.M.O.V.
6. Refluxing
7. Cooling
8. Add. PTSA + Ethyl Acetate
9. Stirring
10. Add. of D.M. Water
11. Reflux the Rx. mixture at 55 ºC
12. Cool the Rx, mixture at 25 ºC
13. Maintain the temperature at 25 ºC
14. Add Ortho Phosphoric Acid
15. Rx/ Mass Quinch in D.M. Water
16. Filtration Process
17. Wash with DM Water
18. Drying
19. Cleaning & Checking of Glass Flask
20. Charging of Acetone

MANUFACTURING PROCESS OF BETAMETHASONE VALERATE

IP/BP/ USP

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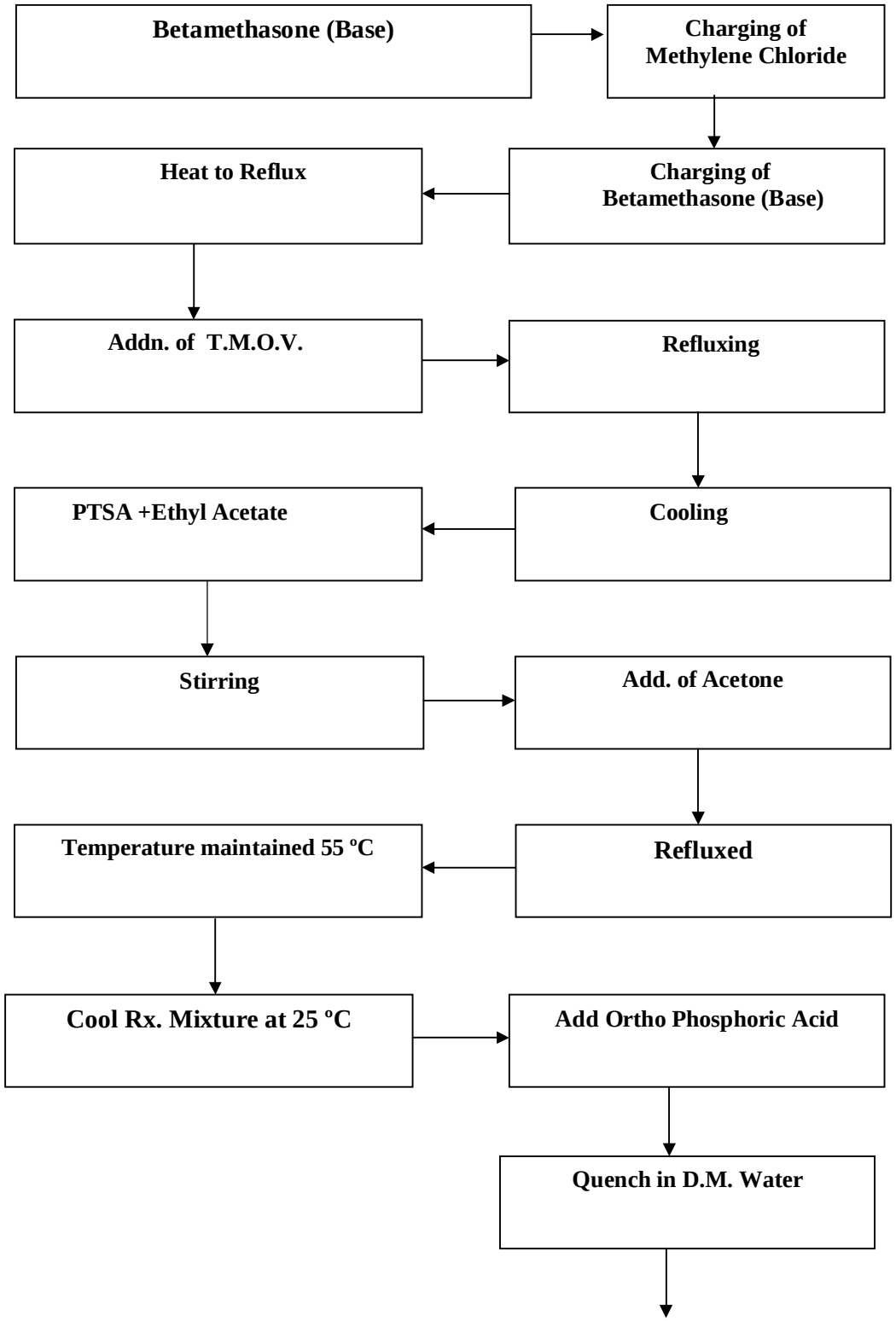
21. Add. Of Betamethasone Valerate (Crude)
22. Stir for Dissolution
23. Add. of Activated Carbon
24. Stirring
25. Filter through Hyflow bed. (Acetone)
26. Wash Hyflow Bed with Acetone
27. Collect filtrate & Washing
28. Add. D.M. Water
29. Stirring
30. Filter and wash with D.M. Water
31. Drying
32. Final Quality Control sampling to be done for complete analysis.
33. Release the material after obtaining the results from Quality Control.
34. Packed in specified containers with proper label.

FLOW CHART OF BETAMETHASONE VALERATE

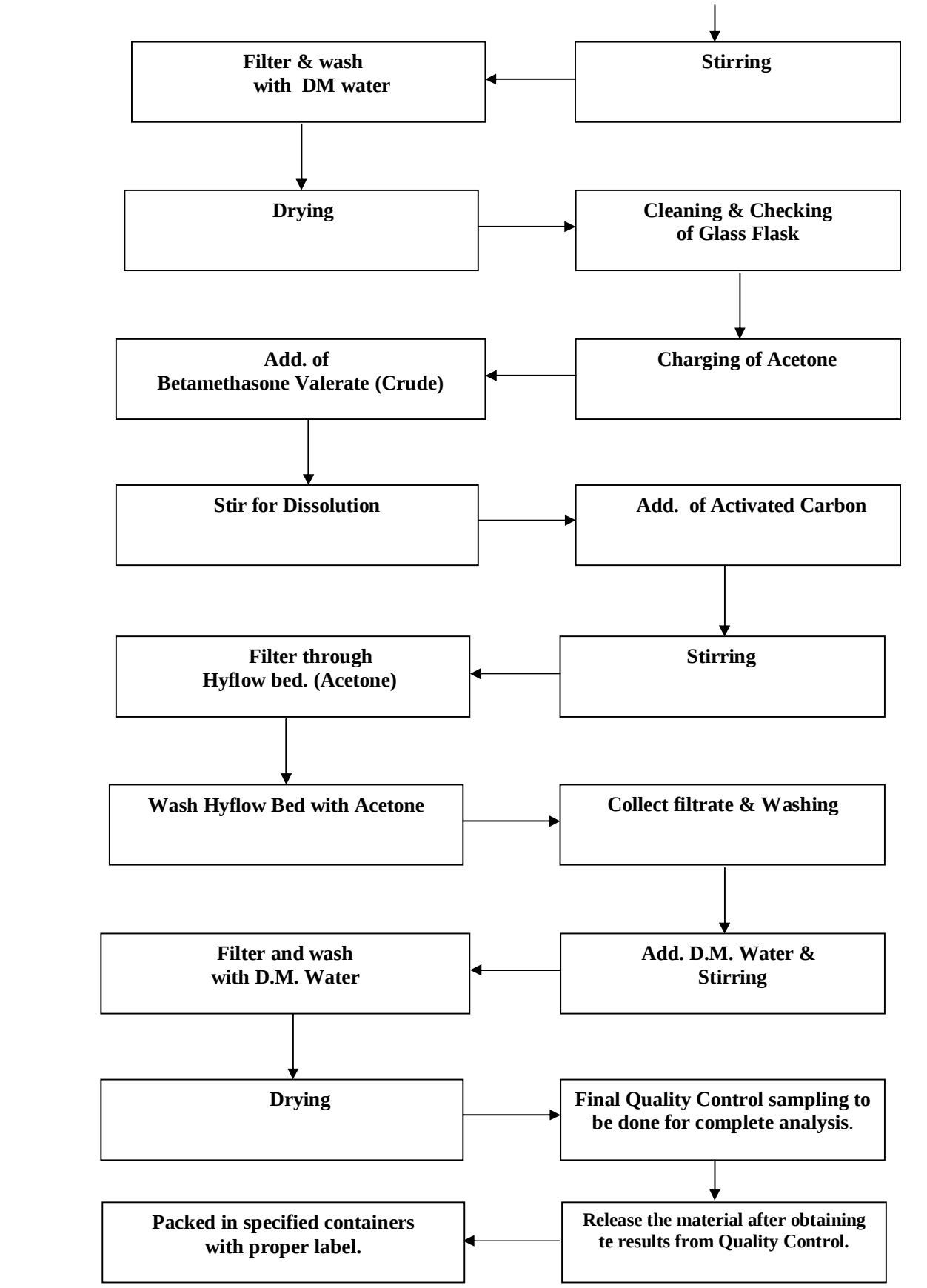
IP / BP/ USP

FLOW CHART



FLOW CHART OF BETAMETHASONE VALERATE

IP / BP/ USP



MANUFACTURING PROCESS OF BECLOMETHASONE DIPROPIONATE

IP/BP/ USP

Raw Material : -

1. DB - XI
2. Hydrochloric Acid (HCL)
3. Potassium Hydroxide (KOH)
4. Chloroform
5. Methylene Chloride
6. Tri Ethyl Ortho Propionate (TEOP)
7. Ethyl Acetate
8. Para Toluene Sulphonic Acid (PTSA)
9. Acetone
10. Ortho Phosphoric Acid
11. Pyridine
12. Propionic Anhydride
13. Activated Carbon
14. Hyflow Supercell
15. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charging of HCL
3. Cool up to -10^0C
4. Addition of DB-XI
5. Stirring for 30 minutes.
6. Rx / mass quenching in D.M. Water
7. Stirring
8. Addn. of KOH solution
9. Stirring 30 minutes
10. Filtration & wash with D. M. Water
11. Washing with Chloroform
12. Washing with Ethyl Acetate
13. Drying , In process testing (Beclo. Base).
14. Charging of Methylene Chloride

MANUFACTURING PROCESS OF BECLOMETHASONE DIPROPIONATE

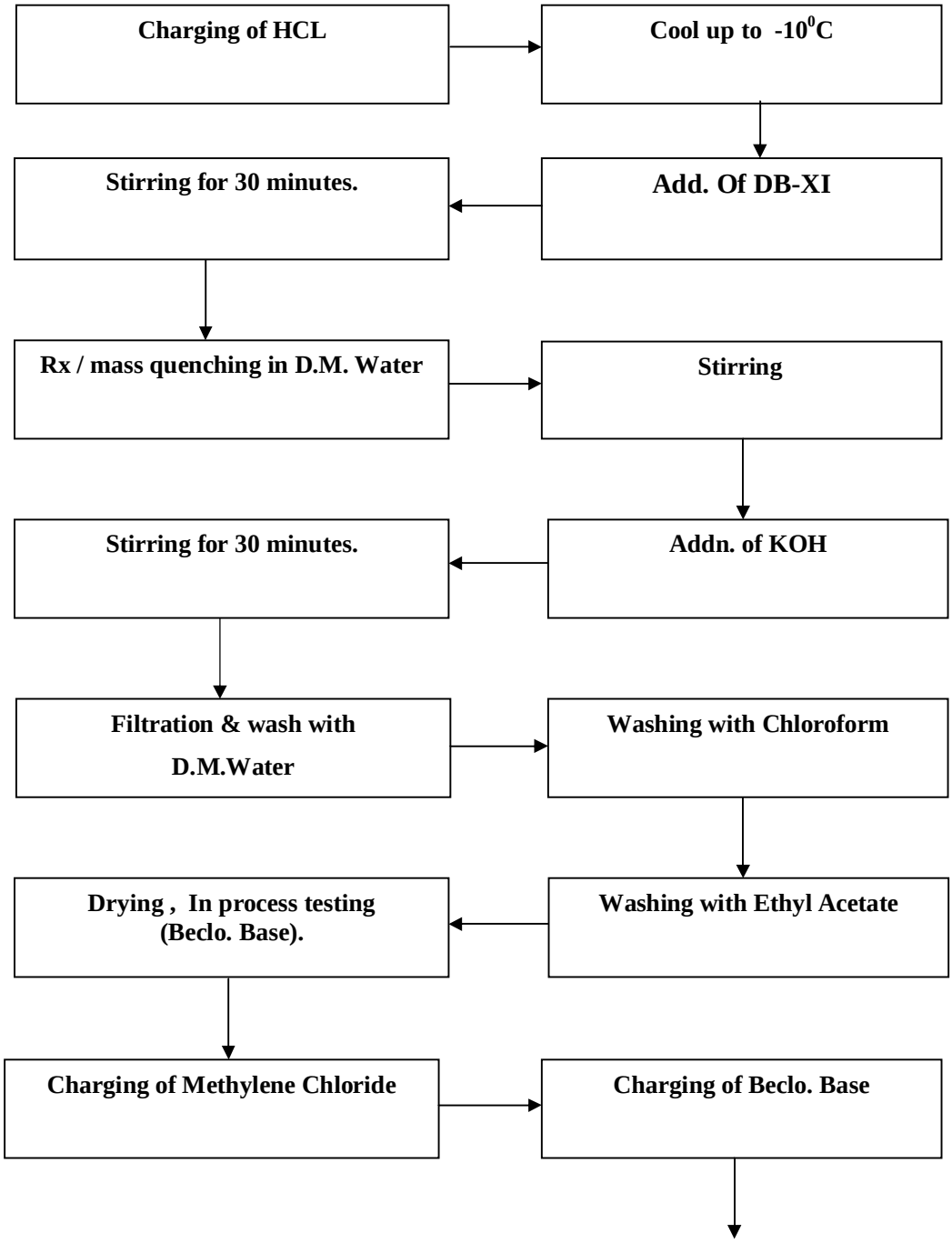
IP/BP/ USP

15. Charging of Beclomethasone Base
16. Heat to Reflux
17. Addn. of T.E.O.P.
18. Distill out Methylene Chloride
19. Addn. of PTSA
20. Addn. of Ethyl Acetate
21. Reflux the Rx. Mixture at 55 ºC
22. Cool the Rx. Mixture at 25 ºC
23. Then add Orthophosphoric Acid
24. And the Rx. Mixture at 25 ºC
25. Filtration & Washing with
26. Charging of Acetone
27. Filtration & Washing with Acetone
28. Charging of Acetone
29. Rx / Mass Quinch in D.M. Water
30. Filtration and Washing with D.M. Water
31. Drying, In process testing (B.M.P.)
32. Charging of Pyridine
33. Charging of B.M.P. (Dry) & cooling
34. Addn. of Propionic Anhydride.
35. Add. D.M. Water
36. Stirring
37. Filtration and washing with DM water.
38. Drying , In process testing (Beclo. Crude)
39. Charging of Acetone
40. Charging of Beclo. Crude
41. Add Activated Carbon and filter it over hyflowbed
42. Cooling
43. Rx / Mass Quench in D.M. Water
44. Filtration & washing with D.M. Water
45. Drying , In Process Testing (Beclomethasone Dipropionate)
46. Final Quality Control sampling to be done for complete analysis.
47. Release the material after obtaining the results from Quality Control.
48. Packed in specified containers with proper label.

FLOW CHART OF BECLOMETHASONE DIPROPIONATE

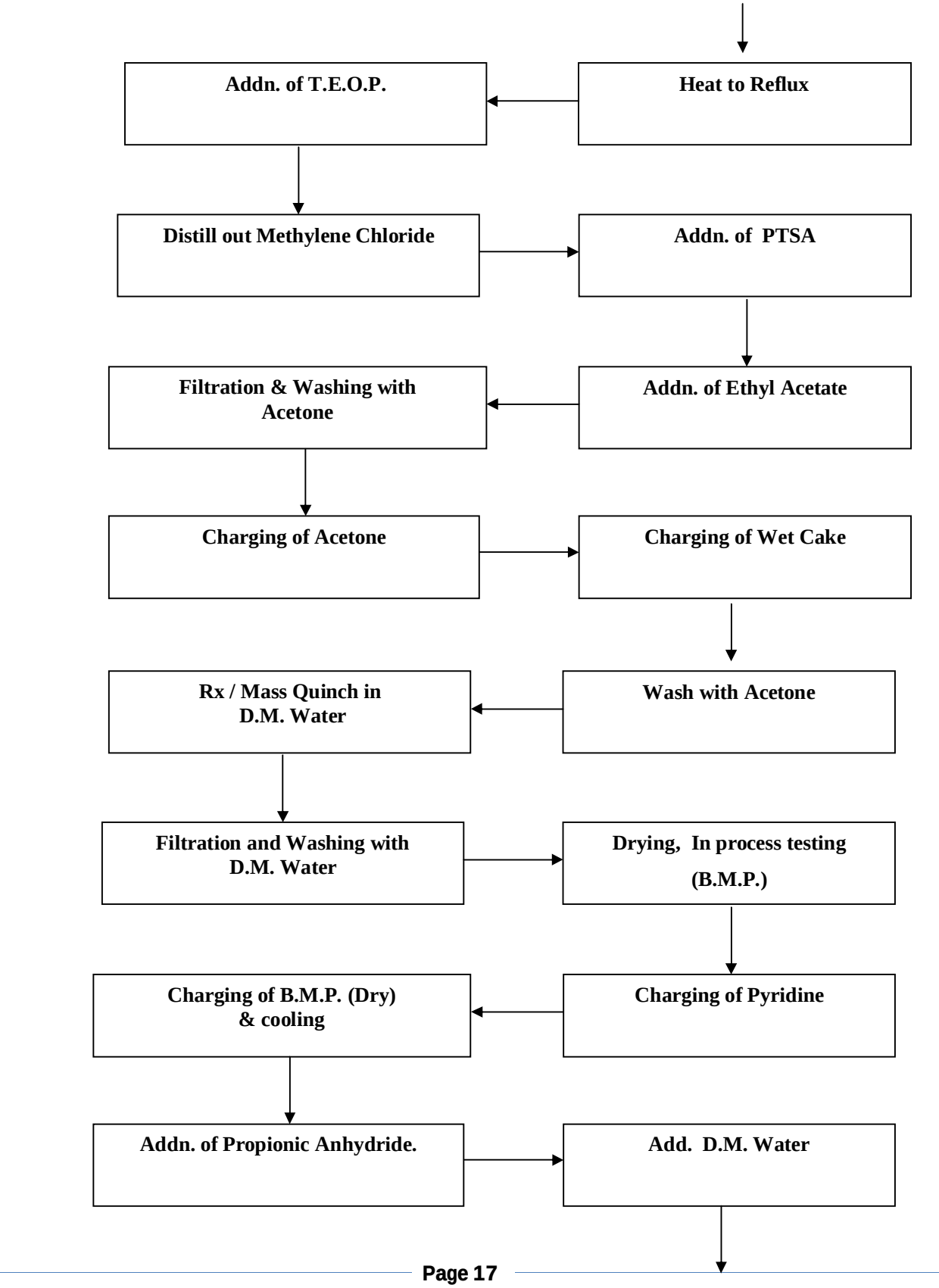
IP/BP/ USP

FLOW CHART



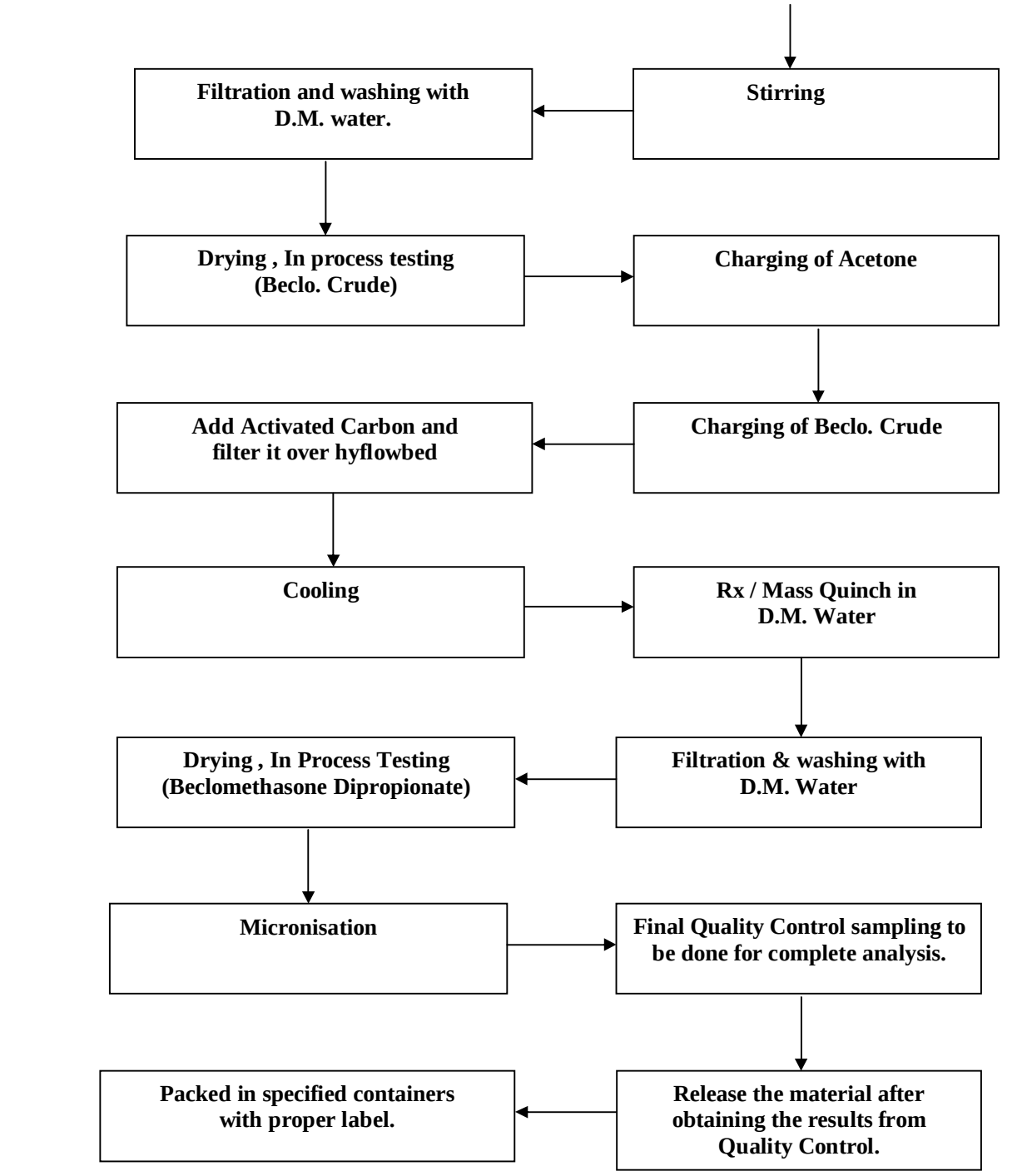
FLOW CHART OF BECLOMETHASONE DIPROPIONATE

IP/BP/ USP



FLOW CHART OF BECLOMETHASONE DIPROPIONATE

IP/BP/ USP



MANUFACTURING PROCESS OF CLOBETASOL PROPIONATE

IP/BP/ USP

Raw Material : -

1. Betamethasone Base
2. Methylene Chloride
3. Tri Ethyl Ortho Propionate.
4. Para Toluene Sulphonyl Chloride + Ethyl Acetate
5. Ortho Phosphoric Acid
6. Acetone
7. Pyridine
8. Methane Sulphonyl Chloride
9. Dimethyl Formamide
10. Lithium Chloride
11. Methanol
12. Chloroform
13. Activated Carbon
14. Hyflow Supercell
15. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charge Methylene Chloride at RT
3. Charge Betamethasone Base at RT
4. Heat up to reflux.
5. Addition of Tri Ethyl Ortho Propionate
6. Addn. of PTSA
7. Addn. of Ethyl Acetate
8. Reflux the Rx. Mixture at 55 ºC
9. Cool the Rx. Mixture at 25 ºC
10. Then add Orthophosphoric Acid
11. And the Rx. Mixture at 25 ºC
12. Filtration & Washing with
13. Charging of Acetone
14. Filtration & Washing with Acetone
15. Charging of Acetone
16. Wet cake quenching in DM water & strring.

MANUFACTURING PROCESS OF CLOBETASOL PROPIONATE

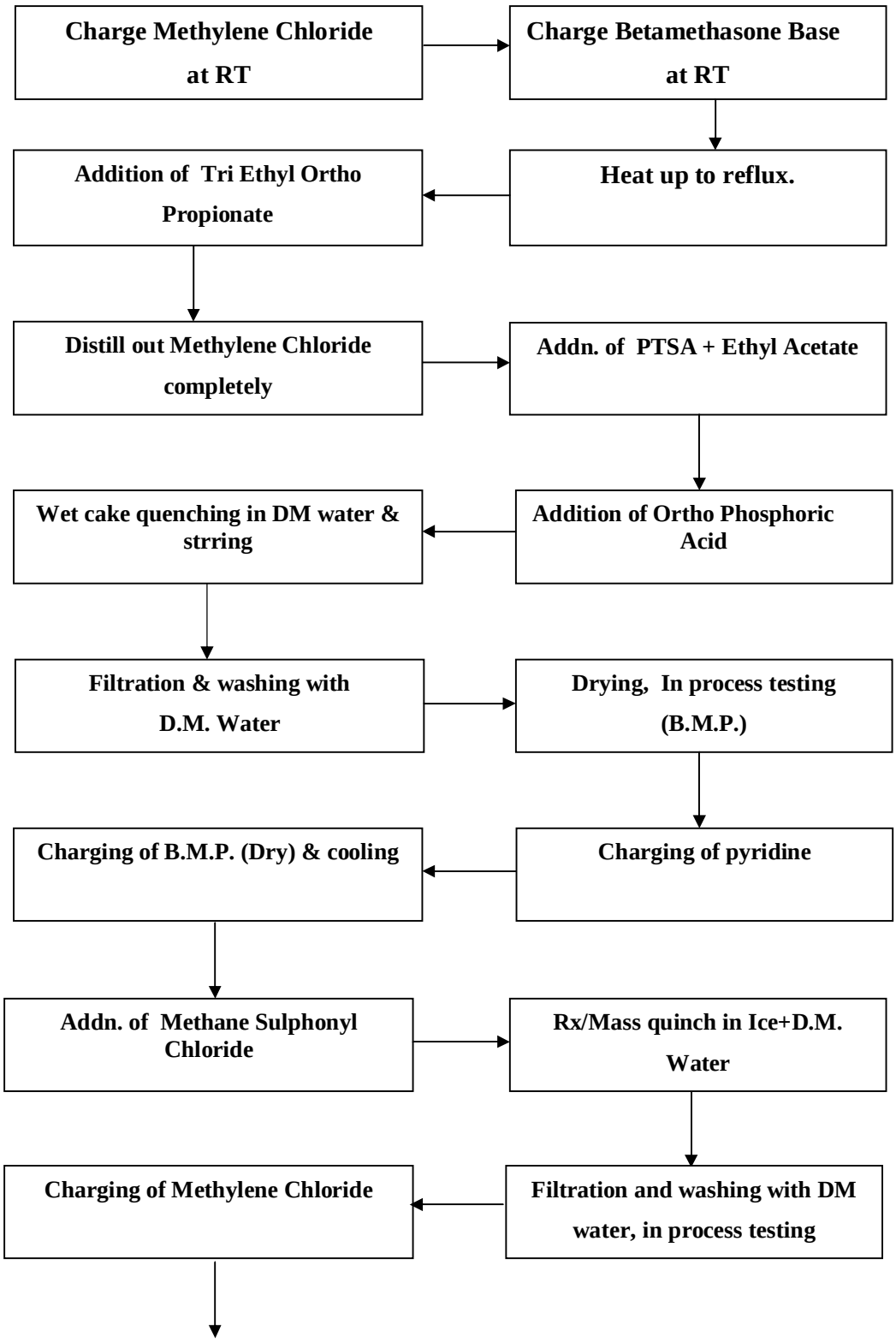
IP/BP/ USP

17. Drying, In process testing (B.M.P.)
18. Charging of pyridine.
19. Charging of B.M.P. (Dry) & cooling
20. Addn. of Methane Sulphonyl Chloride.
21. Rx/Mass quinch in Ice+ D.M. Water
22. Filtration and washing with DM water, in process testing (Mesylate)
23. Charging of Methylene Chloride
24. Add Mesylate
25. Concentration organic layer
26. Add. Di-Methyl Formamide & heating
27. Add. Lithium Chloride & stirring
28. Check T.L.C.
29. Rx/Mass Quinch in Ice + D.M. Water
30. Filtration & washing with D.M. Water, in process testing (Clobetasol Crude)
31. Charging of chloroform
32. Add. Clobetasol Crude
33. Add. Methanol
34. Stirring (Check Clarity)
35. Add Activated Carbon and filter it over hyflowbed
36. Collect organic layer and heat up to 60^0 C
37. Conc. Up to thick mass
38. Filtration and washing with Methanol
39. Drying under vacuum, in process testing (Clobetasol Propionate)
40. Final Quality Control sampling to be done for complete analysis.
41. Release the material after obtaining test results from Quality Control.
42. Packed in specified containers with proper label.

FLOW CHART OF CLOBETASOL PROPIONATE

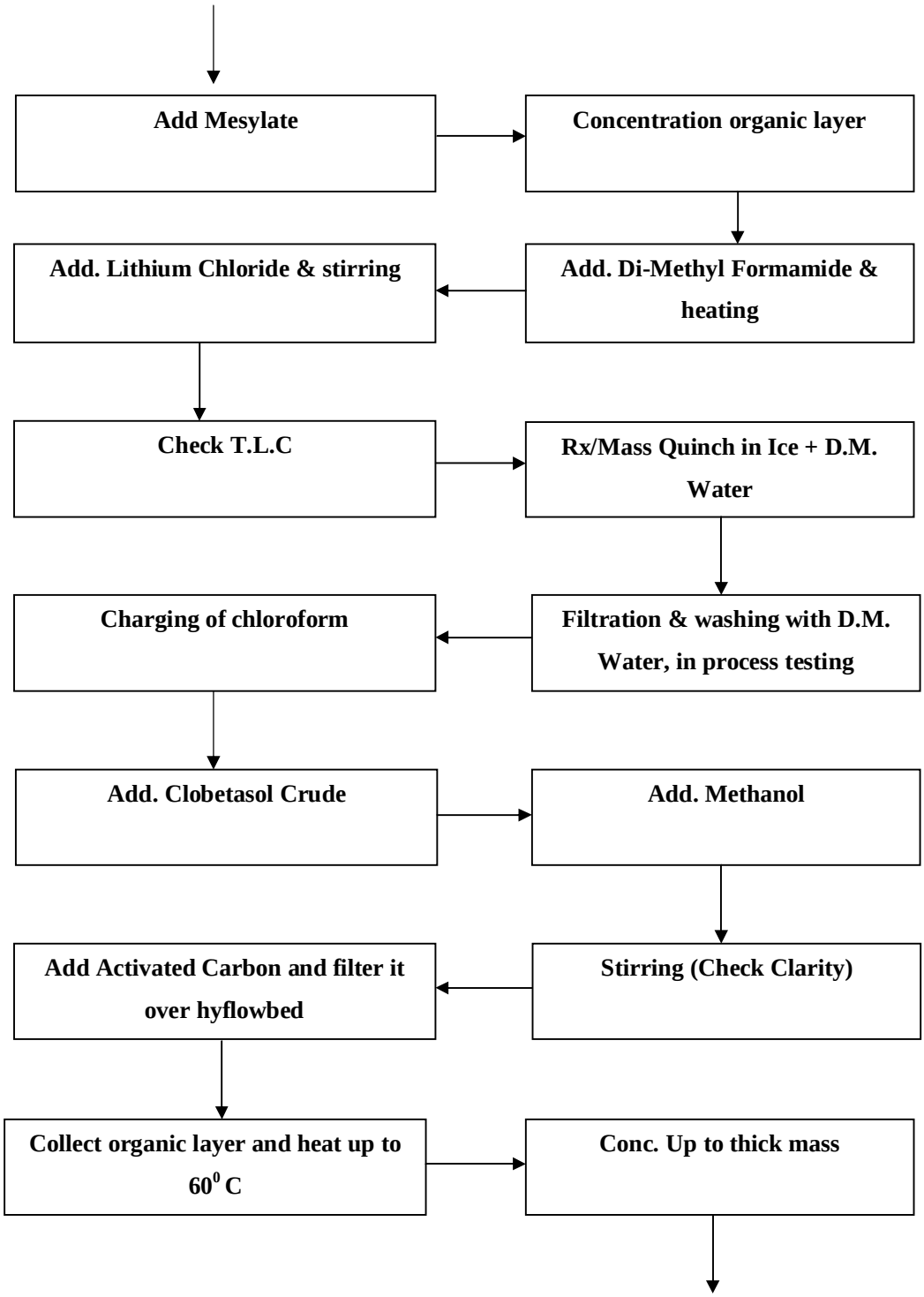
IP/BP/ USP

FLOW CHART



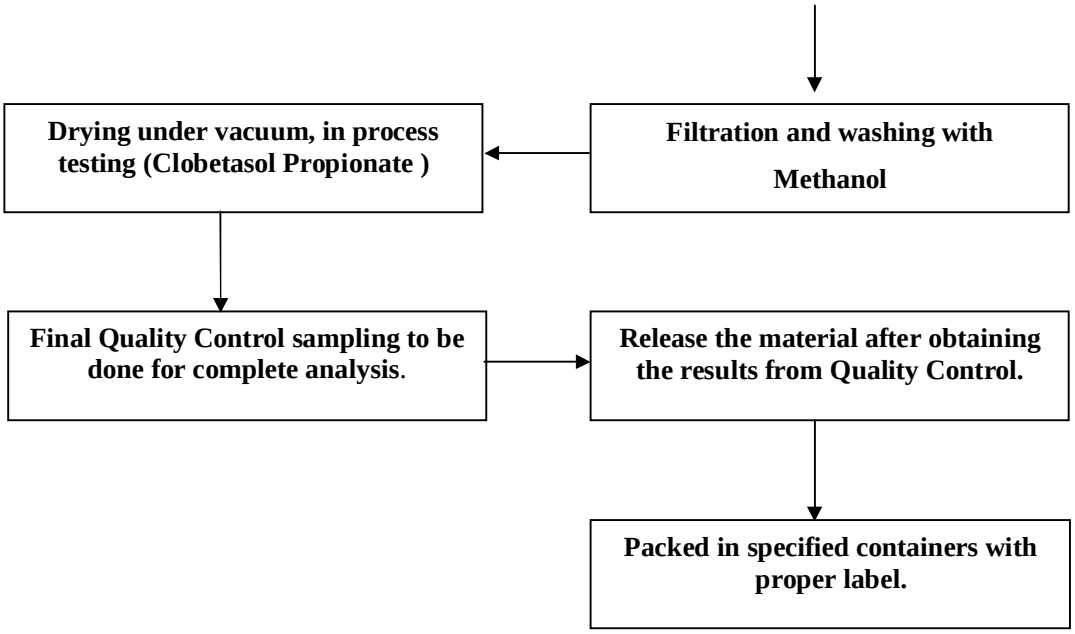
FLOW CHART OF CLOBETASOL PROPIONATE

IP/BP/ USP



FLOW CHART OF CLOBETASOL PROPIONATE

IP/BP/ USP



MANUFACTURING PROCESS OF DEXAMETHASONE SODIUM PHOSPHATE

IP/ BP/ USP

Raw Material : -

1. Dexamethasone (Base)
2. Pyro Phosphoryl Chloride
3. Tetra Hydro Furan (T.H.F)
4. Thinner / Methanol
5. Isopropyl Alcohol
6. Acetone
7. Caustic Flakes (LR)
8. Activated Carbon
9. Hyflow Supercell
10. D. M. Water

Manufacturing Process : -

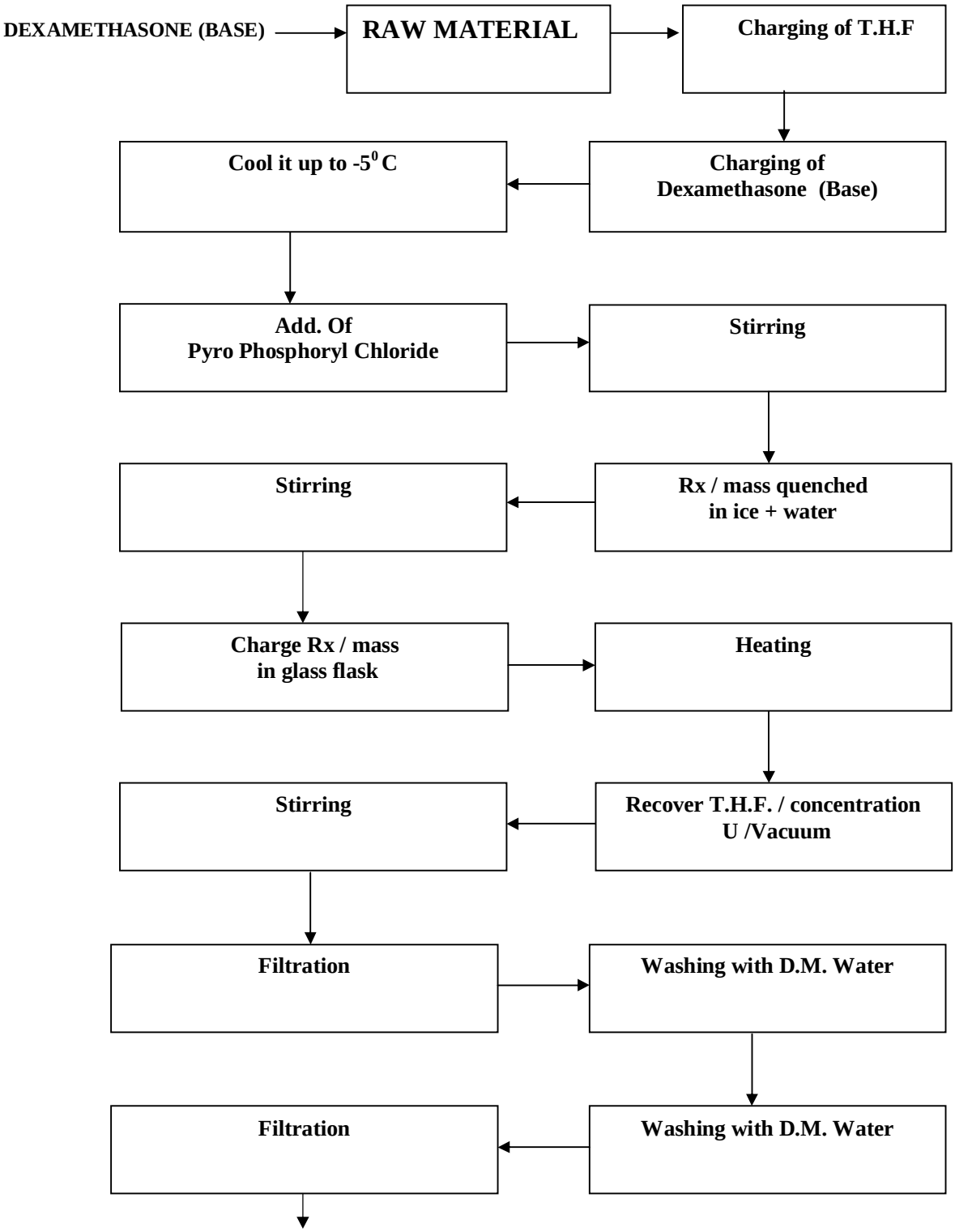
1. Clean & check all the machine used for production in all respect before use.
2. Charging of T.H.F
3. Charging of Dexamethasone (Base)
4. Cool it up to -5^0 C
5. Add. Of Pyro Phosphoryl Chloride
6. Stirring
7. Rx / mass quenched in ice + water
8. Stirring
9. Charge Rx / mass in glass flask
10. Heating
11. Recover T.H.F. / concentration U /Vacuum
12. Stirring
13. Filtration
14. Washing with D.M. Water
15. Drying
16. Cleaning and checking in Glass flask
17. Charging of Thinner / Methanol
18. Add. D.H.P.
19. Heating and Stirring
20. Add. Activated Carbon and then stirring

21. Filtration over hyflowbed
22. Collect filtrate in glass flask
23. Add. of NaOH
24. Stirring
25. Addition of Isopropyl Alcohol
26. Add. of Acetone
27. Stirring
28. Filtration and wash with acetone
29. Drying
30. Final Quality Control sampling to be done for complete analysis.
31. Packed in specified containers with proper label

FLOW CHART OF DEXAMETHASONE SODIUM PHOSPHATE

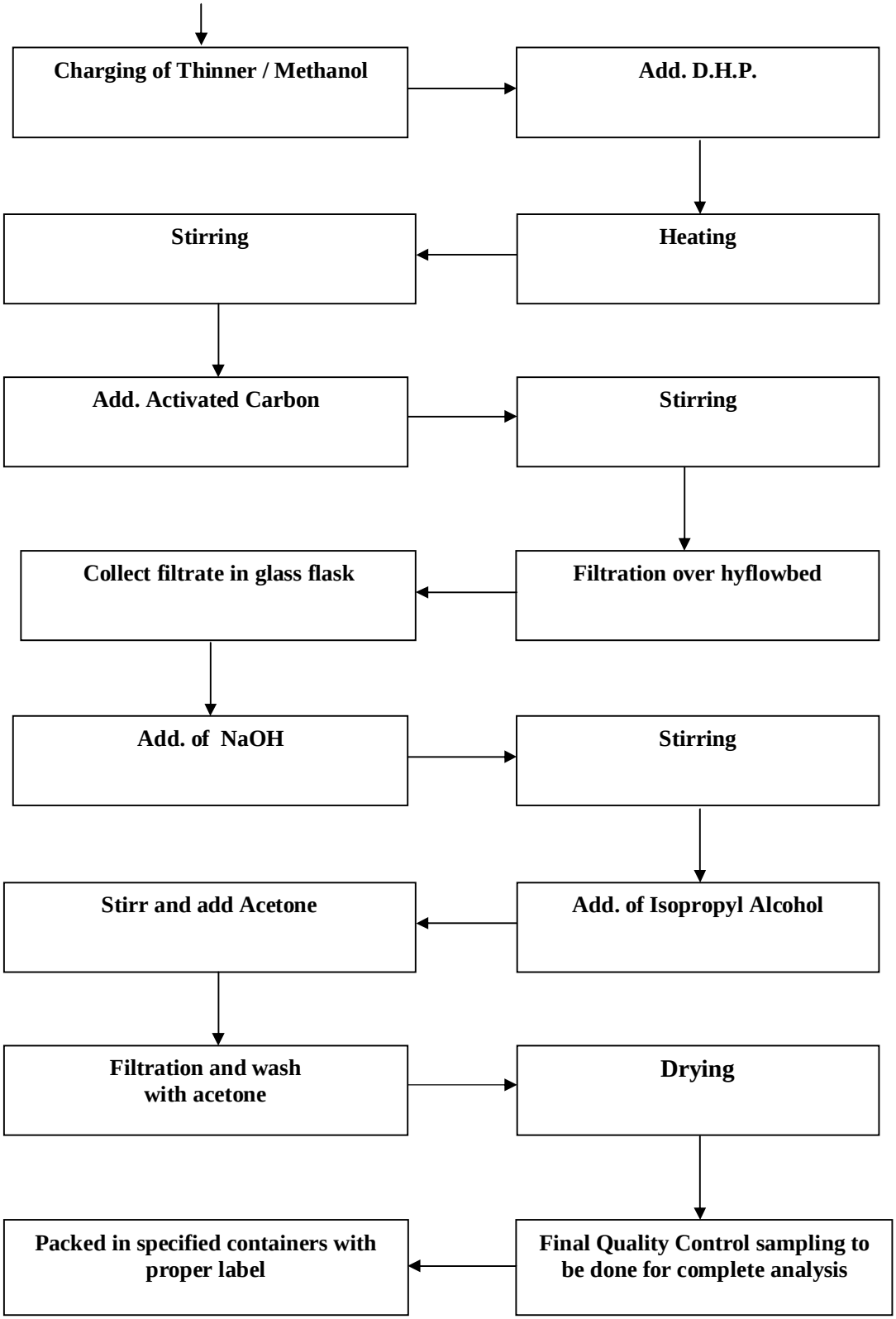
IP/ BP/ USP

FLOW CHART



FLOW CHART OF DEXAMETHASONE SODIUM PHOSPHATE

IP/ BP/ USP



MANUFACTURING PROCESS OF METHYL PREDNISOLONE

IP/ BP/ USP

Raw Material : -

1. Prednisolone
2. Methanol
3. Methyl Magnesium Bromide
4. Acetic Acid
5. Caustic Soda Flakes
6. Acetone
7. Activated Carbon
8. Hyflow Supercell
9. D. M. Water

Manufacturing Process : -

1. Clean & check all the machine used for production in all respect before use.
2. Charging of Methanol at RT.
3. Charging of Prednisolone at RT
4. Cool up to -15^0C
5. Add. of Methyl Magnesium Bromide at -15^0C to 0^0C
6. Stirring 2 hrs. at $+0^0C$ to $+5^0C$
7. Check TLC if Complies
8. Reaction mass quenched in Acidic D.M. Water.
9. Stirring for 60 minutes.
10. Adjust pH 7.0 to 7.5 by Caustic Solution.
11. Centrifuge and washing with D.M. Water
12. Unloaded and dry it. (Methyl Prednisolone Crude)
13. Charging of Acetone at RT.
14. Charging of Methyl Prednisolone (Crude)
15. Heat up to 50^0C
16. Check Clarity and add Activated Carbon.

MANUFACTURING PROCESS OF METHYL PREDNISOLONE

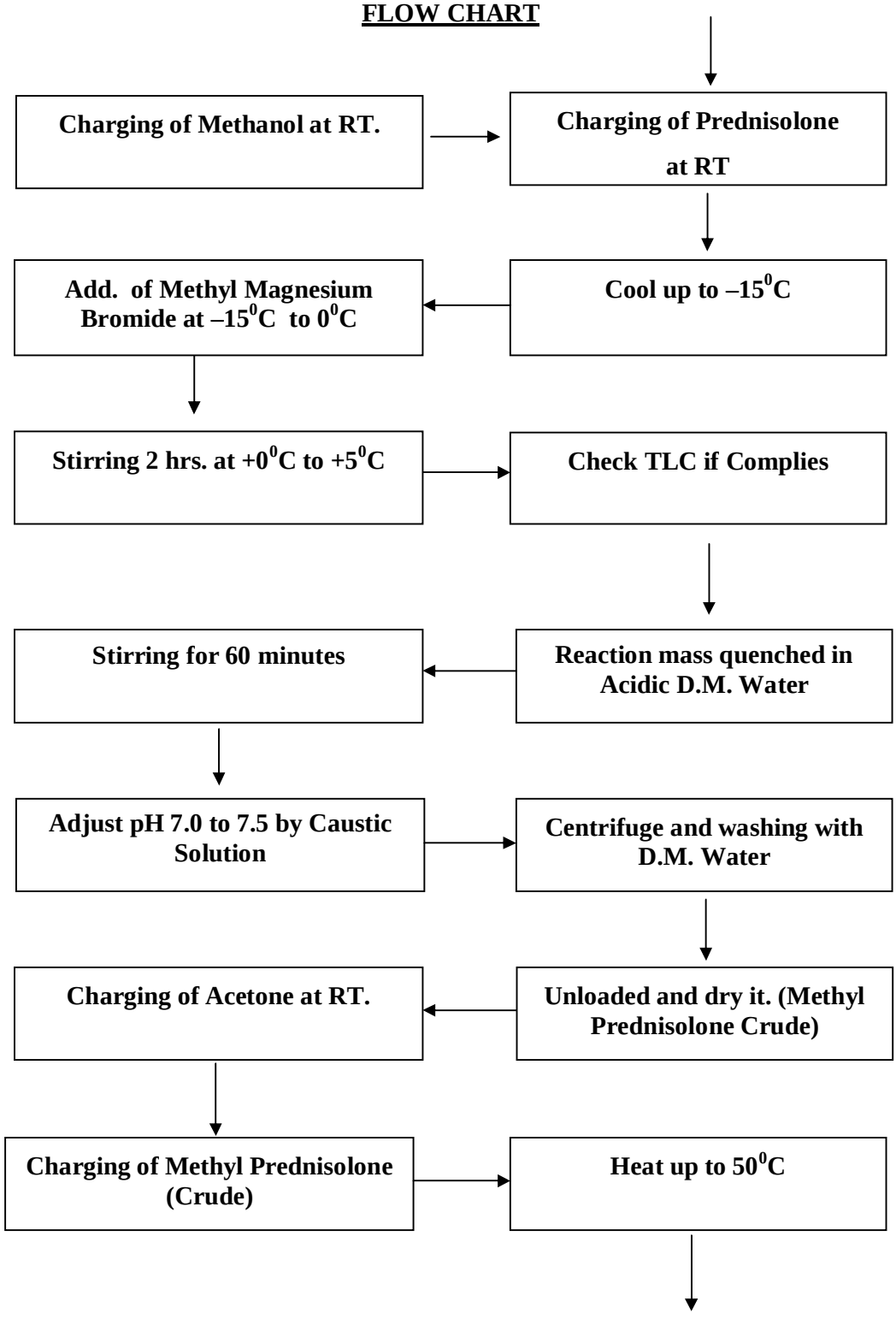
IP/ BP/ USP

17. Filter it over hyflowbed
18. Collect filterate in GLR
19. Add of D.M. Water and Stirr 2 hrs.
20. Cool up to 10^0C
21. Centrifuging
22. Drying (Methyl Prednisolone Pure)
23. Final Quality Control sampling to be done for Complete analysis.
24. Release the material after obtaining the results from Quality Control
25. Micronised the material.
26. Packed in specified containers with proper label.

FLOW CHART OF METHYL PREDNISOLONE

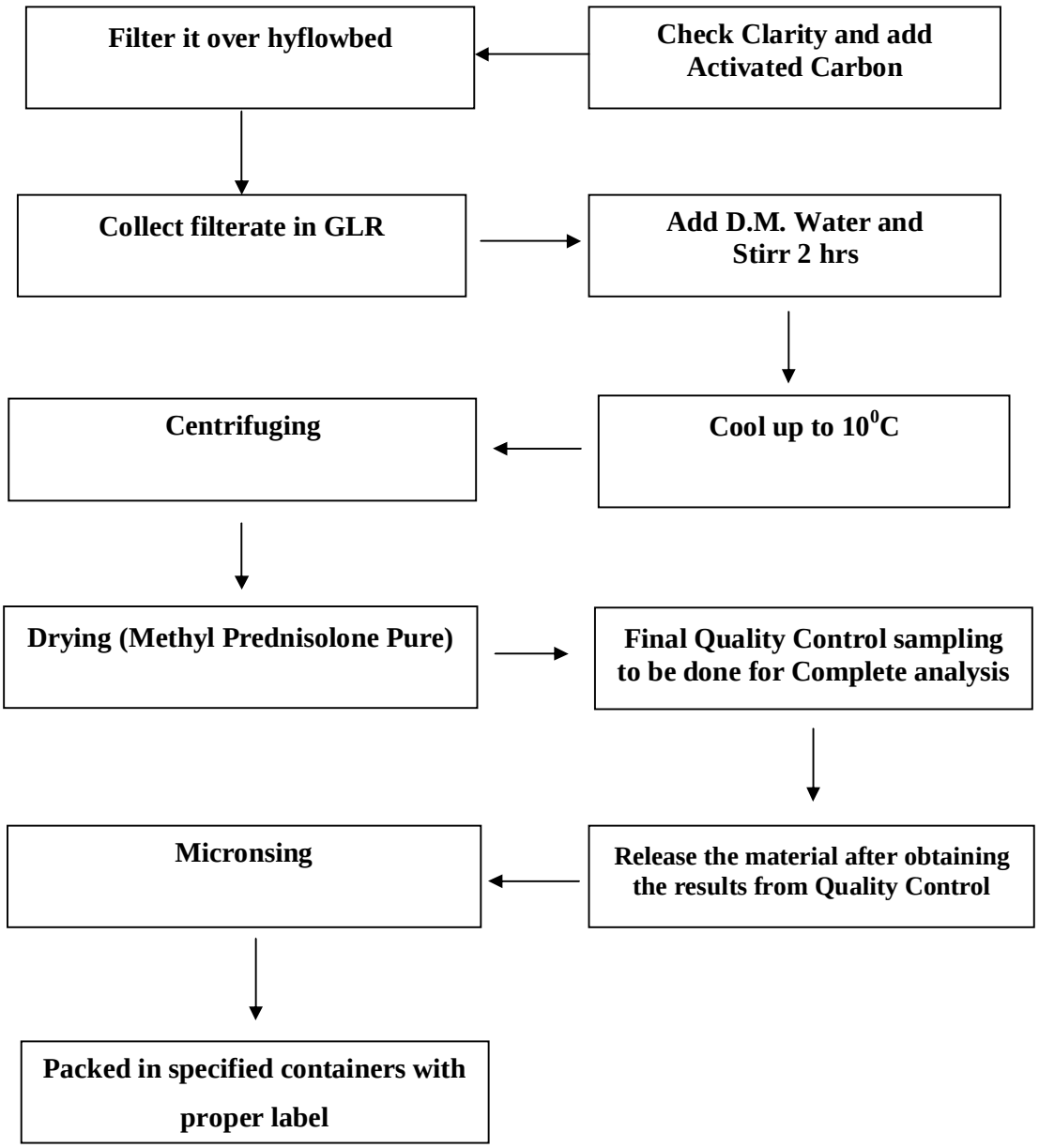
IP/ BP/ USP

FLOW CHART



FLOW CHART OF METHYL PREDNISOLONE

IP/ BP/ USP



MANUFACTURING PROCESS OF PREDNISOLONE ACETATE

IP/ BP/ USP

Raw Material :

1. Prednisolone
2. Methanol
3. Acetyl Chloride
4. Pyridine
5. Sodium Bicarbonate
6. Acetone
7. Activated Carbon
8. Hyflow Supercell
9. D. M. Water

Manufacturing Process :

1. Clean & check all the machine used for production in all respect before use.
2. Charging of Pyridine in GLR / Reaction Vessel at RT.
3. Charging of Prednisolone at RT
4. Cool up to -5^0C
5. Add Acetyl Chloride at -5^0C to 0^0C
6. Stirring 2 hrs. at $+5^0C$
7. Reaction mass quenched in DM Water.
8. Adjust pH 7.0 to 7.5 by sodium Bicarbonate solution
9. Centrifuge and washing with D.M. Water
10. Unloaded and dry it. (Prednisolone Acetate Crude)
11. Charging of Methanol and Acetone in GLR / Reaction Vessel
12. Charging of Prednisolone Acetate (Crude)
13. Heat up to 50^0C
14. Check Clarity and add Activated Carbon
15. Filter it over hyflowbed

MANUFACTURING PROCESS OF PREDNISOLONE ACETATE

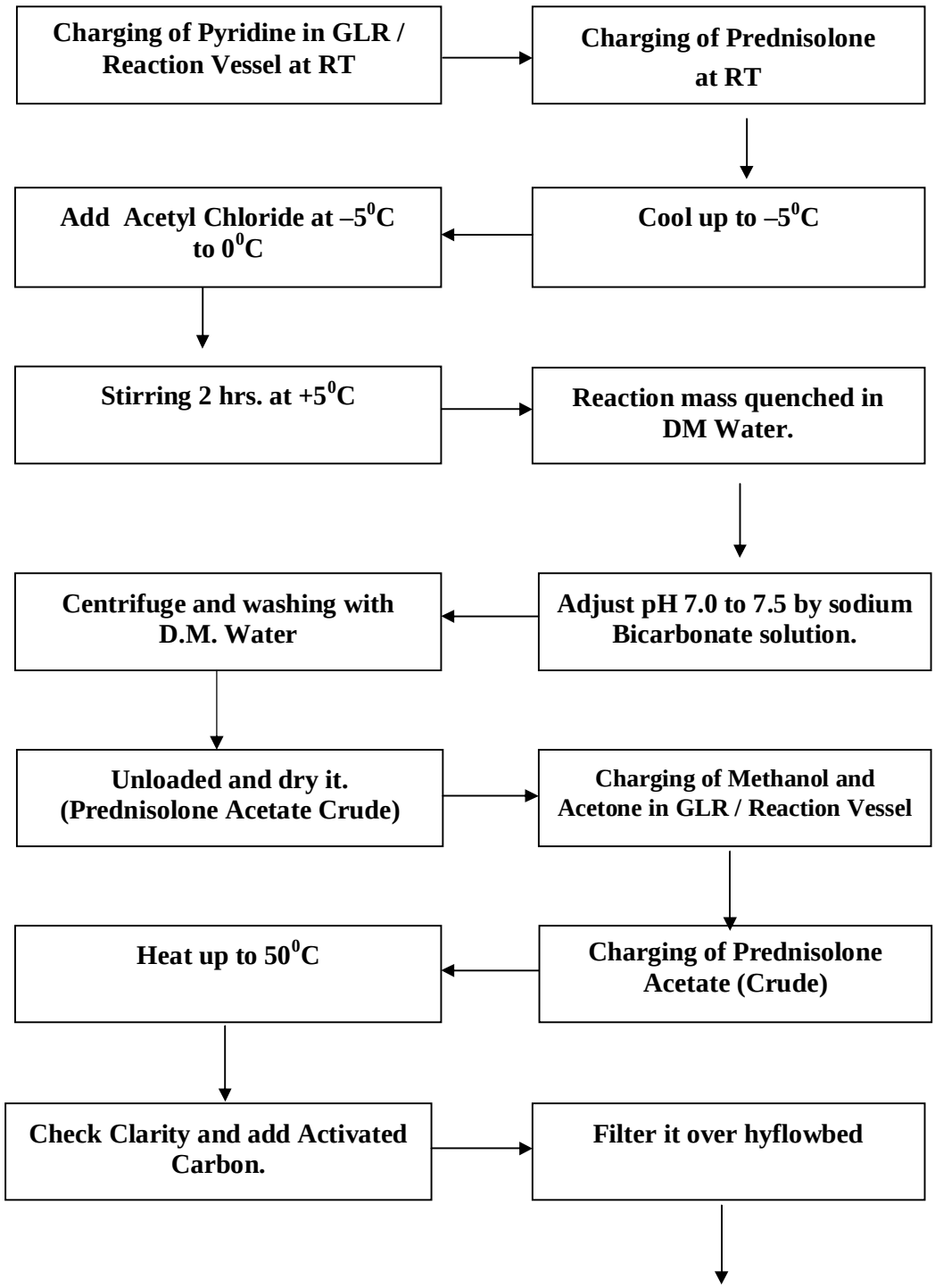
IP/ BP/ USP

16. Collect filterate in GLR
17. Add D.M. Water and Stirr 2 hrs.
18. Cool up to 10^0C
19. Centrifuging
20. Drying (Prednisolone Acetate Pure)
21. Final Quality Control sampling to be done for Complete analysis.
22. Release the material after obtaining the results from Quality Control
23. Micronised the material.
24. Packed in specified containers with proper label

FLOW CHART OF PREDNISOLONE ACETATE

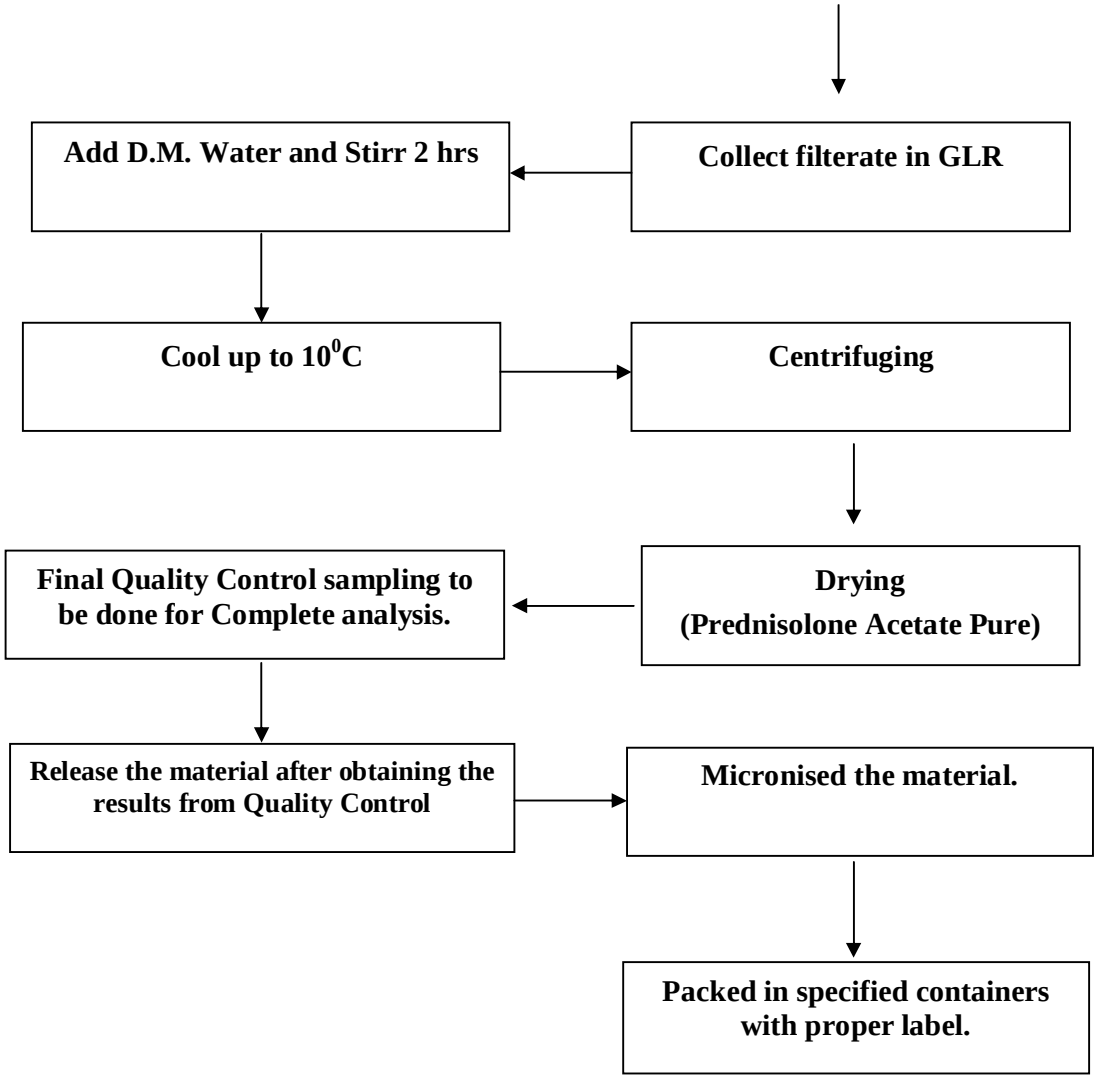
IP/ BP/ USP

FLOW CHART



FLOW CHART OF PREDNISOLONE ACETATE

IP/ BP/ USP



MANUFACTURING PROCESS OF DEFLAZACORT

Raw Material : -

1. 21 beta methyl ,17 nitro, 3,20- dione, 1,4 pregnadiene
2. Methanol .
3. Glacial acetic acid
4. Acetone
5. Potassium acetate
6. Activated carbon
7. Hyflow
8. Nitrogen gas
9. DM Water

Manufacturing Process : -

1. Charging of Methanol in glass flask at RT
2. Heat up to clear solution
3. Cleaning of glass flask
4. Connecting of nitrogen gas cylinder
5. Charging of 21 beta methyl ,17 nitro, 3,20- dione, 1,4 pregnadiene
6. Addition of above solution at 5^0C to 10^0C
7. Stirring for 2 hours at 5^0C to 10^0C
8. Check TLC if ok
9. Addition of Acidic Water solution
10. Stirring for 2 hours 5^0C to 10^0C
11. Filtration and slurry washing with DM Water
12. Drying of Deflazacort crude in oven
13. Charging of Acetone in glass flask at RT
14. Charging of Methanol in glass flask at RT
15. Charging of Potassium Acetate in glass flask at RT
16. Charging of Glacial acetic acid in glass flask at RT
17. Charging of Deflazacort crude
18. Heat up to reflux
19. Reflux for 3 hours at 65 to 70^0C

MANUFACTURING PROCESS OF DEFLAZACORT

20. Check TLC if ok
21. Addition of Activated carbon
22. Stirring for 1 hour
23. Filtration over hyflow bed prepaid in Methanol
24. Concentration of filtrate up to thick mass
25. Cooling up to 10 ^{0}C
26. Filtration and washing with Methanol
27. Drying in oven
28. QC Sampling for complete analysis.

MANUFACTURING PROCESS OF METHYL COBALAMINE / MECOBALAMIN JP

Raw Material : -

1. Cynocobalamine
2. Chloroform
3. Methyl Iodide
4. Sodium Borohydride
5. Phenol
6. Acetone
7. D.M. Water

Manufacturing Process : -

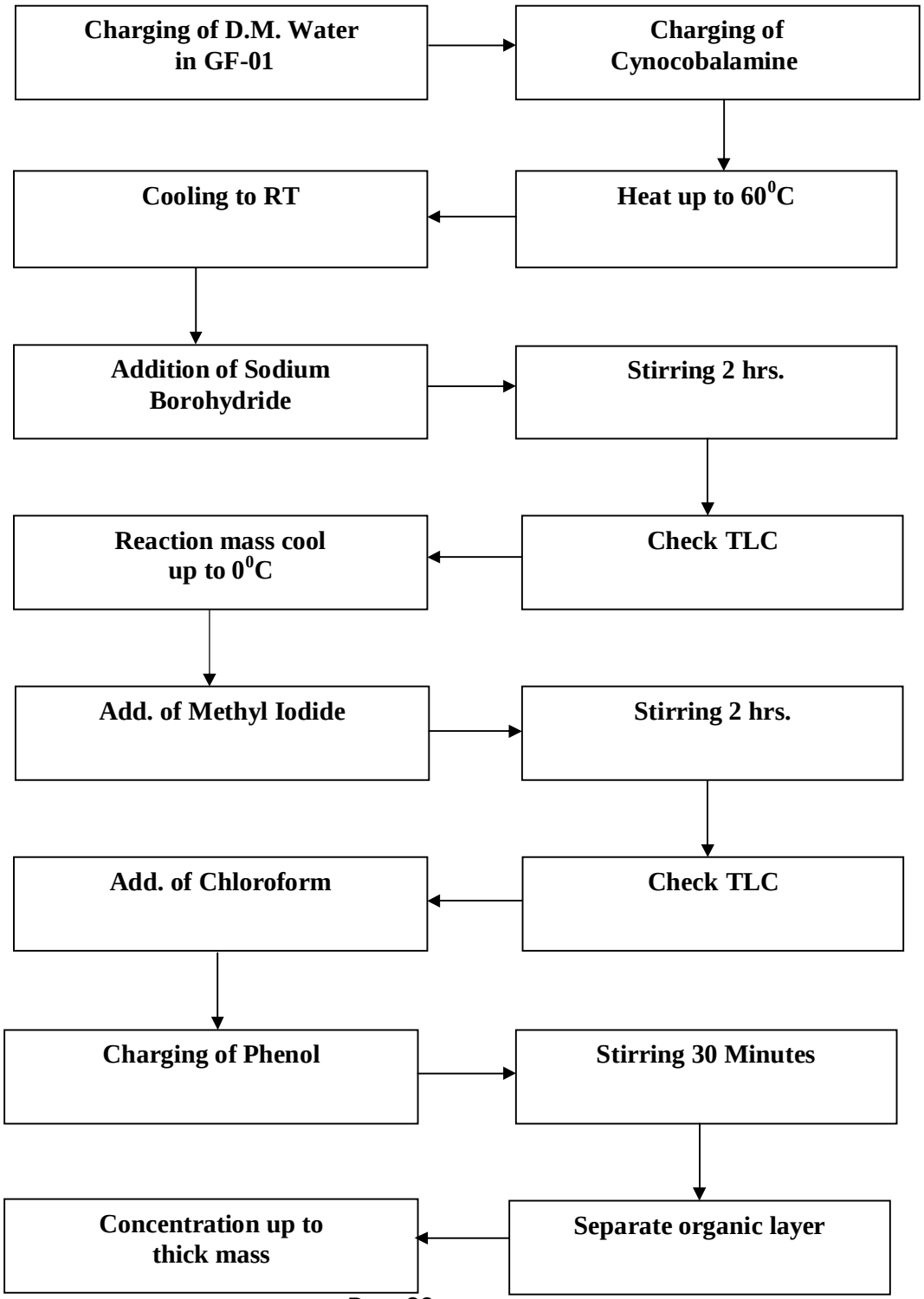
1. Clean & check all the Equipments used for production in all respect before use as per SOP
2. Charge D.M. Water in Glass Flask (GF-01) at RT
3. Charging of Cynocobalamine in GF-01 at RT
3. Heat up to 60^0C and Cool up to RT
5. Addition of Sodium Borohydride in GF-01 at RT
6. Stirring for 2 hrs. at RT
7. Check TLC if OK
8. Reaction mass cool up to 20^0C
9. Addition of Methyl Iodide in RT-01 at RT
10. Stirring 2 hrs.
11. Check TLC
12. Add. of Chloroform in RT-01 at RT
13. Add. of Phenol in RT-01 at RT
14. Stirring for 30 Minutes. at 32-35^0C
15. Separate organic layer
16. Concentration up to thick mass
17. Add. of Acetone in RT-01 at RT
18. Cooling up to 10^0C & Stirring for 30 minutes.
19. Filtration and slurry making with D.M. Water
20. Unloading of wet cake
19. Drying in Electric Tray Drier (ETD-01)
20. Quality Control sampling to be done for complete analysis.
21. Multi milling (MM-01)
23. Release the material for Packing after obtaining the results from Q.C.D.
24. Packed in specified containers with proper label.

25. Sampled for Retesting for preserve a control sample.

FLOW CHART OF METHYL COBALAMINE / MECOBALAMIN

JP

FLOW CHART



FLOW CHART OF METHYL COBALAMINE / MECOBALAMIN

J. P.