ISHA'S GMP CONSULTANCY PVT. LTD.
Ensuring Global GMP Compliance™ ®

PITAVASTATIN CALCIUM

API MASS BALANCE | ALL-SHEETS TECHNICAL REVIEW

Source workbook: 32-Pitvastatin Calcium.xlsx

Material balance sheet • Flow chart • CC • Raw materials • Sheet1

TOTAL INPUT	TOTAL OUTPUT	FINAL API	MASS BALANCE CLOSURE
36.255 kg	36.260 kg	1.000 kg	100.014%
Material balance sheet	Itemised outputs	Pitavastatin Calcium	Calculated from recorded totals

MANUFACTURING PROCESS FLOW • Sequence from Flow chart and Material balance sheet

01 REACTION 1 — Methanol · HCl · NaOH

02 WORK-UP 1 — Ether · cyclohexane

03 REACTION 2 — NaOH · $CaCl_2 \cdot 2H_2O$

04 WORK-UP 2 — Aqueous phase to ETP

05 FILTRATION — Water wash; filtrate

06 DRYING — Evaporation 1.50 kg

07 MILLING & SIFTING — Size reduction

08 FINAL API — Pitavastatin Calcium

INPUT / CHARGE RECORDS • Material balance sheet

Sr.	MB material input	kg
1	Tert-butyl quinoline intermediate [A]	1.180
2	Methanol	6.000
3	Conc.HCl	0.670
4	Water	5.600
5	Sodium hydroxide	0.290
6	Disiopropyl ether [source spelling]	5.900
7	Cyclohexane	5.900
8	Purified water	5.600
9	Sodium hydroxide	0.050
10	Calcium Chloride dihydrate	0.265
11	Purified water	2.400
12	Water	2.400

RAW MATERIAL REGISTER • CC + Raw materials

Sr.	CC raw material	kg
1	Tert-butyl quinoline intermediate [A]	1.180
2	Methanol	6.000
3	Conc.HCl	0.670
4	Sodium Hydroxide	0.340
5	Disiopropyl ether	5.900
6	Cyclohexane	5.900
7	Calcium Chloride dihydrate	0.265

MATERIAL OUTPUTS • Material balance sheet

Sr.	MB output stream	kg
1	Organic layer (disposition TBD)	15.600
2	Evaporation loss	0.700
3	Aqueous layer → ETP	12.400
4	Evaporation loss	2.360
5	Filtrate → ETP	2.500
6	Evaporation loss	0.200
7	Evaporation loss	1.500
8	Pitavastatin Calcium API (final)	1.000

OUTPUT / WASTE RECONCILIATION

CC charge subtotal	**20.255 kg**
MB additional water charges	**16.000 kg**
MB material charges total	**36.255 kg**
Organic layer (reported)	**15.600 kg**
Liquid to ETP (12.40 + 2.50)	**14.900 kg**
Evaporation losses (sum)	**4.760 kg**
Final Pitavastatin Calcium	**1.000 kg**
Recorded solid waste	**NIL**

MOLE / PROPOSED CONSUMPTION • Sheet1

Sheet1 material	kg	MW	mol	ratio	MT/day
KSM intermediate [A]	1.180	517.63	2.28	1.000	0.0983
Methanol	6.000	—	—	—	0.4990
Conc.HCl	0.670	—	—	—	0.0560
Sodium Hydroxide	0.340	40.00	7.50	3.289	0.0280
Disiopropyl ether	5.900	—	—	—	0.4920
Cyclohexane	5.900	—	—	—	0.4920
Ca chloride dihydrate	0.265	110.98	2.43	1.070	0.0230

TECHNICAL REVIEW • VERIFY BEFORE GMP APPROVAL

- Gross balance: outputs exceed inputs by 0.005 kg (closure 100.014%).
- Yield: source 50%; 1.00 / 1.70 kg theoretical = 58.82%.
- Molar record: sodium hydroxide 0.34 kg / 39.997 g/mol ≈ 8.50 mol, versus 7.50 reported.
- $CaCl_2 \cdot 2H_2O$: description and cited MW 110.98 should be reconciled (dihydrate ≈147.0 g/mol).
- Stream disposition: clarify 15.60 kg organic layer; verify charge-sheet versus MB water basis.

[A] Source starting-material description: Ter-butyl 2-((4R, 6S)-6-((E)-2-(2-cyclopropyl-4-(4-flurophenyl) quinolin-3-yl) vinyl-2, 2-dimethyl-1,3-dioxan-4-yl)acetate

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