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

ATORVASTATIN CALCIUM

API MASS BALANCE / WORKBOOK-CONSOLIDATED PROCESS STUDY

Actual figures from Material Balance, FC, CC, RM and Moles | Source discrepancies disclosed

TOTAL MB INPUT	TOTAL MB OUTPUT	FINAL API
46.25 kg	46.25 kg	1.00 kg

01 PROCESS FLOW | FC + Material Balance - stages and reported operations

Reaction / work-up KSM, Raney Ni, NH3, MeOH, water	**Filtration** Solid waste 2.30 kg	**Distillation** MeOH distillate 5.00 kg	**STAGE A** Interstage transfer 1.00 kg	**Reaction** Second intermediate + solvent	**Filtration** Filtrate 15.00 kg	**Drying** Stage B preparation
STAGE B Interstage transfer 1.20 kg	**Reaction** HCl + methanol	**Work-up** NaOH + methanol	**Reaction** Calcium acetate + water	**Filtration** Aqueous filtrate 7.00 kg	**Drying** Loss 0.20 kg	**FINAL API** Atorvastatin calcium 1.00 kg

Note: internal Stage A / Stage B transfers are re-entered as subsequent-step inputs in the MB workbook.

02 MATERIAL REGISTER | CC + RM + Moles - 12 matched material names

No.	RAW MATERIAL	CC kg	MW	Moles	Ratio	Proposed MT/day	Moles remark
01	**KSM-01: (4R,cis) dioxane-4-acetate***	1	269.34	3.71	1	83.33	Starting material
02	Methanol	12.4	--	--	--	1033.33	Solvent
03	Hydrochloric acid	0.35	--	--	--	29.17	Reagent
04	Sodium hydroxide	0.2	40	5	1.35	16.66	Reagent
05	Raney nickel	0.3	85.675	3.5	0.94	24.99	Catalyst
06	MTBE	1.25	--	--	--	104.16	Reagent
07	Aqueous ammonia solution	0.25	--	--	--	20.83	Reagent
08	Calcium acetate	0.2	158.17	1.27	0.34	16.66	Reagent
09	Hyflo	2	--	--	--	166.66	--
10	Pivalic acid	0.1	102.132	0.98	0.26	8.33	Reagent
11	Cyclohexane	10	--	--	--	833.33	Solvent
12	Isopropyl alcohol	8	--	--	--	666.66	Solvent

CC CHARGE SHEET TOTAL **36.05 kg**

* KSM-01 (source): 4R,Cis)-1,1-dimethylethyl-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate. Raw Material sheet (RM) names match the CC list (12 of 12).

Moles values, ratios and proposed MT/day values reproduced as entered; unit/capacity basis requires confirmation.

03 MASS BALANCE OUTPUTS | Material Balance

SOURCE OUTPUT STREAM (14 line items)	kg
10 Solid waste	2.30
11 Filtrate	9.00
12 Evaporation loss (process loss)	0.25
14 Distillate-Methanol	5.00
15 Evaporation loss (process loss)	1.00
18 Stage-A (internal transfer)	1.00
26 Filtrate	15.00
27 Evaporation loss (process loss)	2.20
31 Evaporation loss (process loss)	0.10
34 Stage-B (internal transfer)	1.20
49 Aqueous filtrate to ETP	7.00
50 Evaporation loss (process loss)	1.00
53 Evaporation loss (process loss)	0.20
57 FINAL ATORVASTATIN CALCIUM (API)	1.00

REPORTED MB TOTAL **46.25 kg**

04 GROSS INPUT RECONCILIATION

CC charge	36.05 kg
Water - MB only	+ 8.00 kg
Stage A + B transfer	+ 2.20 kg
MB gross input	46.25 kg

Gross MB includes re-charged intermediates: do not interpret 46.25 kg as fresh external material charged.

05 YIELD & WASTE RECORDS

Theoretical yield (unit unstated)	4.20
Reported yield	23.8%
Methanol recovered	5.00 kg

Liquid ETP	Solid	Fugitive
7.00 kg	2.30 kg	4.80 kg
0.583 MT/day	0.192 MT/day	0.400 MT/day

06 CHECKS REQUIRED BEFORE GMP USE

- CC lists MTBE 1.25 kg; MB instead lists a different 1.25 kg intermediate.
- The 46.25 / 46.25 kg closure is gross; Stage A / B are internal transfers.
- MB evaporation losses total 4.75 kg; waste summary reports 4.80 kg.
- FC calls final material "Solid"; MB names "Atorvastatin calcium".
- Yield 23.8% and theoretical 4.20 require batch / unit confirmation.
- Moles "MT/day" consumption figures need scaling and unit verification.

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