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

TAZAROTENE API | MASS BALANCE

One-page technical overview • Source-based material reconciliation • Five-sheet workbook

PROCESS / GMP TECHNICAL REVIEW

Reference: 40-Tazarotene.xlsx

GROSS INPUT	GROSS OUTPUT	FINAL TAZAROTENE	OVERALL CLOSURE
144.800 kg	144.800 kg	1.000 kg	100.00%
MPCB | includes stage transfers	MPCB | all recovered streams	MPCB | output row	Gross, not stage-wise closure

MANUFACTURING FLOW / INTERMEDIATE TRACKING

Source: FC and MPCB

STAGE A — Reaction → Filter → Workup / distillation

Reaction → Filter | 1.220 kg Stage-A

STAGE B — Stage-A + NaHCO3 + EtOAc + water

Reaction → Workup → Filter | 1.100 kg Stage-B

FINAL STAGE — Stage-B + Hyflo + EtOAc + charcoal

Reaction → Filter → Dry | 1.000 kg Tazarotene

RAW MATERIAL CHARGES

CC / RM | 12 listed materials

NO.	CHARGED MATERIAL	KG
1	Dimethyl Sulfoxide	10.000
2	Palladium Chloride	0.020
3	Triphenyl phosphine	0.100
4	6-ethynyl-4,4-dimethylthiochromane	1.430
5	Ethyl 6-chloronicotinate	1.370
6	Cuprous iodide	0.090
7	Triethyl amine	2.360
8	Ethyl acetate	33.800
9	Ethyl acetate HCl (5%)	14.300
10	NaHCO3	2.070
11	Hyflo	1.000
12	Charcoal	0.140

MOLECULAR / CONSUMPTION SCHEDULE

Moles sheet | blank cells retained

#	INPUT COMPONENT	MW	KG	MOLES	RATIO	MT/DAY	ROLE / REMARK
1	6-ethynyl-4,4-dimethylthiochromane	202.30	1.430	7.068	1.000	0.238	Reagent
2	Palladium Chloride	177.33	0.020	0.113	0.015	0.003	Catalyst
3	Triphenyl phosphine	262.29	0.100	0.382	0.054	0.017	Reagent
4	Dimethyl Sulfoxide	—	10.000	—	—	1.620	Solvent
5	Ethyl 6-chloronicotinate	157.55	1.370	8.700	1.230	0.228	Starting material
6	Cuprous iodide	190.45	0.090	0.480	0.060	0.016	Reagent
7	Triethyl amine	101.00	2.360	23.360	3.300	0.393	Solvent
8	Ethyl acetate	—	33.800	—	—	5.633	Solvent
9	Ethyl acetate HCl (5%)	—	14.300	—	—	2.383	Reagent
10	NaHCO3	84.01	2.070	24.640	2.830	0.345	Reagent
11	Hyflo	—	1.000	—	—	0.167	—
12	Charcoal	—	0.140	—	—	0.023	—

ITEMISED GROSS MATERIAL BALANCE

MPCB | sums include internal Stage-A / Stage-B movements

#	INPUT STREAM / MATERIAL	KG
2	Dimethyl Sulfoxide	10.000
3	Palladium chloride	0.020
4	Triphenyl phosphine	0.100
5	6-ethylene-4,4- dimethylthiochromane	1.430
6	Ethyl 6-chloronicotinate	1.370
7	Cuprous iodide	0.090
8	Triethyl amine	2.360
10	Hyflo	1.000
12	Ethyl acetate	14.300
13	DM water	14.300
16	Ethyl acetate HCl(5%)	14.300
22	Stage-A	1.220
23	NaHCO3	2.070
24	Ethyl acetate	19.500
26	Water	40.000
32	Stage-B	1.100
33	Hyflo	2.000
34	Ethyl acetate	19.500
35	Charcoal	0.140

#	OUTPUT STREAM	KG
9	Solid waste	1.020
10	Evapration loss	2.000
12	Distillate	13.000
13	Evaporation loss	1.500
14	Aq layer to ETP	23.000
18	Filtrate	15.000
19	Evaporation loss	1.000
21	Stage-A	1.220
26	Aq layer-to-ETP	42.000
28	Evaporation loss	1.000
29	Filtrate	18.000
31	Stage-B	1.100
36	Filtrate	15.320
37	Evaporation loss	5.000
38	Solid waste	2.140
40	Evaporation loss	1.500
42	Output	1.000

SOURCE TOTALS — 144.800 kg IN — 144.800 kg OUT

STAGE-WISE RECONCILIATION & EXCEPTIONS

Review required | Source values not adjusted

GROUPED ROWS	INPUT KG	OUTPUT KG	OUT - IN KG
STAGE A (2–21)	59.270	57.740	-1.530
STAGE B (22–31)	62.790	62.100	-0.690
FINAL (32–42)	22.740	24.960	+2.220

- Gross closure masks Stage A/B shortfalls and final-stage excess.
- CC 66.680 kg vs MPCB 144.800 kg: 54.3 water, 19.5 EtOAc, 2 Hyflo, 2.32 transfers.
- Starting-material label: "6-ethylene" (MPCB) vs "6-ethynyl" (RM/CC/Moles).
- Moles sheet: DMSO 10.0 kg; proposed 1.620 MT/day (others imply ~1/6 scale).

GROSS TOTAL — 144.800 kg input = 144.800 kg output — Internal transfers = 2.320 kg | Not external fresh charges

WASTE & YIELD VERIFICATION

MPCB rows 45–56

Liquid effluent to ETP	65.000 kg
Solid waste	3.160 kg
Fugitive / evaporation	12.000 kg
Reported yield	31.34%
Yield if 2.23 kg theoretical	44.84%

REVIEW: 12 kg fugitive monthly/day conversion inconsistent with 5-batch waste basis.

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