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ROPINIROLE API

FOUR-STAGE MASS BALANCE & MANUFACTURING FLOW

Technical illustration based on the uploaded Summary and ROPINIROLE worksheets

TECHNICAL DATA REVIEW

Source: 6- ROPINIROLE.xlsx | 2 worksheets

Reported values preserved • Differences highlighted

SUMMARY BATCH SIZE	RECORDED FINAL-STAGE	MANUFACTURING	GROSS STAGE INPUT	GROSS STAGE OUTPUT
500 kg	100.00 kg	4 stages	21,855.24 kg	21,855.26 kg
Summary sheet	Output labelled “Stage-1”	Detail worksheet	Includes internal transfers	Sum of itemised outputs

PROCESS ROUTE

Intermediate movement between stages

01 STAGE 1 — Reaction • extraction • purification — **129.63 kg Stage-1 transfer** ›

02 STAGE 2 — Reaction • extraction • distillation — **89.45 kg Stage-2 transfer** ›

03 STAGE 3 — Reaction • extraction • distillation — **116.28 kg Stage-3 transfer** ›

04 STAGE 4 — Reaction • salt formation • drying — **100.00 kg recorded final output**

STAGE 1 SYNTHESIS & ISOLATION

Reaction / extraction / purification

INPUT CHARGES • 6 items	kg
4- indole-carboxaldehyde	122.06
Nitro methane	1,220.55
Ammonium acetate	24.41
Ethyl acetate	631.32
Sodium chloride (30% Solution in water)	631.32
cyclohexane	631.32

OUTPUTS / RECOVERIES • 8 items	kg
Effluent water with inorganic salt	703.71
Nitromethane recovery	1,136.38
Ethyl acetate Recovery	599.75
Ethyl acetate Loss	31.57
Cyclohexane Recovery	599.75
Cyclohexane Loss	31.57
Organic Residue Impurities	28.62
Stage-1	129.63

INPUT 3,260.98 kg — **OUTPUT 3,260.98 kg**

DELTA (output - input) **+0.00 kg**

STAGE 2 INTERMEDIATE PROCESSING

Reaction / separation / distillation

INPUT CHARGES • 5 items	kg
Stage-1	129.63
lithium aluminum hydride	156.85
tetrahydrofuran	2,592.62
Water	2,592.62
Ethyl Acetate	1,296.31

OUTPUTS / RECOVERIES • 7 items	kg
Effluent water with inorganic salt	2,768.92
tetrahydrofuran recovery	2,462.99
tetrahydrofuran loss	129.63
Ethyl acetate recovery	1,231.50
Ethyl acetate loss	64.82
Organic residue impurities	20.74
Stage -2	89.45

INPUT 6,768.03 kg — **OUTPUT 6,768.05 kg**

DELTA (output - input) **+0.02 kg**

STAGE 3 INTERMEDIATE PROCESSING

Reaction / extraction / distillation

INPUT CHARGES • 5 items	kg
Stage-2	89.45
Propionic acid	621.65
Sodium borohydride	107.33
Water	2,683.36
Ethyl Acetate	447.23

OUTPUTS / RECOVERIES • 5 items	kg
Effluent water with inorganic salt	3,365.38
Toluene recovery	424.87
Toluene loss	22.36
Organic residue impurities	20.13
Stage -3	116.28

INPUT 3,949.02 kg — **OUTPUT 3,949.02 kg**

DELTA (output - input) **+0.00 kg**

STAGE 4 SALT FORMATION / DRYING

Reaction / filtration / drying

INPUT CHARGES • 6 items	kg
Stage-2	116.28
pyridinium tribromide	202.79
acetic acid 50% solution in water	3,488.37
Water	2,325.58
Ethyl acetate	1,162.79
hydrochloric acid solution in isopropyl alcohol	581.40

OUTPUTS / RECOVERIES • 6 items	kg
Effluent water with inorganic salt	6,108.14
Ethyl acetate Recovery	1,104.65
Ethyl acetate Loss	58.14
Isopropyl alcohol Recovery	465.12
Organic Residue Impurities	41.16
Stage-1 (source output label)	100.00

INPUT 7,877.21 kg — **OUTPUT 7,877.21 kg**

DELTA (output - input) **+0.00 kg**

REPORTED MATERIAL MOVEMENT | AGGREGATED STAGE-OUTPUT STREAMS

Stage-output totals; not a net batch balance

SOLVENTS RECOVERED	AQUEOUS EFFLUENTS	ORGANIC RESIDUES	STATED SOLVENT LOSSES
8,025.01 kg	12,946.15 kg	110.65 kg	338.09 kg
Includes Stage 3 “toluene” entry	Sum of four effluent entries	Across four stages	Sum of explicitly listed loss streams

Grand stage sums: 21,855.24 kg inputs / 21,855.26 kg outputs (+0.02 kg).

Repeated intermediate entries make these sums different from unique external charges.

GMP DATA REVIEW — ITEMS TO RESOLVE BEFORE APPROVAL

NOT AN APPROVED GMP RECORD

01 REFERENCE LABELS

Stage 4 uses “Stage-2” for its 116.28 kg input (equal to Stage 3 output); its 100 kg output is labelled “Stage-1”, not explicitly API.

02 SOLVENT IDENTITY

Stage 3 charges 447.23 kg ethyl acetate, but reports 424.87 kg toluene recovery and 22.36 kg toluene loss.

03 FORMULA / ROUNDING

Several workbook cells contain #REF!; Stage 2 itemised output exceeds input by 0.02 kg. Reported stage totals are rounded.

04 BATCH-SIZE BASIS

Summary batch size is 500 kg; the final stage lists 100 kg output. Confirm scale basis, product identity and solvent reconciliation.

Source: 6- ROPINIROLE.xlsx • Sheets: Summary; ROPINIROLE. All amounts in kg unless otherwise stated.

This is a source-derived illustrative poster, not an approved batch record. GMP acceptance requires verified materials, calculation formulas and stage reconciliation.

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