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

LOPERAMIDE HYDROCHLORIDE

API MASS BALANCE | STAGE-WISE PROCESS & MATERIAL RECONCILIATION

Source: 9-LOPERAMIDE(1).xlsx • Summary + LOPERAMIDE worksheets • Technical review illustration

ONE-PAGE A2

ISSUE: SOURCE RECONCILIATION

BATCH REFERENCE	FINAL API	SUM OF STAGE INPUTS	SUM OF STAGE OUTPUTS	STAGE 5 DIFFERENCE
500 kg	**100.00 kg**	**10,169.57 kg**	**10,128.50 kg**	**41.08 kg**
Summary, not final output	Stage 5: Loperamide HCl	Includes intermediate transfers	Itemised stage outputs	Unreconciled, output shortfall

5-STAGE MANUFACTURING ROUTE

STAGE 1	STAGE 2	STAGE 3	STAGE 4	STAGE 5
Stage-1	Stage-II	Stage-III	Stage-IV	Loperamide HCl
Output 136.95 kg	Output 140.87 kg	Output 159.65 kg	Output 109.59 kg	Output 100.00 kg

STAGE 1 | Reaction > Filtration > Purification > Drying

MATERIAL IN (kg)		MATERIAL OUT (kg)	
4-Bromo 2,2-diphenyl butyronitrile	215.57	Effluent water with inorganic salt	2,466.42
Acetic acid	215.57	Isopropyl alcohol Recovery	722.81
Sulfuric acid	215.57	Isopropyl alcohol Loss	38.04
water	1,990.89	Organic residue impurirties	34.24
Isopropyl alcohol	760.85	Stage-1	136.95

IN 3,398.45 | OUT 3,398.46 kg — **DIFF +0.01 kg**

STAGE 2 | Reaction > Filtration > Drying

MATERIAL IN (kg)		MATERIAL OUT (kg)	
Stage-1	136.95	Acetic acid Recovery	181.30
Hydrobromic acid solution in acetic acid	332.60	Hydrobromic acid and acetic acid loss	104.35
Toluene	26.09	Toluene Recovery	24.78
		Toluene Loss	1.30
		Organic residue impurities	43.04
		Stage-II	140.87

IN 495.64 | OUT 495.64 kg — **DIFF +0.00 kg**

STAGE 3 | Reaction > Distillation

MATERIAL IN (kg)		MATERIAL OUT (kg)	
Stage-II	140.87	Thionyl chloride consumption loss	100.62
Thionyl chloride	112.69	Toluene Recovery	201.24
Dimethyl formamide	6.71	Toluene Loss	10.73
Toluene	211.97	Stage - III	159.65

IN 472.24 | OUT 472.24 kg — **DIFF +0.00 kg**

STAGE 4 | Reaction / Extraction > Separation > Purification > Drying

MATERIAL IN (kg)		MATERIAL OUT (kg)	
Stage-III	159.65	Effluent water with inorganic salt	470.83
Dimethyl amine solution in water	74.41	Chloroform Recovery	1,528.83
Sodium carbonate	81.18	Chloroform Loss	81.18
Water	319.30	Ethyl acetate recovery	324.71
Chloroform	1,610.01	Ethyl acetate loss	20.29
Ethyl acetate	345.00	Organic residue impurities	54.12
		Stage-IV	109.59

IN 2,589.55 | OUT 2,589.55 kg — **DIFF +0.00 kg**

STAGE 5 | Reaction > Salt formation > Filtration > Purification > Drying

MATERIAL IN (kg)		MATERIAL OUT (kg)	
Stage-IV	109.59	Inorganic salt	139.73
4-(4-chloro phenyl) piperidin-4-ol	71.23	Methyl isobutyl ketone Recovery	1,952.05
Sodium carbonate	131.51	Methyl isobutyl ketone Loss	102.74
Methyl isobutyl ketone	2,054.79	Isopropyl alcohol recovery	54.79
Hydrochloric acid solution in isopropyl alcohol	65.75	Ethyl acetate	739.73
Ethyl acetate	780.82	Ethyl acetate	41.10
		Organic Residue Impurities	42.47
		Loperamide Hydrochloride	100.00

IN 3,213.69 | OUT 3,172.61 kg — **DIFF -41.08 kg**

DATA REVIEW / RECONCILIATION NOTES

01 STAGE 5: 41.08 kg OUTPUT SHORTFALL
Itemised output 3,172.61 kg vs. input 3,213.69 kg; source reported output 3,213.70 kg.

02 STAGE 1 TOTALS DIFFER
Itemised input 3,398.45 kg; reported input 3,398.47 kg. Itemised output 3,398.46 kg; reported output 3,398.50 kg.

03 STAGE 3 & 4 ROUNDING / TOTALS
Stage 3 itemised output 472.24 kg vs. reported 472.20 kg; Stage 4 output 2,589.55 kg vs. 2,589.60 kg.

04 SOURCE FORMULAS ARE BROKEN
Per-kg output columns and Summary distillation rows contain #REF! errors; no per-kg results assumed.

05 BATCH REFERENCE IS NOT FINAL OUTPUT
Summary shows 500 kg batch reference; detailed final Stage 5 reports 100 kg. Basis requires confirmation.

06 DISPOSITION / IDENTIFICATION
Stage 5 ethyl acetate entries 739.73 kg and 41.10 kg have the same label; recovery or loss classification is not explicit.

SOURCE BASIS & INTERPRETATION

Detailed mass-balance totals are stage-level sums, NOT a single fresh-charge batch mass; intermediate outputs become inputs in later stages.
The original spreadsheet values are retained for illustration. Reported values, itemised values and broken formula cells require owner QA review.

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