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

EMPAGLIFLOZIN API

MASS BALANCE | RAW MATERIALS, PROCESS FLOW & OUTPUTS

All worksheets reviewed · Source values preserved · One-page A2 technical illustration

FOR TECHNICAL REVIEW

Source: 7- EMPAGLIFLOZIN.xlsx

Summary + EMPAGLIFLOZIN worksheets

SUMMARY BATCH REFERENCE	DETAILED FINAL API	DETAILED MASS BALANCE	STAGE 1 RECORDED DIFFERENCE
500 kg	100.00 kg	3 stages	≈ 300 kg
Summary sheet; basis unconfirmed	Stage 3: Empagliflozin	Summary additionally lists Stage 4	Reported total vs itemised charges

MANUFACTURING PROCESS FLOW

Recorded stages, operations and inter-stage product streams

01 STAGE 1
Reaction • extraction • distillation
1,642.86 kg to Stage 2

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02 STAGE 2
Reaction • separation • crystallisation
500 kg transfer (mislabelled)

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03 STAGE 3
Reaction • separation • purification
100.00 kg final API

STAGE 01 REAGENTS / STAGE 1 INTERMEDIATE

Reaction, extraction, separation & solvent recovery

INPUT / CHARGES • 7 entries	kg
3-{4-[(2-Chloro-5-iodo-phenyl)-methoxy-methyl]-phenoxy}-tetrahydro-furan	714.29
2,3,4,6-tetra-O-trimethylsilyl-D-gluconolactone	1,107.14
Tetrahydrofuran	8,571.43
n-BuLi (2.5 M solution in hexane)	1,785.71
Ammonium chloride (10% solution in water)	2,142.86
Ethyl Acetate	7,142.86
Sodium chloride (10% solution in water)	2,142.86

OUTPUTS / RECOVERIES • 8 entries	kg
Effluent water with inorganic salt	4,821.43
tetrahydrofuran recovery	8,142.86
tetrahydrofuran loss	428.57
Hexane recovery	1,357.14
Hexane loss	71.43
Ethyl acetate recovery	6,785.71
Ethyl acetate loss	357.14
Stage -2	1,642.86

ITEMISED INPUT 23,607.15 kg — OUTPUT 23,607.14 kg

Difference (output - input) -0.01 kg

STAGE 02 TRANSFORMATION / STAGE 2 INTERMEDIATE

Reaction, salt/work-up, crystallisation, filtration

INPUT / CHARGES • 8 entries	kg
Stage-1	1,642.86
Methane sulfonic acid	214.29
Methanol	12,142.86
Sodium carbonte (10% solution in water)	1,428.57
Ethyl acetate	21,428.57
Water	10,714.29
Sodium chloride (10% solution in water)	10,714.29
hydrochloric acid solution in isopropyl alcohol	3,571.43

OUTPUTS / RECOVERIES • 9 entries	kg
Effluent water with inorganic salt	23,650.00
Methanol Recovery	11,535.71
Methanol Loss	607.14
Ethyl acetate Recovery	20,357.14
Ethyl acetate Loss	1,071.43
Cyclohexane Recovery	3,392.86
Cyclohexane Loss	178.57
Organic Residue Impurities	564.29
Stage-1	500.00

ITEMISED INPUT 61,857.16 kg — OUTPUT 61,857.14 kg

Difference (output - input) -0.02 kg

STAGE 03 FINAL API / PURIFICATION

Reaction, extraction, crystallisation & drying

INPUT / CHARGES • 9 entries	kg
Stage-II	500.00
Acetonitrile	5,000.00
Methylene dichloride	5,000.00
Triehylsilane	425.00
Boron triflouride etherate	300.00
Sodium carbonte (10% solution in water)	10,000.00
Ethyl acetate	10,000.00
Sodium chloride (10% solution in water)	10,000.00
Isopropyl acetate	6,000.00

OUTPUTS / RECOVERIES • 11 entries	kg
Effluent water with inorganic salt	20,785.00
Acetonitrile Recovery	4,750.00
Acetonitrile Loss	250.00
Methylene dichloride Recovery	4,750.00
Methylene dichloride Loss	250.00
Ethyl acetate Recovery	9,500.00
Ethyl acetate Loss	500.00
Isopropyl acetate Recovery	5,700.00
Isopropyl acetate Loss	300.00
Organic Residue Impurities	340.00
Empagliflozin	100.00

ITEMISED INPUT 47,225.00 kg — OUTPUT 47,225.00 kg

Difference (output - input) +0.00 kg

SOURCE VERIFICATION / GMP RECONCILIATION

REQUIRES SOURCE CORRECTION

01 STAGE 1 TOTALS
Recorded Stage 1 input/output: 23,907.1 kg each. Itemised amounts: input 23,607.15 kg; output 23,607.14 kg. Approx. 300 kg not explained.

02 STAGE 2 ROUNDING
Stage 2 reported output 61,857.20 kg; itemised 61,857.14 kg. Itemised input is 61,857.16 kg, producing a 0.02 kg shortfall.

03 SOLVENT IDENTITY
Stage 2 charges HCl solution in isopropyl alcohol (3,571.43 kg), but lists cyclohexane recovery/loss totalling the same 3,571.43 kg. Confirm identity.

04 STAGE / STREAM LABELS
Summary lists Stage 4 but no detailed Stage 4. Stage 2 500 kg output is labelled “Stage-1”; Stage 3 input is “Stage-II”. Verify transfers.

05 FORMULA / SCALE
Summary contains #REF! cells. Summary batch size is 500 kg while detailed final API is 100 kg. Confirm calculation and scale basis.

Source: 7- EMPAGLIFLOZIN.xlsx | Detailed data: EMPAGLIFLOZIN worksheet | Summary provides 500 kg batch reference and additional Stage 4 heading.

Technical reference only. Source text/spelling preserved; do not use as an approved GMP batch record until stage totals, stream identities, formula errors and batch basis are verified.

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