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

CANAGLIFLOZIN

API MASS BALANCE / FOUR-STAGE PROCESS

Client workbook review | Stage-wise charges, recoveries, intermediate transfers and reconciliation

01 REACT · 02 SEPARATE · 03 RECOVER · 04 DRY

BATCH SIZE - SUMMARY	FINAL API - DETAILED SHEET	MANUFACTURING STAGES	STAGE 4 OUTPUT-ROW GAP
500 kg	100.00 kg	04	35.20 kg

01 STAGE 1

Reaction / separation / THF-hexane recovery

CHARGED INPUTS / kg	3,040.01
2-(4-Fluoro-phenyl)-5-(5-iodo-2-methyl-benzyl)-thiophene	180.95
2,3,4,6-tetra-O-trimethylsilyl-D-gluconolactone	255.14
Tetrahydrofuran (THF)	1,357.15
(trimethylsilyl) methyl lithium (1 M solution in hexane)	884.86
Sodium bicarbonate (10 solution in water)	361.91

RECOVERIES / OUTPUTS / WASTE / kg	
Aqueous effluent / inorganic salts	554.62
THF recovery	1,289.29
THF loss	67.86
Hexane Recovery	756.39
Hexane Loss	39.81
Organic residue / impurities	33.48
Stage-1	298.57

WORKBOOK RECORDED TOTALS
In: 3,040.01 kg Out: 3,040.03 kg

02 STAGE 2

Reaction / extraction / EDC-ethyl acetate

CHARGED INPUTS / kg	3,228.98
Stage-1	298.57
Ethylene dichloride	900.87
Triethylsilane	169.88
Boron trifluoride etherare (source)	122.26
Water	1,029.57
Ethyl Acetate	386.09
Sodium bicarbonate (10 solution in water)	321.74

RECOVERIES / OUTPUTS / WASTE / kg	
Aqueous effluent / inorganic salts	1,764.80
Ethylene dichloride Recovery	855.83
Ethylene dichloride Loss	45.04
Ethyl Acetate Recovery	366.78
Ethyl Acetate Loss	19.30
Organic residue / impurities	24.07
Stage-2	153.15

WORKBOOK RECORDED TOTALS
In: 3,228.98 kg Out: 3,228.97 kg

03 STAGE 3

Reaction / recovery / filtration / drying

CHARGED INPUTS / kg	4,365.65
Stage-2	153.15
4-methyl morpholine	186.61
DMAP	4.18
Tetrahydrofuran (THF)	1,608.70
Acetic anhydride	160.87
Phosphoric acid (10% solution in water)	386.09
Ethyl acetate	900.87
Toluene	321.74
Sodium bicarbonate (10% solution in water)	321.70
Methanol	321.74

RECOVERIES / OUTPUTS / WASTE / kg	
THF recovery	1,525.04
THF loss	83.65
Acetic acid Recovery	102.96
Aqueous effluent / inorganic salts	942.05
Ethyl acetate Recovery	855.83
Ethyl acetate Loss	45.04
Toluene Recovery	305.65
Toluene Loss	16.09
Methanol Recovery	305.65
Methanol Loss	16.09
Organic residue / impurities	19.63
Stage-3	148.00

WORKBOOK RECORDED TOTALS
In: 4,365.65 kg Out: 4,365.68 kg

04 STAGE 4

Reaction / extraction / solvent recovery

CHARGED INPUTS / kg	2,673.06
Stage-3	148.00
Tetrahydrofuran (THF)	656.00
Methanol	984.00
Lithium Hydroxide	5.06
Ethyl Acetate	680.00
Sodium chloride (30% solution in water)	200.00

RECOVERIES / OUTPUTS / WASTE / kg	
THF recovery	624.00
THF loss	32.00
Methanol Recovery	934.80
Methanol Loss	49.20
Aqueous effluent / inorganic salts	253.06
Ethyl Acetate Recovery	646.00
Ethyl Acetate Loss	34.00
Organic residue / impurities	35.20
Canagliflozin	100.00

WORKBOOK RECORDED TOTALS
In: 2,673.06 kg Out: 2,673.10 kg

05 STAGE MASS BALANCE RECONCILIATION

Stage	Input (kg)	Output (kg)	Rows out (kg)	Rows diff.	In-Out
1	3,040.01	3,040.03	3,040.02	-0.01	-0.02
2	3,228.98	3,228.97	3,228.97	0.00	+0.01
3	4,365.65	4,365.68	4,365.68	0.00	-0.03
4	2,673.06	2,673.10	2,708.26	+35.16	-0.04

CRITICAL STAGE 4: REPORTED OUTPUT EXCLUDES A LISTED WASTE STREAM
Listed Stage-4 outputs sum to 2,708.26 kg vs recorded total 2,673.10 kg; 35.20 kg organic residue is present but appears omitted from the total.

06 STAGE TRANSFERS & STREAM TOTALS

Stage 1 298.57 kg › Stage 2 153.15 kg › Stage 3 148.00 kg › Final API 100.00 kg

Recorded solvent / acid recoveries	8,568.22 kg
Recorded solvent losses	448.08 kg
Aqueous effluent streams	3,514.53 kg
Organic residue streams	112.38 kg

Summary Total Volume (unit unstated): 3,040.03 / 1,491.58 / 343.94 / 1,640.00

07 SOURCE REVIEW / REQUIRED GMP CHECKS

01 Summary batch = 500 kg; detailed final API = 100 kg. Confirm the basis.
02 Stage 4: 35.20 kg organic residue is excluded from recorded total.
03 Several quantity-per-kg cells show #DIV/0! (Stages 2-4).
04 Stage 1 listed output sum differs slightly from recorded total (rounding).
05 Material names and stage yields require batch-record verification.

NOT AN APPROVED GMP BATCH RECORD
Verify charges, recovery basis, formulas and independent QA sign-off.

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info@ishasgmp.com • +91 86675 89984
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