MASTER FORMULA RECORD

Product Name: Fluorouracil Injection BP 50 mg/ml (500mg/10ml)

MFR No.	Revision no.	Supersedes No.	Effective Date	Review date
FU/MFR/002	03	02	05/02/2025	04/01/2027

MASTER FORMULA RECORD

	PREPARED BY	CHECKED BY	APPROVED BY	AUTHORIZED BY
NAME	Sachin kumar	Vikas Kumar	Harpinder Singh	Akhil Sharma
DESIGNATION	Sr. Officer	Executive	Asst. Manager	Dy. Manager
SIGNATURE				
DATE	05/02/2025	05/02/2025	05/02/25	05/02/25

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1.0 Product Information:

Each ml contains:

Fluorouracil BP 50 mg

Water For Injection BP q. s.

Description of Solution	A clear Colourless solution.
Packing Presentation:	A clear colourless solution filled 10 ml Clear colour moulded glass vial USP type -1st, stoppered with 20 mm non slotted Bromo butyl rubber plug and 20 mm Aluminum Flip off Seal having Blue Colour.
Storage Condition	Store below 25°C. Protect from light. Do not Refrigerate
Shelf Life:	36 Months
Market:	Export
Mfg License No.:	BNZ/08/41
Neutral Code:	HP/DRUGS/08/40-41
Category of drug	Cytotoxic
Batch Manufacturing Record No.:	FU/MFR/002
PH Limit:	8.5 to 9.1
Assay Limit:	90.0% to 110.0%

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2.0 MFR Index:

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3.0 List of Equipment's and Instruments:

Sr. No	Equipment Name	Make	Equipment Id. No.
1.	Sampling & Dispensing Isolator	Klenzide	KPL/WH/013
2.	Reverse Laminar Air Flow	New Brehz Engineering Works	KPL/WH/005
3.	Weighing Balance	A & D company Limited	KPL/WH/006
4.	Vial washing machine	Kailas machine tools	KPL/CI/010
5.	Bung Washing Machine	Parth Engineering	KPL/CI/011
6.	Homogenizer	IKA	KPL/CI/017
7.	Pressure Vessel –I	————	KPL/CI/018
8.	Pressure Vessel –II	————	KPL/CI/019
9.	Pressure Vessel –III(Jacketed)	————	KPL/CI/020
10.	Pressure Vessel –IV	————	KPL/CI/021
11.	SS 316 Membrane Holder-I	————	KPL/CI/022
12.	SS 316 Membrane Holder-II	————	KPL/CI/023
13.	SS 316 Membrane Holder-III	————	KPL/CI/024
14.	Automatic Vial Filling Machine	Keshav Pharmapack	KPL/CI/025
15.	Sealing machine	Keshav Pharmapack	KPL/CI/026
16.	Rotary Evaporator	IKA	KPL/CI/027
17.	Cold Room	Blue Star	KPL/CI/028
18.	Bubble point tester	Pall life science	KPL/CI/029
19.	Compounding Isolator	Klenzaids	KPL/CI/030
20.	Lyophilizer-I	Lyophilization System India	KPL/CI/031
21.	Lyophilizer-II	Lyophilization System India	KPL/CI/032
22.	Manufacturing Tank –I	Komal	KPL/CI/033
23.	Manufacturing Tank –II	Komal	KPL/CI/034
24.	Fogger	————	KPL/CI/035
25.	Three bucket system	————	KPL/CI/036
26.	Vacuum pump	————	KPL/CI/039
27.	Closer Processing System Cum HPHV	Machin Fabrik	KPL/CI/040
28.	Dynamic Pass Box –I	P.S. Air Technology	KPL/CI/041
29.	Dynamic Pass Box –II	P.S. Air Technology	KPL/CI/042

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Sr. No	Equipment Name	Make	Equipment Id. No.
30.	Dynamic Pass Box –III	P.S. Air Technology	KPL/CI/043
31.	Dynamic Pass Box –IV	P.S. Air Technology	KPL/CI/044
32.	Dynamic Pass Box –V	P.S. Air Technology	KPL/CI/045
33.	Dynamic Pass Box –VI	P.S. Air Technology	KPL/CI/046
34.	Dynamic Pass Box –VII	P.S. Air Technology	KPL/CI/047
35.	Dynamic Pass Box –VIII	P.S. Air Technology	KPL/CI/048
36.	Mobile Trolley- I	P.S. Air Technology	KPL/CI/049
37.	Mobile Trolley-II	P.S. Air Technology	KPL/CI/050
38.	Sterile garments cubicle -I	_____	KPL/CI/051
39.	Sterile garments cubicle -II	_____	KPL/CI/052
40.	Laminar Air Flow	P.S. Air Technology	KPL/CI/053
41.	Particle Counter	Shreedhar instruments	KPL/CI/054
42.	Laminar Air Flow	P.S. Air Technology	KPL/CI/055
43.	Laminar Air Flow	P.S. Air Technology	KPL/CI/056
44.	Laminar Air Flow	P.S. Air Technology	KPL/CI/057
45.	Laminar Air Flow	P.S. Air Technology	KPL/CI/058
46.	Laminar Air Flow	P.S. Air Technology	KPL/CI/059
47.	Laminar Air Flow	P.S. Air Technology	KPL/CI/060
48.	Laminar Air Flow	P.S. Air Technology	KPL/CI/061
49.	Laminar Air Flow	P.S. Air Technology	KPL/CI/062
50.	SS Membrane holder	_____	KPL/CI/066
51.	Housing filter	_____	KPL/CI/067
52.	Table Mount LAF	_____	KPL/CI/074
53.	Laminar Air Flow	P.S. Air Technology	KPL/CI/075
54.	Dry Heat Sterilizer	Machine Fabrik	KPL/CI/076

4.0 PROCESS FLOW DIAGRAM

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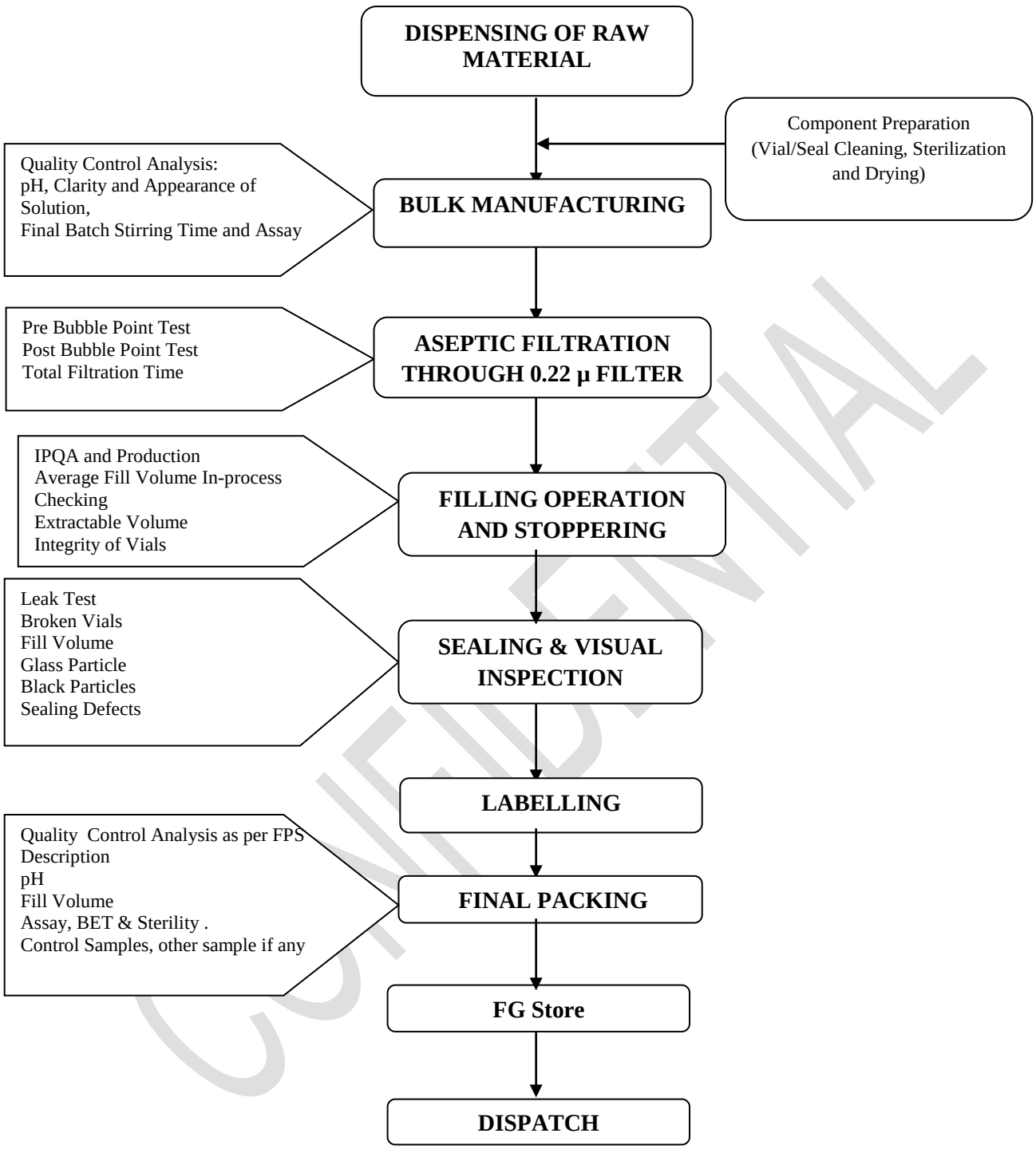

5.0 Calculation Sheet:

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Sr. No.	Active Ingredients	A.R. No.	Assay %	LOD/ Water	Checked by
1	Fluorouracil BP				

Quantity of Fluorouracil for batch (In gm) =

$$\frac{100 \times \text{Label Claim (mg per vial)} \times \text{Batch Size (in vial)} \times \text{Factor} \times 100}{\text{Potency} \times 1000 \times (100 - \text{LOD})} = \text{gm}$$

Calculation: $\frac{100 \times \quad \times \quad \times 100}{\quad \times 1000 \times (100 - \quad)} = \_\_\_\_\_$ gm

Calculated by Production (Sign & Date)	**Checked by Store (Sign & Date)**	**Checked by Production Head (Sign & Date)**	**Approved by Head QA (Sign & Date)**

Standard Batch Formulation:

Sr. No.	Ingredient	Specification	Item Code	Label claim per ml	Quantity for 500 vials
1.	Fluorouracil	BP	AC/130R	50.00 mg	250.0 gm
2.	Disodium Edetate	BP	E/0216	1.00 mg	5.000 gm
3.	Tromethamine	BP	E/0228	84.00 mg	420.00 gm
4.	Sodium hydroxide	BP	E/0157	6.00 mg	30.00 gm
5.	Sodium hydroxide	BP	E/0157	q. s. to pH adjust	q. s. to pH adjust
6.	Water for Injection	BP	E/0084	q.s to 1.0 ml	q. s. to 5.0 Liters

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6.0 Dispensing Sheet:

Sr. No.	Item codes	Ingredients & Specification	Qty. Each ml	Std Qty. in gm for 500 vial	Overage	Qty. Required	Vendor Name	A. R. No.	Dispensed quantity			Dispensed By (Store)	Checked By (Prod.)	Verified By (QA)
									Gross Wt.	Tare Wt.	Net Wt.			
1.	AC/130 R	Fluorouracil	50.00 mg	250.0 gm	NIL									
2.	E/0216	Disodium Edetate	1.00 mg	5.000 gm	NIL									
3.	E/0228	Tromethamine	84.00 mg	420.00 gm	NIL									
4.	E/0157	Sodium hydroxide	6.00 mg	30.00 gm	NIL									
5.	E/0157	Sodium hydroxide	q. s. to pH adjust	q. s. to pH adjust	NIL									
6.	E/0084	Water for Injection	q.s to 1.0 ml	q. s. to 5.0 Liters	NIL									

6.2 Primary Packing Materials:

Sr. No.	Item codes	Name of Materials	Overage	Qty. Required	Vendor Name	Dispensed quantity	A. R. No.	Dispensed By (Store)	Checked By (Prod.)	Verified By (QA)
1.	P/V/002	____ ml clear glass vial USP type-1st								
2.	P/S/006	20 mm Gray Bromo Butyl rubber stopper								
3.	P/S/008	20mm Flip-off seal having _____ colour								

* Refer approved QBD for detail of primary packaging material as per customer requirement.

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6.3 All In process auto print generated should be attached With Sign/Date:

- Dispensing Slip & Label
- RM COA
- PM COA
- Isolator generated print
- In process reports & Rinse/Swab
- QB

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7.0 Manufacturing Process:

7.1 MANUFACTURING

Room Name	Compounding Area	Room ID	RO/FF/CI/023
Equipment Name	Compounding Isolator	Equipment ID:	KPL/CI/030

Instructions:

1. Setup and operate the equipment's as per SOP. No. CI043
2. All the workers should wear protective cloth, dust mask and gloves while handling raw materials as per SOP.No.CI001.
3. Care should be taken at every stage to avoid extraneous matter getting into the products per SOP. No. QA017.
4. Check the name of the Product and Batch No. written on each dispensing label of each material. Put a tick mark against the name of the Product and Batch No. on the tag per SOP.No.QA004.

Batch Manufacturing Procedure: -

Sr. No.	Procedure	Time		Done By Sign./Date	Checked By Sign./Date	Verified by Sign/Date
		From	To			
1	Take freshly collected Water for Injection _____Liters in dry and cleaned sterile S.S. manufacturing tank and cool at temperature between 30ºC - 40ºC with Continue nitrogen purging throughout the compounding process.					
2	Now transfer Disodium Edetate_____ gm in manufacturing tank with continues stirring until a clear solution is obtained and check the clarity of the solution.					
3	Now add Tromethamine_____ gm in manufacturing tank with continues stirring and clear the solution.					
4	Stir the solution for 20 minutes and check the complete dissolution and clarity of the solution.					
5	Add fluorouracil_____ gm in manufacturing tank and continue stirring to disperse it completely.					
6	Now add sodium hydroxide _____ gm slowly in manufacturing tank under continues stirring and stir the solution to obtain clear solution.					
7	Check the pH of the solution in between 8.6-9.0. If required adjust the pH of solution with sodium					

	hydroxide.					
8	Make up the final batch volume_____ liters with water for injection.					
9	Send the Sample to QC for chemical analysis (Attach the bulk report in the BMR). If results found within limit than proceed further process.					

Note:
Remarks:

CPP and CQA for Batch Manufacturing:

Critical Parameter Process (CPP)	Critical Quality Attributes (CQA)	Specifications
Quality of WFI for Bulk- manufacturing	Description	A clear colourless solution filled in 10 ml clear moulded glass vial USP Type – I.
	pH	Between 8.5 to 9.1
	Conductivity (100 ml)	NMT 1.3 µS/cm^2
	BET (10ml)	NMT 0.33 EU/ml
	Bioburden (100 ml)	10 CFU/100ml
Mixing speed (RPM) & Time	Description	A clear colourless solution filled in 10 ml clear moulded glass vial USP Type – I.
	Assay	90.0 % to 110.0 %
	pH	Between 8.5 to 9.1

8.0 Filtration of Solution: (Reference SOP No. CI041)

Room Name	Filtration room	Room ID	RO/FF/CI/33
Equipment Name	SS 316 Membrane Holder-I	Equipment ID:	KPL/CI/022
	SS 316 Membrane Holder-II		KPL/CI/024

CPP and CQA for Filtration Process:

Critical Parameter Process (CPP)	Critical Quality Attributes (CQA)	Specifications
Bulk Filtration	Filters	0.22 micron Nylon filter
	Nitrogen pressure during filtration	1.0 to 2.5 Kg/cm^2

9.0 Filling of vials:

S. No.	Parameter	Standard	Frequency of Check
1.	Appearance	Clear Colourless Solution	At Starting
2.	Fill Volume	NLT 10.0 ml	Initial and Every One Hour Production Initial and Every Two Hours QA
4.	LAF	Pressure Limit (0-25 mm/wc)	Initial and Every One Hour Production Initial and Every Two Hours QA

CPP and CQA for Filling Stage:

Critical Parameter Process (CPP)	Critical Quality Attributes (CQA)	Specifications
Filling Parameters	Speed of filling m/c	40-60 vials/min
	Pre nitrogen flow	1.0 to 2.5 $Kgcm^2$
	Post nitrogen flow	1.0 to 2.5 $Kgcm^2$
	Fill volume at minimum filling speed	NLT 10.0 ml
	Fill volume at maximum filling speed	NMT 10.0 ml
	Assay	90.0 % to 110.0 %
	pH	Between 8.5 to 9.1
	Sterility	No growth should be observed

10.0 Sealing of Vials:

CPP and CQA of Sealing Stage:

Critical Parameter Process (CPP)	Critical Quality Attributes (CQA)	Specifications
Sealing Parameters	Sealing Speed	40-60 vials/min.
	Leak Test	Should be Complies

11.0 Abbreviation:

Sr. No.	Abbreviation:	Full Form
1.	QA	Quality Assurance
2.	USP	United State Pharmacopoeia
3.	DHS	Dry Heat Sterilizer
4.	BMR	Batch Manufacturing Record
5.	MFR	Master Formula Record
6.	NA	Not Applicable
7.	RFU	Ready For Use
8.	IPQA	In Process Quality Assurance
9.	NF	National Formulary
10.	PC	Paclitaxel
11.	PP	Primary Packing
12.	API	Active Pharmaceutical Ingredient
13.	RM	Raw Material
14.	BET	Biological Endotoxins tests
15.	QC	Quality Control
16.	SOP	Standard Operating Procedure
17.	A.R. No.	Analytical Report Number