



KWALITY PHARMACEUTICALS LIMITED

1-A, INDUSTRIAL AREA, RAJA KA BAGH, TEHSIL NURPUR,
KANGRA-176201 (INDIA)

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PROCESS VALIDATION PROTOCOL

PRODUCT NAME: Gemcitabine for Injection USP 200mg/ vial

PROTOCOL NO.: GM/PVP/001-00

Supersedes No.: 00

Effective Date

05/02/21

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PROCESS VALIDATION PROTOCOL

PRODUCT NAME

GEMCITABINE FOR INJECTION

USP 200 mg / VIAL

STANDARD BATCH SIZE

5.0 Liters

PROTOCOL NO.

GM/PVP/001-00



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1. PROTOCOL APPROVAL

Signing of this approval page of process validation Protocol No. GM/PVP/001-00 indicates agreement with the Process Validation Approach described in this document. Any modification to the process validation will be prepared and approved as an addendum.

Prepared By

Name	Designation	Signature	Date
Vinayak Kanshal	Officer QA		05/02/21

Checked By

Name	Designation	Signature	Date
Harpinder Singh	Mfg. Chemist		05/02/21
Naresh Kumar	Head QC		05/02/21
B. B. Pandey	Manager Engg		05/02/21

Approved By

Name	Designation	Signature	Date
SURAJ GIR	Executive-QA		05/02/21

Authorized By

Name	Designation	Signature	Date
N. P Mishra	Head QA		05/02/21



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2. OBJECTIVE:

To conduct the process validation of the manufacturing process for the **Gemcitabine for Injection USP 200mg / vial** manufactured at Cytotoxic Injection block. The validation study shall be conducted for the generation of sufficient data to establish documentary evidence and to provide assurance that the product can be manufactured on a commercial scale, meeting all its quality attributes in a consistent manner.

3. SCOPE:

This protocol shall be applicable for first three consecutive batches manufactured with specific batch size and equipment and operating parameters for the **Gemcitabine for Injection USP 200mg/ vial** at Kwality Pharmaceuticals Limited Raja Ka Bagh.

4. VALIDATION APPROACH:

The validation approach shall be prospective and following things shall be reviewed:

- 4.1 Review the qualification documents of equipment and related utility systems which shall be employed for the manufacturing of batch.
- 4.2 Review the Analytical method validation.
- 4.3 Review the calibration record of instruments used in validation.
- 4.4 Review the master formula records.
- 4.5 Review the specification and analytical procedures of raw materials and packing materials.
- 4.6 Review the specification and analytical procedures for in-process & finished products.

5. REASON FOR VALIDATION:

Process Validation shall be carried out due to modification in equipments.

6. REVALIDATION:

The manufacturing process is subjected to revalidation when following changes occur.

- 6.1 When change in quantity and change in Excipients
- 6.2 Any Change in batch size
- 6.3 Change in master formula.
- 6.4 Change in manufacturing site
- 6.5 Any modification in any critical equipment
- 6.6 Any change in the specification and change in the source of active Pharmaceuticals Ingredient.
- 6.7 Any change in primary packing material
- 6.8 Any major change in the manufacturing process which may affect the quality of the product.



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7. RESPONSIBILITY :

Following validation team is responsible for carrying out the process validation.

7.1 Quality Assurance shall be responsible for:

- Preparation, approval and training of validation protocol, review of the data compiled, review of deviations (if any), monitoring the process as per the process parameters and for withdrawal of validation samples.
- Review of facility, equipment qualification and utility validation reports.
- cGMP compliance during the manufacturing process, review and evaluation of the data/results generated during the validation process.
- Preparation of process validation summary report, review and its approval.

7.2 Production shall be responsible for:

- To execute the batches as per the batch production record and process validation protocol.
- Compilation of data related to manufacturing area and furnishing the same for review.
- Review of protocol and summary report.

7.3 Quality Control shall be responsible for:

- Raw material and packing material analysis
- In process and finished product samples analysis as per the sampling plan.
- Collection and review of in process and finished product analysis data.
- Submission of data /results to QA for review and evaluation.



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8. Product & Batch Detail:

Process Validation of **Gemcitabine for Injection USP 200mg/ vial** shall be carried out on any three consecutive batches. The details are as under:

Product/ Generic Name	:	Gemcitabine for Injection
Strength	:	200 mg/vial
Product Code	:	GM/001
Batch Size	:	5.0 Liters
Dosage Form	:	Sterile lyophilized Injection
Composition	:	Each vial contains: Gemcitabine Hydrochloride USP Eq. to Gemcitabine 200mg Excipients q.s.
Packing Detail	:	A white colour lyophilized cake filled in 10ml clear molded vial USP type -1 Glass vial, stoppered with 20mm slotted Bromo butyl rubber plug and 20mm Aluminum Flip off seal having red grain color.
Storage Condition	:	Store below 25°, Protect from light.

Batch Detail for validation

3 consecutive batches are selected

Sr. No.	Batch No.	Batch Size	Batch Manufacturing Date	Mfg. Date	Exp. Date
1.					
2.					
3.					



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9. Equipment and Machinery List

9.1 Production Equipment

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.	Refrigerator 2 -8 °C	_____	KPL/WH/009
4.	Weighing Balance	A & D company Limited	KPL/WH/006
5.	Vial Washing Machine	Kailas machine tools	KPL/CI/010
6.	Dry Heat Sterilizer	_____	KPL/CI/012
7.	Closer Processing System cum HPHV	Machin Fabrik	KPL/CI/040
8.	Compounding Isolator	Klenzide	KPL/CI/030
9.	Manufacturing Tank	Komal	KPL/CI/033
10.	Bubble Point	Pall Life Science	KPL/CI/029
11.	Filling Tank	_____	KPL/CI/005
12.	Automatic Vial Filling and stopering machine	Parth Engineering	KPL/CI/025
13.	Pressure vessel	_____	KPL/CI/019
14.	Vial Sealing Machine	Parth Engineering	KPL/CI/005
15.	Visual Inspection Table	_____	KPL/CI/001
16.	Labeling & Coding machine	Parth Engineering	KPL/CI/002
17.	Dynamic Pass Box -VIII	PS Air technology	KPL/CI/048
18.	Dynamic Pass Box -II	PS Air technology	KPL/CI/042
19.	Dynamic Pass Box -I	PS Air technology	KPL/CI/041
20.	Dynamic Pass Box -V	PS Air technology	KPL/CI/045
21.	Dynamic Pass Box -VI	PS Air technology	KPL/CI/046
22.	Mobile Trolley	PS Air technology	KPL/CI/049
23.	Mobile Trolley	PS Air technology	KPL/CI/050
24.	Sterile Garment Cubicle	_____	KPL/CI/051
25.	Sterile Garment Cubicle	_____	KPL/CI/052
26.	Vial Washing Area LAF	PS Air technology	KPL/CI/055



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Sr. No	Equipment Name	Make	Equipment Id. No.
27.	Filtration LAF	PS Air technology	KPL/CI/056
28.	Cooling Zone LAF	PS Air technology	KPL/CI/057
29.	Vial Filling & Stoppering Machine LAF	PS Air technology	KPL/CI/058
30.	Sealing Area LAF	PS Air technology	KPL/CI/059
31.	Non Viable Particle counter	Sridhar Instruments	KPL/CI/054
32.	Lux Meter	HTC	KPL/ENG/017
33.	pH Meter	Lab India	KPL/CI/060
34.	Lyophilizer – 1 st	Lyophilization system India	KPL/CI/031
35.	Lyophilizer – 2 nd	Lyophilization system India	KPL/CI/032

9.2 Engineering Equipment

Sr. No	Equipment Name	Make	Equipment Id. No.
36.	Purified Water system	Komal	KPL/ENG/014
37.	Water for Injection System	Komal	KPL/ENG/015
38.	Pure steam System	Komal	KPL/ENG/016
39.	Compressed Air System	Ingersoll Rand	KPL/ENG/001
40.	Nitrogen System	Allied Air and gas Engineers	KPL/ENG/007
41.	Air Handling Unit	ZECO	AHU/HAC02/CI/001
42.	Air Handling Unit	ZECO	AHU/HAC02/CI/004
43.	Air Handling Unit	ZECO	AHU/HAC02/CI/005
44.	Air Handling Unit	ZECO	AHU/HAC02/CI/006
45.	Air Handling Unit	ZECO	AHU/HAC02/CI/007
46.	Air Handling Unit	ZECO	AHU/HAC02/CI/008
47.	Air Handling Unit	ZECO	AHU/HAC02/CI/009
48.	Air Handling Unit	ZECO	AHU/HAC02/CI/010
49.	Air Handling Unit	ZECO	AHU/HAC02/CI/011



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9.3 Quality Control Instrument

Sr. No	Equipment Name	Make	Equipment Id. No.
50.	High Performance Liquid Chromatography	Shimadzu 2030	KPL/QC/105
51.	High Performance Liquid Chromatography	Shimadzu 2030	KPL/QC/053
52.	Weighing Balance	Shimadzu	KPL/QC/054

10. Raw Material Sheet:

Batch Size: 5.0 Liters

Name of Ingredients	Specifications	Std. Qty per vial.	O.A (%)	Qty required for Batch (in gm)
Gemcitabine Hydrochloride	USP	200.0 mg	NIL	200.00 gm
Mannitol	BP	200.0 mg	NIL	200.00 gm
Sodium Acetate	USP	12.5 mg	NIL	12.5 gm
Sodium Hydroxide	BP	1.0 mg	NIL	1.00 gm
Hydrochloric Acid	BP	For pH Adjustment	NIL	For pH Adjustment
Water for Injection	USP	5.0 ml	NIL	5.0 liters

11. Approved Raw and Packing Material:

The raw or packing material uses in manufacturing process are from approved vendor.

Raw Material:

Raw Material	Spec.	Item Code	Vendor
Gemcitabine Hydrochloride	USP	AC/092R	Aspen Biopharma Labs Pvt Ltd.
Mannitol	BP	E/0192	Qingdao Bright Moon Seaweed Group Co. Ltd
Sodium Acetate	USP	E/0141	Avarice Quality Delivered
Sodium Hydroxide	BP	E0157	Avarice Quality Delivered
Hydrochloric Acid	BP	E/0029	Bright way Store
Water for Injection	USP	E/0087	In House

Packing Material:

Packing material	Spec.	Item Code	Vendor
10 ml clear moulded Glass vial USP Type I	IHS	P/V/001	S.GD Pharma India Ltd.
20 mm Bromo butyl slotted Rubber Stopper	IHS	P/S/004	Bharat Rubber Works Pvt Ltd.
20 mm Flip Top Red Grain Finish Aluminium Seal.	IHS	P/F/001	Shakai Packing Private Limited



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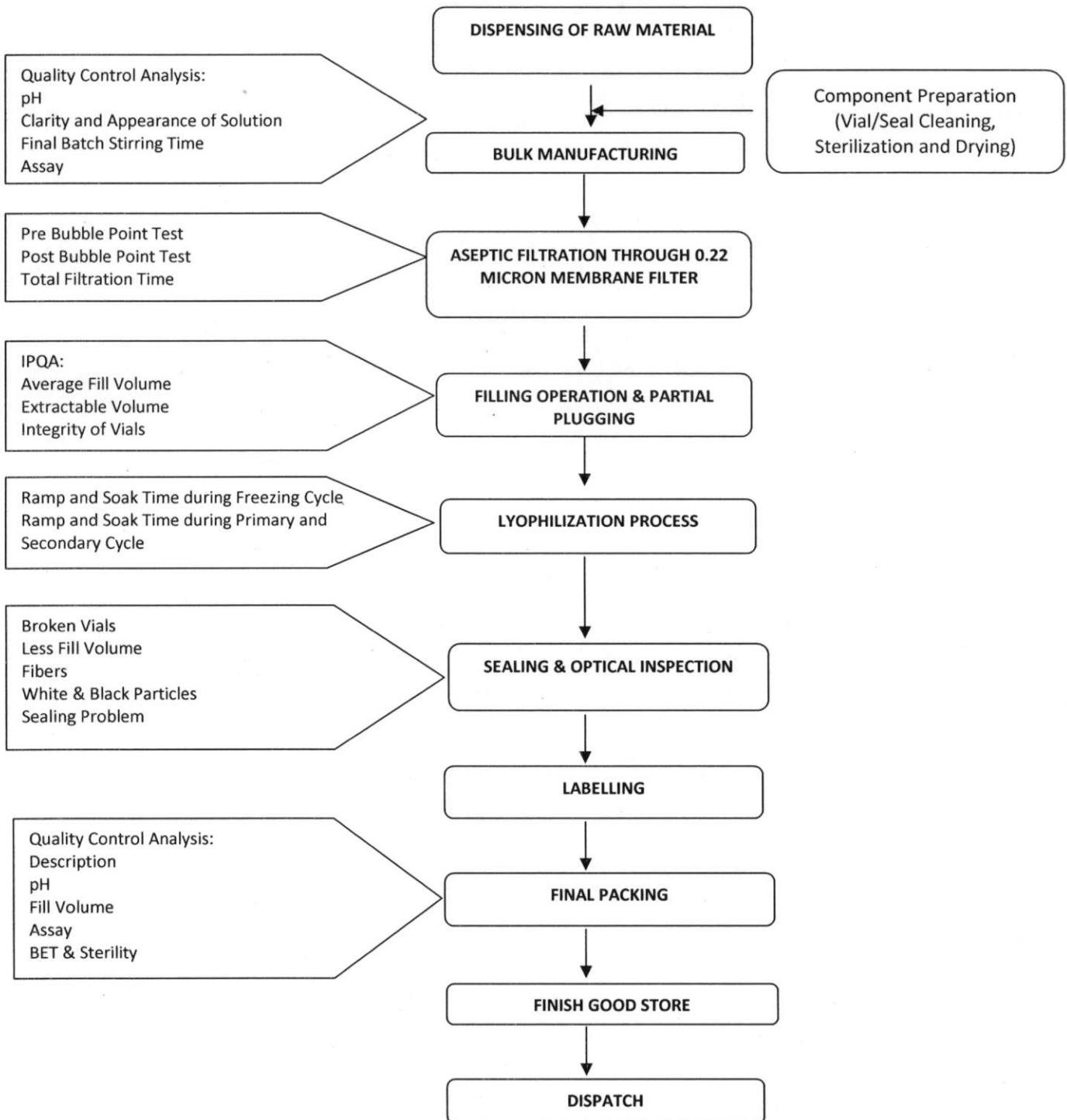
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12. Process Flow Diagram

Process Controls

Process Steps





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13. Manufacturing process

Check the Equipment for Cleanliness prior to use before manufacturing process and check the status label displayed. Take line clearance from IPQA for cleanliness

- 13.1 Now add dispensing sodium acetate anhydrous with continuous stirring till completely dissolved. Check the clarity of the solution.
- 13.2 Transfer Mannitol to manufacturing tank with continuous stirring. Till clear solution obtained & Check the Clarity of the solution.
- 13.3 Transfer Gemcitabine Hydrochloride slowly to manufacturing tank with continuous stirring. Stir for 30 minutes, till the clear solution obtained.
- 13.4 Now add solution of prepared sodium hydroxide solution slowly in the manufacturing tank with continuous stirring to clear the solution.
- 13.5 Now add solution of prepared hydrochloric solution slowly in the manufacturing tank with continuous stirring to clear the solution.
- 13.6 Send the bulk sample to QC for testing. If found satisfactory. Filter the solution through 0.22 micron Nylon filter & fill accordingly.

Speed S.S. Mechanical Stirrer (RPM)	Sample Volume (ml)	Appearance and Clarity of Solution	pH	Final Batch Stirring Time
400	20 ml each at different stirring time	Clear colorless solution	2.7 to 3.3	15 minutes
				20 minutes
				25 minutes

- 13.7 After getting Approval from Quality Control Department, take line clearance form IPQA personal for filtration of bulk solution.
- 13.8 Carry out Pre and Post bubble point test to confirm the Integrity of the 0.22 Micron Membrane Filter

Test	Nitrogen Pressure
Pre Bubble Point Test	1.2 kg/cm ² to 1.5 kg /cm ²
Post Bubble Point Test	1.5 kg/cm ² to 1.8 kg /cm ²

- 13.9 Filter the solution aseptically and collect the solution in the sterile pressure vessel. Total Filtration time shall be recorded.



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14. Filling & Partial Plugging:

- 14.1 After Bubble point test, take line clearance from IPQA personal for Filling and partial plugging and for the machines and equipments to be used during the filling and partial plugging. Total Filtration Time shall be recorded.
- 14.2 Set the Filling and Sealing Machine at slow, medium & high speed and aseptically fill not less than 5.0 ml of Solution in 10 ml clear moulded glass vials. Inform IPQA personal for sampling of Filled Vials.

Sample Quantity	Average Fill Volume	Extractable Volume	Integrity of Vials
10 Vials at the Minimum, Optimum & Maximum Machine speed of operation	NLT 5.0 ml	5.0 ml to 5.3 ml	Should be properly Plugged

- 14.3 IPQA personal shall draw 10 Vials for Sample at the beginning, middle and end of the filling operation and carry out in process check for individual fill volume, minimum and maximum and average fill volume.



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15. Lyophilization Process:

- 15.1 Take line clearance from IPQA personal before Lyophilization Process.
- 15.2 Vials are aseptically loaded into the Lyophilizer, Run Preliminary check points before loading the vials in to the Lyophilizer.
- 15.3 Control and record the following Preliminary check parameters. These include: shelf temperature, product temperature, condenser temperature, chamber pressure and condenser pressure and leak test rate.

Preliminary Check Points

Process Control Parameters		Limits
Shelf Temperature		25 ± 5 ° C
Product Temperature		25 ± 5 ° C
Condenser Temperature		25 ± 5 ° C
Chamber Pressure		687580 mT
Leak Test Rate	Condenser Temp	- 80 ° to -40°
	Vacuum Set Point	10 to 500 mT
	Test Time	10 to 90 minutes
	Leak Rate	Less than 30 mT

- 15.4 Load the vials aseptically into the Lyophilizer and run freezing cycle

Freezing Cycle:

1. It is desirable after freezing and during primary drying to hold the drying temperature (in the product) at least 4-5° C below the Eutectic point.
2. Set the Vacuum rate at 500 millitors and run Freezing Cycle and record the Ramp and Soak time for all the three batches in the table given below.

Parameters for Freezing Cycle Parameters (Ramp and Soak Time)

Ramp/Soak Time (°C) Time	(Shelf Time)	Cycle Run Time (mins)	Vacuum Rate (mT)
Ramp Time at -20 °C		90 ± 15 mins	NA
Soak Time at -20 °C		60 ± 15 mins	
Ramp Time at -45 °C		90 ± 15 mins	
Soak Time at -45 °C		280 ± 15 mins	



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Primary and Secondary Cycle:

Set the Primary and Secondary Cycle and record the Ramp and Soak time results for the three batches in the table given below

Parameters for Primary and Secondary Cycle Parameters (Ramp and Soak Time)

Ramp/Soak Time (°C) (Shelf Temp)	Cycle Run Time (mins)	Vacuum Rate (mT)
Ramp Time at -30 °C	120 ± 15 mins	200 mT
Soak Time at -30 °C	240 ± 15 mins	200 mT
Ramp Time at -20 °C	120 ± 15 mins	150 mT
Soak Time at -20 °C	900 ± 15 mins	150 mT
Ramp Time at -10 °C	120 ± 15 mins	150 mT
Soak Time at -10 °C	600 ± 15 mins	150 mT
Ramp Time at -0 °C	120 ± 15 mins	150 mT
Soak Time at -0 °C	240 ± 15 mins	150 mT
Ramp Time at 10 °C	120 ± 15 mins	100 mT
Soak Time at 10 °C	180 ± 15 mins	100 mT
Ramp Time at 20 °C	120 ± 15 mins	70 mT
Soak Time at 20 °C	180 ± 15 mins	70 mT
Ramp Time at 30 °C	120 ± 15 mins	50 mT
Soak Time at 30 °C	240 ± 15 mins	50 mT
Ramp Time at 35 °C	120 ± 15 mins	30 mT
Secondary Cycle		
Shelf Temp at 40 °C	2000 ± 15 mins	30 mT



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16. Visual Inspection

- 16.1 Remove the Plugged Vials aseptically from the Lyophilizer and Seal the Vials with Aluminium Flip off Seal having Red colour.
- 16.2 Filled and Sealed Vials are inspected against white and black board to check the absence of any extrinsic particles such as fibers, white and black particles and less volume and other physical defects such as broken vials and improper sealing at the beginning, middle and end of the filling and sealing operation at different speed of sealing machine.
- 16.3 Inform the IPQA personal for Sampling of Filled and Sealed vials for Optical Inspection. Following Parameters are to be checked during the Optical Inspection.

Sample Quantity	Physical Defects / Rejections	Results
10 Vials at the beginning, middle and end of operation	Broken Vials Less Volume Fibers White Particles Black Particles	Should be Nil



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Sr. No.	Stage/ Critical Process Steps	Control Variables	Sampling time/ Qty.	Test/ Process Parameter	Acceptance Criteria
3.	Filtration	Pressure Control of Nitrogen	After Filtration (From Filling Vessel) (25 ml) *This sample also consider as initial sample i,e '0' hour for hold time study)	Sterility	No growth should be observed
			After Filtration (From Filling Vessel) (25 ml) *This sample also consider as initial sample i,e '0' hour for hold time study)	BET	NMT 0.05 EU/mg
			For Description, Assay and pH		As per Specification
4.	Filling & Half Stoppering	Temperature and humidity Machine speed Feed rate of rubber stopper Movement of vials on the machine Nitrogen gas pressure Machine Speed seal a feed rate	Nitrogen	Bioburden	As per Specification
			Initial Middle & end (02 filled vials at each stage)	Assay	As per Specification
			pH		As per Specification
			Initial Middle & end (04 filled vials at each stage)	Sterility	No growth should be observed
			At Minimum, Optimum and Maximum machine speed (12 filled vials at each stage)	Fill Volume (to be checked by IPQA)	NLT 5.0 ml
			Before filling & Sealing operation	Viable & non viable count	As per Guideline ISO: 14644
			Initial, Middle & end (21 Empty Depyrogenated vials at each stage)	BET	As per Specification
				Sterility	
			Initial, Middle & end (22 bungs at each stage)	Sterility	As per Specification
				BET	
			Nitrogen	Sterility	As per Specification
			Initial, Middle & end (20 Flip – off seal at each stage)	Sterility	As per Specification



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17. Sampling Plan:

Sr. No.	Stage/ Critical Process Steps	Control Variables	Sampling time/ Qty.	Test/ Process Parameter	Acceptance Criteria
1.	Vial Washing & Depyrogenation	Quality of Purified water	Purified water (Routine Sampling)	pH, Conductivity, description	As per Specification
			Water for injection Routine Sampling)	pH, Conductivity, description	As per Specification
		Quality of WFI	BET and Bioburden		
			Compresses air	Bioburden	NMT 100 cfu/ml
		Quality of Compressed air	Before Washing (20 vials)	Bioburden	For informative purpose
			After Washing (20 vials)	Bioburden	For informative purpose
		Sterilization Temperature	Washed vials (10 vials)	LBPC	>10 μ = NMT 60/ml >25 μ = NMT 60/ml
2.	Manufacturing	Quality of WFI for Bulk – Manufacturing	Vials Depyrogenation	Sterilization Temperature and time	At 250°C hold for 120 minutes.
				Description, pH, Conductivity (100 ml)	As per Specification
				BET (10 ml)	
				Bioburden (100 ml)	
		Mixing speed (RPM) & Time	During Mixing – after 15, 20 and 25 minutes (10 ml each stage) (Before Filtration *Last sample also consider as initial sample i,e '0' hour for hold time study)	For Description, Assay and pH	As per Specification
			(Before Filtration *Last sample also consider as initial sample i,e '0' hour for hold time study)	Bioburden (10 ml)	NMT 100 cfu/ml



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Sr. No.	Stage/ Critical Process Steps	Control Variables	Sampling time/ Qty.	Test/ Process Parameter	Acceptance Criteria
5.	Lyophilization process	Temperature	During Cycle	Ramp and Soak Time during Freezing	To be complies as per protocol complies as per finish product specification
		Pressure		Ramp and Soak Time during Primary and Secondary Cycle	
		Vacuum	From all loaded shelve	Description, pH & Assay	
		Freezing		Composite sample	
		Drying	Complete testing		

18. Hold time Study Sampling Plan

Sr. No.	Stage	Interval	Sample Quantity	Test	Acceptance
1.	Hold time Study – Before Filtration (from Holding tank)	Initial at "0" hours (Already covered above)	10 ml	For chemical Analysis: description, Assay and pH	As per Specification
		At 06 Hour	10 ml	For Bioburden	NMT 100 cfu/ml
2.	Hold time Study - After filtration (From Holding tank)	Initial at "0" hours (Already covered above)	25 ml	Sterility	No growth should be observed
		At 06 Hours At 12 Hours At 24 Hours At 48 Hours		BET	NMT 0.05 EU/mg

Note:

- Hold time study before filtration shall be conducted for 06 hours.
- Hold time study after filtration shall be conducted for 48 hours.



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19. ACCEPTANCE CRITERIA

Stage	Test / Process parameter	Acceptance criteria
Vial washing and Depyrogenation	Compressed air - Bioburden	NMT 100 cfu/ml
	Sterile vial for sterility	No growth should be observed
	Sterile vial for LBPC	>10 µm = NMT 6000 per container >25 µm = NMT 600 per container
Bulk Manufacturing	Clarity and Appearance of Solution	To Verify the clarity and Appearance of bulk solution
	pH	2.7 to 3.3
	Assay	95.0 % to 105.0 %
Aseptic Filtration (Pre and Post Bubble Point Test and Total Filtration time)	N2 Pressure (Pre Bubble Point Test)	1.2 kg/cm ² to 1.5 kg /cm ² (Filter should not burst)
	N2 Pressure (Post Bubble Point Test)	1.5 kg/cm ² to 1.8 kg /cm ² (Filter should not chock and burst)
	Total Filtration Time	Within 15 minutes
Hold time Study – Before filtration – “0” hour & “06” hours.	Chemical analysis – (10ml)	As per specification
	Bioburden – (10 ml)	NMT 100 cfu/ml
Hold time Study – After filtration – “0” hour & “06” hours, “12” hour, “24” hour and “48” hour.	Chemical analysis – (10ml)	As per specification
	Sterility and BET – (25ml)	As per specification & BET limit: NMT 5.04 EU/ml
Filling & Sealing	Average Fill Volume	NLT 5.0 ml
	Extractable Volume	NLT 5 ml
Lyophilization Process	Ramp and Soak Time during Freezing	Ramp and Soak time should be within the limit
	Ramp and Soak Time during Primary and Secondary Cycle	
Optical Inspection	Broken Vials	Should be absent or Nil
	Less Volume	
	Fibers	
	White Particles	
	Black Particles	
Quality Control Attributes after Lyophilization	Description Before reconstitution	White coloured lyophilized cake filled in clear colourless transparent glass tubular vials USP type 1.
	Identification By HPLC	The retention time of the major peak of the sample corresponds to that of the standard solution, as obtained in the assay
	Identification By UV	The UV spectrum obtained from sample solution should be corresponds to that of the standard solution.



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	pH	2.7 to 3.3
	Completeness and color of injection	The sample should be clear and colorless after reconstitution and it should not be significantly less clear than an equal volume of diluents.
	Uniformity of dosage units	For L1 stage , AV =NMT 15 and for L2 stage , AV = NMT 25
	Cytosine	NMT 0.1 %
	Any individual unspecified impurity	NMT 0.2%
	Total impurities	NMT 0.3%
	Bacterial endotoxins test	NMT 0.05 endotoxin units/mg
	Sterility	No growth should be observed
	Particulate Matter	For 10µm =NMT 6000 per container For 25 µm =NMT 600 per container
	Assay : Each vial contains:	
	Gemcitabine Hydrochloride USP Eq. to Gemcitabine 200mg	95 to 105% (950mg to 1050mg)

Quality Control Attributes	Description	A white colour lyophilized cake filled in 10 ml clear moulded vial USP Type - I
	Identification:	
	By UV	The UV absorption spectrum of the major peak of the sample solution and the standard solution exhibit maxima and minima at the same wave length.
	By HPLC	In the Assay, the retention time of the major peak of the sample solution corresponds to that of the standard solution.
	pH	2.7 to 3.3
	Uniformity of Dosage units	For L1 Stage, AV = NMT 15 and L2 Stage, AV = NMT 25
	Sterility	No growth should be observed
	Bacterial Endotoxins test	NMT 0.05 EU/mg
	Particulate Matter	For 10 µm to less than 25 µm – NMT 6000 particles For 25 µm to greater – NMt 600 particles
	Impurities	
	Cytosine	NMT 0.1%
	Gemcitabine	NMT 0.1 %
	Any Individual unspecified impurity	NMT 0.2 %
	Total impurities	NMT 0.3 %



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20. REFERENCE DOCUMENTS

S. No.	Document name	Document No.
1.	Master Formula Record	GM/MFR/001
2.	Batch Manufacturing Record	GM/BMR/001
3.	Product Standard Testing Procedure	KPL/STP/IN/016-00
4.	Stability Protocol	STP/20/011
5.	Gemcitabine Hydrochloride Standard Testing Procedure	KPL/STP/RM/003-00
6.	Mannitol Standard Testing Procedure	KPL/STP/RM/026

21. STABILITY :

If acceptance criteria at all the stages of 3 batches are satisfied, the process to be accepted as validated for manufacturing the product at site, Kwality Pharmaceuticals Limited. The validation batches shall be introduced for complete stability studies protocol.

22. Deviation Report:

23. Change Control:

24. Abbreviation:

- KPL : Kwality Pharmaceuticals Ltd.
PVP : Process Validation Protocol
IPQA : In-process Quality Assurance
QA : Quality Assurance



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mg	:	milligram
kg	:	Kilogram
ml	:	mille liter
q.s	:	quantity sufficient
mm	:	millimeter
CI	:	Cytotoxic Injection
QC	:	Quality Control
BP	:	British Pharmacopoeia
USP	:	United State Pharmacopoeia
RPM	:	Rotation per Minute
S.S	:	Stainless Steel
NLT	:	Not less than
ENG	:	Engineering