

BATCH MANUFACTURING RECORD
(A2 BLOCK)

PRODUCT	BATCH NUMBER
Y1 (PRODUCTION FERMENTATION)	

PRODUCT CODE : Y1	ISSUED BY : QUALITY ASSURANCE
DOCUMENT CODE : XX/BMR/YYYY/VN	SIGNATURE : DATE :
EFFECTIVE DATE :	PAGE : 1 OF 48

LABORATORY SEED BATCH No. :

SEED FERMENTATION BATCH No. :

MEDIA PREPARATION BATCH No. :

Note 1: Encircle the appropriate type of batch number.

MANUFACTURING SITE ADDRESS:

Site-2

PHARMA Limited,

PHARMA Special Economic Zone,

RECEIVED BY: PRODUCTION

SIGNATURE:

DATE:

PREPARED BY:

CHECKED BY:

APPROVED BY:

DATE :

DATE :

DATE :

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RAW MATERIAL CONSUMPTION SUMMARY

ITEM CODE	ITEM NAME	CON.	UOM	STD. QTY.	ACTUAL QTY.	BATCH No.	CKD BY
ITC1	RM1	01	Kg	10			
ITEM CODE	ITEM NAME	CON.	UOM	STD. QTY.	ACTUAL QTY.	PREPARATION No.	CKD BY
ITC2	RM2	01	Kg	50			
ITC3	RM3	01	Kg	70			
ITC4	RM4	01	Kg	60			
ITC5	RM5	01	Kg	60			

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ITEM CODE	ITEM NAME	CON.	UOM	STD. QTY.	ACTUAL QTY.	PREPARATION No.	CKD BY
ITC6	RM6	01	Kg	700			

***Note 2.:** Based on the performance of the batch, the quantity of material marked with * may vary from the standard quantity.

RAW MATERIAL CONSUMPTION SUMMARY FOR CLEANING

ITEM CODE	ITEM NAME	CON.	UOM	STD. QTY.	ACTUAL QTY.	PREPARATION No.	CKD BY
ITC7	RM7	01	Kg	600			

Batch started on: _____

Batch completed on: _____

Reviewed by:

PRODUCTION :

DATE :

QUALITY ASSURANCE :

DATE :

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Note 3: Refer below listed reference documents as and when required.**LIST OF REFERENCES****LIST OF SOPs**

DOCUMENT NAME	DOCUMENT CODE
pH meter	A2/PROD/SOP/006
Waste disposal	A2/PROD/SOP/008
Sterility check procedure	A2/PROD/SOP/009
Production planning	A2/PROD/SOP/010
Emergency shutdown procedure	A2/PROD/SOP/011
Batch failure	A2/PROD/SOP/013
Usage of filters	A2/PROD/SOP/014
Alarms and actions	A2/PROD/SOP/015
Solution preparation	A2/PROD/SOP/016
Material entry	A2/PROD/SOP/018
DO ₂ probe failure identification	A2/PROD/SOP/020
Re-cleaning frequency for equipment	A2/PROD/SOP/021
Sampling procedure	A2/PROD/SOP/022
Miscellaneous items cleaning	A2/PROD/SOP/023
Decontamination procedure	A2/PROD/SOP/025
Calibration of pH and DO ₂ Probes	A2/PROD/SOP/030
Procedure for taking fermentation process trend printouts	A2/PROD/SOP/031

LIST OF EOPs

1kL Fermenter	A2/PROD/EOP/002
10kL Fermenter	A2/PROD/EOP/003
100kL Fermenter	A2/PROD/EOP/004
5kL NDV	A2/PROD/EOP/005
10kL NDV	A2/PROD/EOP/006
CIP System	A2/PROD/EOP/007

LIST OF ECCs

1kL Fermenter	A2/PROD/ECC/12
10kL Fermenter	A2/PROD/ECC/15
100kL Fermenter	A2/PROD/ECC/13
5kL NDV / 10kL NDV	A2/PROD/ECC/05

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ABBREVIATION LIST

<	Less than	kL	Kilo Liter
%	Percentage	L	Liter
&	And	mg	Milli gram
>	Greater than	mm	Millimeter
±	Plus or minus	MSDS	Material safety data sheet
°C	Degree Celsius	NA	Not applicable
A.R.No.	Analytical reference number	NDV	Nutrient Dosing Vessel
A1	Media preparation block	NLT	Not less than
A2	Fermentation block	Nm ³ /hr	Normal meter cube per hour
BMR	Batch manufacturing record	NMT	Not more than
CIP	Clean in place	No.	Number
CKD By	Checked by	OCP	Operational Control Procedure
CKL	Checklist	PCV	Packed cell volume
CON.	Configuration	PIS	Pre inoculation sample
D1	Extraction block (Downstream 1)	POIS	Post inoculation sample
DO ₂	Dissolved oxygen	QC	Quality control
ECC	Equipment cleaning checklist	QTY. / Qty.	Quantity
EOF	End of fermentation	RPM	Revolutions per minute
EOP	Equipment operating procedure	SOP	Standard operating procedure
g	Gram	SP	Set point
HDPE	High-density polyethylene	STD. / Std.	Standard
Hr / hr / hrs.	Hours	UOM	Unit of measurement
Kg	Kilo gram	W/W	Weight /Weight

SAFETY PRECAUTION

Wear gloves, goggle, masks and apron while handling alkali, fine powders or acids. Refer respective MSDS before handling the respective material.

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3. LEAKAGE TEST

3.1. Replace the rubber septa of the inoculation ports with new ones.		_____	_____
3.2. Replace the vessel isolation actuated valve on the related RM solution feed lines with manual valve.	Yes NA	_____	_____
3.3. Charge XX Kg of Potable water into the fermenter: _____ Kg A.R.No. _____		_____	_____
3.4. Set the Air flow to YY Nm ³ /hr	Process value _____ Nm ³ /hr	_____	_____
3.5. Pressurize the fermenter to ZZ bar.	process value _____ bar	_____	_____
3.6. Start the leakage check.			

Note 4: All unions connected to the vessel and all vessel isolation valves should be checked for leakage. Soap solution should be sprayed on the unions using spray bottle. If there is a leakage, bubble formation will occur, if not, it is confirmed that there is no leakage. Valve leakage (valve passing) is confirmed by holding water in a beaker beneath the open drain valve, which is next to vessel isolation valve (tip of the drain line is immersed in the water). If there is a leakage bubble formation will occur, if not, it is confirmed that there is no leakage in the vessel isolation valve.

3.7. LEAKAGE CHECK RESULT

Note 5: 'P' represents PASS, 'F' represents FAIL.

Note 6: For any leakage, inform the maintenance personnel about leakage. After rectification, restart the test. If there is a leakage in harvesting valve, level transmitter or Bottom flange, drain the water and inform the maintenance personnel about leakage. After rectification, charge potable water then restart the test and enter the result in the below column.

Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.1. Charge XX Kg of potable water.	NA	_____ Kg/NA A.R.No. _____	_____ Kg/NA A.R.No. _____	_____ Kg/NA A.R.No. _____
3.7.2. Test start time and Date	_____ hrs Date _____	_____ hrs Date _____	_____ hrs Date _____	_____ hrs Date _____
3.7.3. Diaphragm of Harvesting valve.	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

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Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.4. Bottom flange	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.5. Level transmitter	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.6. 25 mm port 1	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.7. 25 mm port 2	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.8. 25 mm port 3	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.9. 25 mm port 4	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.10. 25 mm port 5	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.11. 25 mm port 6	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.12. Sampling valve	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.13. Man hole lid	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.14. Sight glass	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

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Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.15. Steam supply union to sight glass	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.16. Spare nozzle 1	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.17. Spare nozzle 2	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.18. Header E	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.19. Header F	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.20. Header A	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.21. Header B	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.22. Partial Harvest line	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.23. Header C	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.24. Header D	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.25. Transfer line from seed fermenter	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

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Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.26. Transfer line from 10kL fermenters.	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.27. Transfer line from 100L fermenters.	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.28. Light glass	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.29. Steam supply union to light glass	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.30. Dip rod sample valve	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.31. Foam sensor	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.32. Header G	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.33. Spare nozzle 4 / NA	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.34. Spare nozzle 5 / NA	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.35. Spare nozzle 6 / NA	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.36. Additional Sparger line /NA	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

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Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.37. Pressure transmitter	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.38. Bursting disc	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.39. CIP Port 1	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.40. CIP Port 2	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.41. 19 mm port 1	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.42. 19 mm port 2	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.43. 19 mm port 3	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.44. 19 mm port 4	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.45. 19 mm dummy port	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.46. Air line (After Air fine filter)	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.47. Exhaust view glass	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

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Details	Test -1	Test-2/NA	Test-3/NA	Test -4/NA
3.7.48. Exhaust valve before filter	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.49. Exhaust filter housing Joints	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.50. Exhaust Filter top clamp	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.51. Exhaust Filter bottom clamp	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.52. Valve before exhaust control valve	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.53. Exhaust bypass valve	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.54. Exhaust control valve joint flanges	P / F Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____	P / F / NA Rectified by _____
3.7.55. Test end time and Date	_____ hrs Date _____	_____ hrs Date _____	_____ hrs Date _____	_____ hrs Date _____
3.8. Test result	P / F	P / F / NA	P / F / NA	P / F / NA
Done by :	_____	_____	_____	_____
Checked by :	_____	_____	_____	_____

Note 7: If there is any leakage observed after the 4th leak test, enter those details in the section 3.9.**3.9. Details of failure and rectification / NA**

Done by : _____ Checked by : _____

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4. VESSEL PRESSURE TEST -1 (PRESSURE HOLD TEST)**4.1. CRITERIA:** Pressure drop should not be > 0.2 bar in 10 minutes to pass the test.

Parameter	Std.set point	Actual set point	Process value for Test	Process value for Test repeat / NA	Done by	Checked by
4.2. Test SP 1	000 bar					
4.3. Test Time	10 minutes		NA			
4.4. Air flow set Point	YY Nm³/hr					
4.5. De-pressurise set point	0.1 bar					
4.6. Test Hysteresis	0.2 bar		NA			

4.7. Confirm the parameters and start the test.

Details	Pressure test	Repeat pressure test / NA
4.8. Test start Time and Date	_____ hrs Date_____	_____ hrs Date_____
4.9. Test End Time and Date	_____ hrs Date_____	_____ hrs Date_____
4.10. Pressure at the end	_____ bar	_____ bar
4.11. Test result	P / F	P / F / NA
4.12. Accept the prompt	Yes	Yes / NA
Done by :	_____	_____
Checked by :	_____	_____

Note 8: If there is any leakage observed after the repeat test, enter those details in the section 4.13.**4.13. Details of failure and rectification / NA**

Done by : _____ Checked by : _____

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DATE :	DATE :	DATE :

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DATE/TIME		PROCEDURE	OBSERVATION	Done by	Checked by																														
From	To																																		
		<p><u>5. ADDITIONAL SPARGER FINE FILTER STERILISATION / NA (Applicable only for F104-D)</u></p> <p><u>Note 9:</u> Place the sterilisable grade Air fine filters on the filter housing.</p> <p><u>Note 10:</u> Pre-sterilisation of the Air fine- filter should be done without pressurising the filter by just passing steam through the filter for 15 to 17 minutes.</p> <p>5.1. Fix the Air fine filters</p> <p>5.2. Give YY Nm³/hr set point to Air flow control valve of additional sparger.</p> <p>5.3. Start the filter sterilisation</p> <p>5.4. Pre-sterilisation of the additional sparger fine filter should be done for 15 to 17 minutes without pressure</p> <div style="border: 1px solid black; padding: 5px; margin: 10px 0;"> <p>5.5. Sterilise the additional sparger fine filter by passing steam and maintain the steam pressure at 1.1 to 1.3 bar for 30 to 35 minutes.</p> </div> <p><u>Note 11:</u> Sterilise the additional sparger fine filter for 30 to 35 minutes. Record the details in the chart provided below.</p>	<p>Yes NA</p> <p>_____ Nm³/hr / NA</p> <p>Yes NA</p> <p>_____ bar</p> <p>_____ bar</p>	<p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	<p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>																														
<p>5.6. ADDITIONAL SPARGER FINE FILTER STERILISATION CHART / NA</p> <table border="1"> <thead> <tr> <th>Interval</th> <th>Time</th> <th>Pressure (bar)</th> <th>Done by</th> <th>Checked by</th> </tr> </thead> <tbody> <tr> <td>5.6.1. Initial</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>5.6.2. After 10 minutes</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>5.6.3. After 20 minutes</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>5.6.4. 30th to 35th minute</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td colspan="3">5.6.5. Cool the filter to ambient temperature.</td> <td></td> <td></td> </tr> </tbody> </table>						Interval	Time	Pressure (bar)	Done by	Checked by	5.6.1. Initial					5.6.2. After 10 minutes					5.6.3. After 20 minutes					5.6.4. 30 th to 35 th minute					5.6.5. Cool the filter to ambient temperature.				
Interval	Time	Pressure (bar)	Done by	Checked by																															
5.6.1. Initial																																			
5.6.2. After 10 minutes																																			
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5.6.5. Cool the filter to ambient temperature.																																			

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From	To				
		<u>6. MEDIA PREPARATION</u> Note 12: Media solution should be prepared in A1 block and the same is transferred to respective equipment in A2 block. The media preparation details are recorded in the respective BMR of A1 Block. <div style="border: 1px solid black; padding: 2px;">6.1. Batch size</div> 6.2. Receive media solution from A1 Block to the fermenter in A2 Block. Simultaneously switch 'ON' agitator of the fermenter and set the RPM to YY ± Y 6.3. Total Qty. (XX Kg) of Product media solution transferred from A1 Block. 6.3.1. A1 Block Media Preparation Batch No. <u>7. Vessel pressure test – 2</u> <u>7.1. CRITERIA:</u> Pressure drop should not be > 0.2 bar in 10 minutes to pass the test.	<div style="border: 1px solid black; padding: 2px;">XX Kg</div> RPM _____ _____ Kg _____		
Parameters		Std. set point	Actual set point	Process value for Test	Process value for Test repeat / NA
7.2. Test Pressure		1.8 bar			
7.3. Test Time		10 minutes		NA	
7.4. Air flow set point		YY Nm ³ / hr			
7.5. De-pressurise set point		0.1 bar			
7.6. Test Hysteresis		0.2 bar		NA	
7.7. Confirm the parameters and start the test					
Details		Pressure test		Repeat pressure test / NA	
7.8. Test start time and Date		_____ hrs Date _____		_____ hrs Date _____	
7.9. Test End Time and Date		_____ hrs Date _____		_____ hrs Date _____	
7.10. Pressure at the end		_____ bar		_____ bar	
7.11. Test result		P / F		P / F / NA	
7.12. Accept the prompt		Yes		Yes / NA	
Done by :		_____		_____	
Checked by :		_____		_____	
PREPARED BY:		CHECKED BY:		APPROVED BY:	
DATE :		DATE :		DATE :	

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From	To				

Note 13: If pressure test fails inform the maintenance personnel about the leakage. After rectification repeat the test.

Note 14: If there is any leakage observed after the repeat test, enter those details in the section 7.13.

7.13. Details of failure and rectification / NA

Done by : _____ Checked by : _____

8. MEDIA STERILISATION AND COOLING

8.1. Set the recipe parameters.

Parameters	Std. set point	Actual set point	_____	_____
8.2. Heating 1 SP	H1 °C	_____ °C		
8.3. Heating 2 SP	H2 °C	_____ °C		
8.4. Sterilisation time	10 minutes	_____ minutes		
<div>8.5. Sterilisation holding temperature and pressure</div>	<div>Temperature 120-135 °C Pressure 1.1 – 1.3 bar</div>	Temperature _____ °C Pressure _____ bar		
8.6. Heating hysteresis	H1 ° C	_____ °C		
8.7. Exhaust close temperature	T1 ° C	_____ °C		
8.8. Back pressure SP	ZZ – ZZ bar	_____ bar		
8.9. Air flow SP	YY ± YY Nm ³ / hr	_____ Nm ³ / hr		
8.10. Air pressure set point	ZZ – ZZ	_____ bar		
8.11. Cooling 1 SP	C1 – C1 °C	_____ °C		
8.12. Cooling 2 SP	C2 °C	_____ °C		
8.13. Filter checked	Yes	Yes		
8.14. Confirm the parameters and start sterilisation.				
8.15. Media sterilisation start time _____ hours 8.15.1. Date : _____				

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From	To																													
		<p><u>8.16. AIR FINE FILTER STERILISATION</u></p> <p>Note 15: Pre-sterilisation of the Air fine filter should be done without pressurising the filter by just passing steam through the filter for 15 to 17 minutes.</p> <p>8.16.1. Start the filter sterilisation</p> <p>8.16.2. Pre-sterilisation of the Air fine filter should be done for 15 to 17 minutes without pressure.</p> <div style="border: 1px solid black; padding: 5px;"> <p>8.16.3. Sterilise the Air fine filter by passing steam and maintaining the steam pressure at 1.1 to 1.3 bar for 30 to 35 minutes</p> </div> <p>Note 16: Sterilisation of the Air fine filter done for 30 to 35 minutes. Record the details in the chart provided below.</p> <p>8.16.4. AIR FINE FILTER STERILISATION CHART</p> <table border="1"> <thead> <tr> <th>Interval</th> <th>Time</th> <th>Pressure (bar)</th> <th>Done by</th> <th>Checked by</th> </tr> </thead> <tbody> <tr> <td>8.16.4.1. Initial</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>8.16.4.2. After 10 minutes</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>8.16.4.3. After 20 minutes</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>8.16.4.4. 30th to 35th minute</td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p>8.16.5. Accept the prompt for completion of sterilisation</p> <p>8.16.6. Cool the filter to ambient temperature</p> <p>8.16.7. Accept the prompt for completion of cooling</p>	Interval	Time	Pressure (bar)	Done by	Checked by	8.16.4.1. Initial					8.16.4.2. After 10 minutes					8.16.4.3. After 20 minutes					8.16.4.4. 30 th to 35 th minute							
Interval	Time	Pressure (bar)	Done by	Checked by																										
8.16.4.1. Initial																														
8.16.4.2. After 10 minutes																														
8.16.4.3. After 20 minutes																														
8.16.4.4. 30 th to 35 th minute																														
<p>Note 17: Ensure that the exhaust valve is closed when the media sterilisation temperature reaches H1 °C.</p> <p>Note 18: Once temperature reaches H1 °C send steam through additional sparger continuously (for F104-D).</p> <p>8.17. Open the vessel isolation valves on G Header line, Edenor feed line and L-Leucine feed line once the temperature reaches H1 °C.</p>																														
Parameters		Process value	Attaining time																											
8.18. Heating 1 SP (H1 – H1 °C)		_____ °C	_____ hrs																											
8.19. Heating 2 SP (H2±1 °C)		_____ °C	_____ hrs																											
8.20. Sterilisation time (ST – ST minutes)		_____ minutes	From _____ hrs To _____ hrs																											
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	Interval	Time	Temperature (°C)	Pressure (bar)	Done by	Checked by
8.21. Sterilisation Holding temperature and pressure	Initial					
	After 10 minutes					
	After 20 minutes					
	After 30 minutes					
	After 40 minutes					
	After 50 minutes					
	End					

8.22. CHECK POINTS DURING STERILISATION (Tick in the appropriate box)**Note 19:** During sterilisation holding, following points to be checked for the temperature using thermo melt pen of range 121°C.**Note 20:** When media cooling sequence is started, close steam and send Air through the additional sparger (only for F104-D).

8.22.1. Air sparger lines		8.22.16. Header A			
8.22.2. Air bypass lines		8.22.17. Header B			
8.22.3. Steam supply line to light glass		8.22.18. Header C			
8.22.4. Steam supply line to sight glass		8.22.19. Header D			
8.22.5. Partial harvest line		8.22.20. Header E			
8.22.6. Transfer line from 10kL fermenter		8.22.21. Header F			
8.22.7. Transfer line from 1kL fermenter		8.22.22. Header G			
8.22.8. Exhaust Filter housing		8.22.23. Spare nozzle 1			
8.22.9. Exhaust Filter drain line		8.22.24. Spare nozzle 2			
8.22.10. Exhaust line		8.22.25. Transfer line from 100L Fermenter.			
8.22.11. Exhaust bypass line		8.22.26. Spare nozzle 4 / NA (Applicable for F104-A,B,C only)			
8.22.12. Sampling valve		8.22.27. Spare nozzle 5 / NA (Applicable for F104-A,B,C only)			
8.22.13. Harvest valve steam cross outlet line		8.22.28. Spare nozzle 6 / NA (Applicable for F104-D only)			
8.22.14. Man hole lid		8.22.29. Additional sparger line/ NA (Applicable for F104-D only)			
8.22.15. Sampling dip rod line				_____	_____
8.23. Close the vessel isolation valves on G Header line, RM and RM feed line.				_____	_____
8.24. Start cooling.				_____	_____

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From	To					
Parameters		Process value		Attaining time		
8.25. Air flow through additional Sparger (YY±Y Nm ³ /hr)		_____ Nm ³ /hr / NA		NA		
8.26. Back pressure SP (ZZ-ZZ bar)		_____ bar		NA		
8.27. Air flow SP (YY±YY Nm ³ / hr)		_____ Nm ³ /hr		NA		
8.28. Air pressure set point (ZZ – ZZ bar)		_____ bar		NA		
8.29. Cooling 1 SP (C1 – C1 °C)		_____ °C		_____ hrs		
8.30. Cooling 2 SP (C2±C2 °C)		_____ °C		_____ hrs		
_____		8.31. Start nutrient dosing and accept the prompt.				
_____		8.32. Set back pressure to 1.1 ± 0.2 bar..		_____ bar		
_____	_____	8.33. Line up sterilised Antifoam SAG 471 solution.		Yes NA		
_____		8.34. Close the Air bypass line.				
_____	_____	8.35. Sparge Air through the media for 10 ± 2 minutes (If foaming occurs, dose Antifoam SAG 471 solution)		_____ minutes		
_____		8.36. Check the pH of the media.		pH _____		
_____		8.37. pH of the media has to be adjusted to pH1 ± pH1 using sterilised 10% Base solution (w/w) or 10% acid solution (w/w).				
_____	_____	8.38. pH of the media after adjustment.		pH _____ / NA		
_____		8.39. Qty of 10% Base solution (w/w) / 10% Nitric acid solution used (w/w).		_____ Kg		
_____		8.39.1. Solution preparation No.		_____		
_____		8.40. Take pre-inoculation sample (PIS).				
		<u>9. INITIAL PARAMETERS SETTING</u>				
_____	9.1. Set Back pressure to ZZ bar		_____ bar			
_____	9.2. Set Air flow to YY Nm³/ hr		_____ Nm ³ / hr			
_____	9.3. Set Temperature to T1 °C		_____ °C			
_____	9.4. Set Agitator speed to A1 RPM		_____ RPM			
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<div style="border: 1px solid black; width: 100%; height: 100%;"></div>	<div style="border: 1px solid black; width: 100%; height: 100%;"></div>	9.5. Calibrate the 1 st DO ₂ to 100%. 9.6. Calibrate the 2 nd DO ₂ to 100%. <u>10. ALARMS SETTING</u> 10.1. Temperature Low: T1 ° C / High: T1 ° C 10.2. Air flow Low: YY Nm ³ /hr / High: YY Nm ³ /hr 10.3. Back pressure Low: ZZ bar 10.4. Agitation : Trip off 10.5. Enable the Foam Switch/Sensor <u>11. INOCULATION</u> 11.1. Set and confirm the recipe parameters. 11.2. Seed fermenter code. 11.3. pH of the inoculum. 11.4. PCV of the inoculum. 11.5. Age of the inoculum. <div style="border: 1px solid black; padding: 2px; margin: 5px 0;">11.6. Inoculate the fermenter.</div> 11.7. Start production. 11.8. Take post inoculation sample (POIS). 11.9. Check the pH of the post inoculation sample.	<div style="border: 1px solid black; width: 100%; height: 100%;"></div>	<div style="border: 1px solid black; width: 100%; height: 100%;"></div>	<div style="border: 1px solid black; width: 100%; height: 100%;"></div>
<u>12. MONITORING THE FERMENTER</u>					

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13.4. Preparation of RM Solution

Use 5kL / 10kL nutrient dosing vessel for preparation, sterilisation and dosing of both the solutions. For Preparation of RM solution refer solution preparation checklist. The solution should be sterilised at 121-123° C and 1.1 to 1.3 bar for 45 minutes followed by cooling the same to <30°C and all the details should be recorded in the respective solution preparation checklist.

16. HARVESTING CRITERIA**16.3. INSTRUCTION BY THE MANAGER / PRODUCTION INCHARGE**

16.3.1. Stop feeding at: _____ Log hr 16.3.2. Signature: _____ 17.3.3. Date: _____

17. SAMPLES FOR MICROBIOLOGICAL ANALYSIS:

17.1. In addition to the PIS and POIS samples, take sterile sample from 100kL fermenter every day starting from the 1st day onwards, until End of fermentation to check the contamination.

Note 30: For checking contamination samples should be collected in the pre labeled sterile culture tubes/flasks containing the sample identification, reference Batch No., sample status, equipment code and date marked with permanent marker pen.

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18. SAMPLES TO CHECK PRODUCT CONTENT (Pr.Cont.):

From the first hour of feeding, collect sample from 100kL fermenter every 1 - 2 hrs, till End of fermentation. Send the samples to QC for product content analysis. Record the details of the samples in the product content analysis details chart (Page 25 to 30).

Note 31: One Technical Information Sheet should be raised for the samples generated every 24 hours.

19. CHECKING pH AND PCV OF THE BROTH

Check pH and PCV of the broth from the 1st day till EOF. PCV of the broth should be checked using the Centrifuge at XXX rpm for 30 minutes and pH of the broth should be checked using pH meter.

Note 32: For checking pH, PCV and product content, sample should be collected in the fresh HDPE container with 'sample for analysis' label having relevant information.

IN PROCESS SAMPLE DETAILS CHART

Date	Time	Sample Stage	Log Hr	Sample		pH	PCV (%)	Checked by
				Done by	Checked by			
		PIS	NA				NA	NA
		POIS					NA	NA
		1 st day						
		2 nd day						
		3 rd day						
		4 th day						
		5 th day						
		6 th day						
		7 th day						
		8 th day						
		9 th day						
		10 th day						
		11 th day						
		12 th day						
		13 th day						
		EOF						

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BATCH No.:

[illegible]

Checked by _____

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DATE/TIME		PROCEDURE	OBSERVATION	Done by	Checked by
From	To				
		<u>20. HARVESTING DETAILS</u>			
		20.1. Total fermentation log hours	_____ hrs	_____	_____
_____		20.2. pH of the broth at EOF	pH _____	_____	_____
		20.3. Before transfer, steam the broth transfer line to D1 Block		_____	_____
		<u>Note 33:</u> The broth can be collected in one or two different broth collection tanks			
_____	_____	20.4. Transfer the broth to D1 Block		_____	_____
		20.5. Equipment code at D1 Block	1. T403 - ____/NA 2. T403 - ____/NA	_____	_____
		20.6. Total quantity of Broth harvested.	_____ Kg	_____	_____
_____	_____	20.7. Flush the fermenter thoroughly to remove residual broth using potable water.			
_____	_____	20.8. Transfer the flushing to D1 Block		_____	_____
		20.9. Total quantity of Potable water used for flushing the fermenter.	_____ Kg A.R.No. _____	_____	_____
		<u>Note 34:</u> Clean the fermenter after the process as per relevant ECC.			

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21. DEVIATION DETAILS:						
Note 35: Document the details of Deviation observed / occurred during the manufacturing.						
Sl No.	Date	Summary of deviation	Deviation type (Planned / Unplanned)	Deviation No.	Reference Page No.	Sign
PREPARED BY:		CHECKED BY:		APPROVED BY:		
DATE :		DATE :		DATE :		