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CLIENT: **TAKEDA**	
PROJECT **BURITI EPCMV PROJECT**	

DRUG SUBSTANCE
CHILLED GLYCOL SYSTEM (PROCESS)
DESCRIPTION REPORT

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1. REVISION HISTORY 3
2. PURPOSE 3
3. REFERENCE 3
4. PROCESS DESCRIPTION 3
4.1 CHILLERS 5
4.2 PRIMARY PUMPS 6
4.3 BUFFER TANK 6
4.4 MAKE-UP SYSTEM – LOOP 1 7
4.5 AIR SEPARATOR – LOOP 1 7
4.6 CHEMICAL DOSING SYSTEM – LOOP 1 7
4.7 SECONDARY PUMPS – LOOP 1 7
4.8 HEAT EXCHANGER 8
4.9 SECONDARY PUMPS – LOOP 2 9
4.10 MAKE-UP SYSTEM – LOOP 2 9
4.11 PRESSURIZED EXPANSION TANK – LOOP 2 10
4.12 AIR SEPARATOR – LOOP 2 10
4.13 CHEMICAL DOSING SYSTEM – LOOP 2 10
4.14 BALANCING VALVES 10
4.15 CONSUMERS 11
4.15.1 LOOP 1 11
4.15.2 LOOP 2 12

1. REVISION HISTORY

Rev	Reason For Change
A	90% DD ISSUE
0	ISSUED FOR CONSTRUCTION
1	AS PER N+1 UPDATE

2. PURPOSE

This document is intended to describe the process characteristics for the Chilled Glycol System (Process), Building 7B – Bulk Drug Substance – BDS, intended to Buriti Project, located at Hemobrás site in Goiana – Pernambuco state, Brazil.

3. REFERENCE

The following documents were used as reference:

Item	Number	Process Equipment List – Building 7B
01	PRD-MEC-CLC-004	CHILLED GLYCOL AND CHILLED WATER SYSTEM CALCULATION (PROCESS)
02	7B-M-0-5-44	P&I DIAGRAM DRUG SUBSTANCE CHILLED GLYCOL GENERATION SYSTEM
03	7B-M-0-5-45	P&I DIAGRAM DRUG SUBSTANCE CHILLED GLYCOL DISTRIBUTION SYSTEM (1/4)
04	7B-M-0-5-52	P&I DIAGRAM DRUG SUBSTANCE CHILLED GLYCOL DISTRIBUTION SYSTEM (2/4)
05	7B-M-0-5-53	P&I DIAGRAM DRUG SUBSTANCE CHILLED GLYCOL DISTRIBUTION SYSTEM (3/4)
06	7B-M-0-5-54	P&I DIAGRAM DRUG SUBSTANCE CHILLED GLYCOL DISTRIBUTION SYSTEM (4/4)

4. PROCESS DESCRIPTION

The Chilled Water/Glycol Generation System was designed to meet all the equipment in building 7B and will be located on the second floor.

The thermal load required for this building is 228 TR. To meet this thermal load, the generation system will have the following equipment:

- 1 chiller of 300 TR at Loop 1;
- 1 primary pump at Loop 1;
- 1 buffer tank at Loop 1;
- 1 make-up system at Loop 1;
- 1 air separator at Loop 1;
- 1 chemical dosing system at Loop 1 with:

  - a chemical dosing tank;
  - a chemical dosing pump;
  - a spill containment pallet.
- 1 secondary pump at Loop 1;
- 1 heat exchanger between Loops 1 and 2;
- 1 secondary pump at Loop 2;
- 1 make-up system at Loop 2
- 1 pressurized expansion tank at Loop 2;
- 1 air separator at Loop 2;
- 1 chemical dosing system at Loop 2 with:
  - a chemical dosing tank;
  - a chemical dosing pump;
  - a spill containment pallet.

The distribution system for process equipment consists in two loops with the following philosophy:

- Loop 1 - designed for chilled water service, but with the possibility for future implementation of a glycol mixture to replace chilled water.
- Loop 2 - designed for chilled water service, without the possibility for future implementation of a glycol mixture to replace chilled water.

At Loop 1 are allocated the users for all process systems (minus the bioreactor jacket loop skids). The current low temperature requirement for process vessels is 5 degrees Celsius. This can be accommodated by chilled water. However, if there is a future design change to meet a lower temperature (i.e., 2 degrees Celsius), then a glycol mixture (lower freezing point) will need to be used. Therefore, the process vessels are serviced by loop 1.

At Loop 2 are allocated the bioreactor jacket loop skids and the clean utilities systems. The bioreactor jacket loops must drain chilled water in their recirculation loop every batch to be replaced with plant steam. It was determined to be undesirable to implement this practice with a glycol solution due to the cost of replacing discarded glycol. Therefore, all jacket loop skids are serviced by loop 2.

The clean utility systems do not share the potential future requirement to achieve a lower temperature than 5 degrees Celsius. Therefore, the clean utilities are serviced by loop 2. While it would not have been inappropriate to place these systems on loop 1, it was desirable to more evenly distribute the load requirements across the two loops.

Based on the system philosophy, the chilled water system will have the following conditions:

Loop 1 – chilled water supply = 4 °C / chilled water return (glycol) = 7.2 °C

Loop 2 – chilled water supply = 6 °C / chilled water return = 10.7 °C

If this temperature will not sufficient to keep the process working correctly, the installation shall be prepared to operate with Propylene Glycol at the first Loop.

In this case, the chilled water system will have the following conditions:

Loop 1 – chilled water supply (glycol) = 0 °C / chilled water return (glycol) = 3.2 °C

Loop 2 – chilled water supply = 4 °C / chilled water return = 8.7 °C

To guarantee a balancing and a good distribution, static balancing valves were considered throughout the system:

- At by-passes at the end of the distribution headers;
- At the beginning of the distribution headers;
- At the process equipment inlet;
- At the chiller´s outlet.

4.1 CHILLERS

The chilled water system will have ONE chiller (PCH-7B-1) of nominal capacity of 300 TR (one operating).

The simultaneous peak load is 2,734,944.0 BTU/h (689,194.0 kcal/h) and it is equivalent to 228 TR.

So, the chiller has an oversizing of 24 % (72 TR) of thermal load, where the excess of flow rate is diverted to a future expansion (tie-in). The oversizing was considered at Loop 1 and at Loop 2 individually.

The chiller has the following instruments:

EQUIPMENT	FLUID	INLET LINE		OUTLET LINE	
		INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
PCH-7B-1	CHILLED WATER	TIT-980029	Temperature Indication High Temperature Alarm Low Temperature Alarm	TIT-980001	Temperature Indication High Temperature Alarm Low Temperature Alarm
		FIT-980029	Flow Rate Indication Low Flow – shut down the chiller	XV-980001	Automatic Valve to be closed when the chiller is shutted down
		PIT-980029	Pressure indication	PIT-980001	Pressure indication
		PDSHL-9800252 – High Differential Pressure or Low Differential Pressure shut down the chiller			
	COOLING WATER (1)	TIT-980013	Temperature Indication High Temperature Alarm Low Temperature Alarm	TIT-980014	Temperature Indication High Temperature Alarm Low Temperature Alarm
		-	-	XV-980014	Automatic Valve to be closed when the chiller is shutted down
		-	-	FIT-980014	Flow Rate Indication Low Flow – shut down the chiller
		PIT-980013	Pressure indication	PIT-980014	Pressure indication
		PDSHL-9800253 – High Differential Pressure or Low Differential Pressure shut down the chiller			

Notes:

1. For cooling water system, see the Description Report (PRD-PRO-MDE-009 - Drug Substance – Cooling Water System Description Report).

4.2 PRIMARY PUMP

The primary pump (P-PCH-7B-2) is centrifugal and was designed for a flowrate of 4725 LPM (283 M3/HR) and a manometric height of 15 mcl. For this operating condition the pump was selected with a motor of 18.5 kW.

The primary pump operates at a fixed speed for the design condition and for the maximum condition. The excess flow rate for the other conditions of the system will be directed to supply the Chiller through the Buffer Tank where the overflow occur from the cold side to the hot side of the tank.

The pump has the following instruments:

EQUIPMENT	SUCTION LINE		DISCHARGE LINE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
P-PCH-7B-2	TIT-980022	Temperature Indication High Temperature Alarm Low Temperature Alarm	-	-
P-PCH-7B-2	PI-980023	Pressure Indication	PI-980024	Pressure Indication
	SC-980023 – Speed controler for start-up of the pump			

4.3 BUFFER TANK

The Buffer Tank (BT-7B-1) was designed for an autonomy of 3 minutes to guarantee the thermal load when the chiller shuts down, considering that the chiller´s supplier recommended the minimum stabilization time of 2 minutes.

The tank was divided in two sides (cold side and hot side).

The design flow rate of the chilled water system considered for the sizing of the tank was 4725 LPM (283 M3/HR).

That way, the buffer tank will have a total volume of 30 M3 (15 M3 each side).

The buffer tank has the following instruments:

EQUIPMENT	COLD SIDE		HOT SIDE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
BT-7B-1	LG-9800250	Level sight glass	LG-9800251	Level sight glass
	LIT-980005A	Level Indication High Level – close the make-up valve (LV-980005) and stop de dosing pump (BM-7B-1) Low Low Level – open the make-up valve (LV-980005) and start de dosing pump (BM-7B-1)	LIT-980005B	Level Indication High Level – close the make-up valve (LV-980005) and stop de dosing pump (BM-7B-1) Low Low Level – open the make-up valve (LV-980005) and start de dosing pump (BM-7B-1)
	-	-	FIT-980021	Flow Rate Indication Low Flow Alarm
	-	-	PIT-980021	Pressure Indication
	-	-	TIT-980021	Temperature Indication

EQUIPMENT	COLD SIDE		HOT SIDE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
				High Temperature Alarm Low Temperature Alarm

4.4 MAKE-UP SYSTEM – LOOP 1

The make-up system will monitor and maintains system pressure, replacing water whenever there is a loss in the system.

The control of the replacing water is made by the level of the buffer tank (LIT-980005 A/B – for cold and hot side), that opens or closes the make-up line valve (LV-980005) whenever the level of the tank fluctuates.

4.5 AIR SEPARATOR – LOOP 1

The air separator is used to eliminate continuously the air dissolved at the chilled water. It is used to avoid noise problems, corrosion, pump cavitation and mechanical breakdowns.

It was designed for the flow rate of 4725 LPM (283 M3/HR) and will be installed at the primary pumps suction line.

The pressure drop of the air separator, considering the flow rate and the diameter of the line is 0,05 bar, according to the supplier information.

4.6 CHEMICAL DOSING SYSTEM – LOOP 1

The chemical dosing system is efficient to prevention slime generation, scaling, corrosion and to remove already formed slimes of the chilled water system.

The system is composed for one chemical dosing tank (TK-7B-2), one chemical dosing pump (BM-7B-1) and one spill containment pallet (CN-7B-1).

The chemical dosing system has the following instruments:

EQUIPMENT	INSTRUMENT	FUNCTION
TK-7B-2	LSL-980031	Low Level Alarm
BM-7B-1	HS-980005	Stops and starts the pump (LSH-980005 A/B – LSLL-980005 A/B)
CN-7B-1	LSH-980032	High Level Alarm

4.7 SECONDARY PUMP – LOOP 1

The secondary pump (P-PCH-7B-3) is centrifugal and was designed for a flow rate of 4725 LPM (283 M3/HR) and a manometric height of 20 mcl. For this operating condition the pump was selected with a motor of 30 kW.

The secondary pump will forward the chilled water until the equipment of Loop 1 and through the heat exchanger between loops.

The pump is controlled by a differential pressure transmitter PDIT-980010, maintaining constant the pressure drop of 1.5 bar at the main distribution header. The instrument is installed at a distance of 2/3 of the main distribution pipe total length, to guarantee a good control.

Each pump has the following instruments:

EQUIPMENT	SUCTION LINE		DISCHARGE LINE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
P-PCH-7B-3	FIT-980005	Flow Rate Indication Low Flow Alarm	-	
	PIT-980005	Pressure Indication	-	
	TIT-980005	Temperature Indication High Temperature Alarm Low Temperature Alarm	-	
P-PCH-7B-3	PI-980006	Pressure Indication	PI-980007	Pressure Indication
	SC-980006 – Speed controller of the pump (PDIT-980010)			

4.8 HEAT EXCHANGER

The heat exchanger (HX-7B-2) uses the chilled water of the Loop 1 to chill the water of Loop 2.

With Chilled water at Loop 1 at 4.0 °C, the water at Loop 2 will chill from 10.7 °C to 6.0 °C. With Propylene Glycol at Loop 1 at 0.0 °C, the water at Loop 2 will chill from 8.7 to 4.0 °C.

The design thermal capacity is 3,102,799.0 BTU/h (781,892.0 kcal/h).

The heat exchanger has the following instruments:

EQUIPMENT	INLET LINE		OUTLET LINE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
HX-7B-2 Loop 1 Side	FIT-070065	Flow Rate Indication Low Flow Alarm	PIT-070066	Pressure Indication
	PIT-070065	Pressure Indication	TIT-070066	Temperature Indication High Temperature Alarm Low Temperature Alarm
	TIT-070065	Temperature Indication High Temperature Alarm Low Temperature Alarm	TV-070001	Temperature Control Valve – controlled by TIT-070001
HX-7B-2 Loop 2 Side	TIT-070003	Temperature Indication High Temperature Alarm Low Temperature Alarm	FIT-070001	Flow Rate Indication Low Flow Alarm
	-	-	PIT-070001	Pressure Indication
	-	-	TIT-070001	Temperature Indication High Temperature Alarm Low Temperature Alarm

EQUIPMENT	INLET LINE		OUTLET LINE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
				Control the temperature control valve (TV-070001), installed at the return line at loop 1 side

4.9 SECONDARY PUMPS – LOOP 2

The secondary pump (P-PCH-7B-5) is centrifugal and was designed for a flowrate of 2800 LPM (168 M3/HR) and a manometric height of 34 mcl. For this operating condition the pump was selected with a motor of 30 kW.

The secondary pump will forward the chilled water until the equipment's of Loop 2.

The pump is controlled by a differential pressure transmitter PDIT-070001, maintaining constant the pressure drop of 2.0 bar at the main distribution header. The instrument is installed at a distance of 2/3 of the main distribution pipe total length, to guarantee a good control.

The pump has the following instruments:

EQUIPMENT	SUCTION LINE		DISCHARGE LINE	
	INSTRUMENT	FUNCTION	INSTRUMENT	FUNCTION
P-PCH-7B-5	FIT-070002	Flow Rate Indication Low Flow Alarm	-	
	PIT-070002	Pressure Indication Low Pressure Alarm High Pressure – close the make-up valve XV-070062) and stop de dosing pump (BM-7B-2) Low Pressure – open the make-up valve XV-070062) and start de dosing pump (BM-7B-2)	-	
	TIT-070002	Temperature Indication High Temperature Alarm Low Temperature Alarm	-	
P-PCH-7B-5	PI-070002	Pressure Indication	PI-070003	Pressure Indication
	SC-070002 – Speed controller of the pump, controlled by PDIT-070001			

4.10 MAKE-UP SYSTEM – LOOP 2

The make-up system will monitor and maintains system pressure, replacing water whenever there is a loss in the system.

The control of the replacing water is made by the pressure of the system, controlled at the pump suction line (PSHL-070002), that opens or closes the make-up line valve (XV-070062) whenever the pressure of the system fluctuates.

This system works together with the pressurized expansion tank to guarantee the pressure of the chilled water system.

4.11 PRESSURIZED EXPANSION TANK – LOOP 2

The pressurized expansion tank (TK-7B-1) is used to keep the system pressurized (together with the make-up system) and to absorb thermal expansions of the fluid.

According to supplier, for this system with a volume 5.8 m³ and static height 1.9 m, a tank with nominal capacity of 0.14 m³ is required.

The pressurized expansion tank (TK-7B-1) will work pressurized at 0.25 bar and has a safety valve (PSV-070056) that will response at 3 barg, according supplier reference.

4.12 AIR SEPARATOR – LOOP 2

The air separator is used to eliminate continuously the air dissolved at the chilled water. It is used to avoid noise problems, corrosion, pump cavitation and mechanical breakdowns.

The air separator was designed for the flow rate of 2800 LPM (168 M3/HR) and will be installed at the primary pumps suction line.

The pressure drop of the air separator, considering the flow rate and the diameter of the line is 0,09 bar, according to the supplier information.

4.13 CHEMICAL DOSING SYSTEM – LOOP 2

The chemical dosing system is efficient to prevention slime generation, scaling, corrosion and to remove already formed slimes of the chilled water system.

The system is composed for one chemical dosing tank (TK-7B-3), one chemical dosing pump (BM-7B-2) and one spill containment pallet (CN-7B-2).

The chemical dosing system has the following instruments:

EQUIPMENT	INSTRUMENT	FUNCTION
TK-7B-3	LSL-070063	Low Level Alarm
BM-7B-2	HS-070002	Stops and starts the pump (PSHL-070002)
CN-7B-2	LSH-070064	High Level Alarm

4.14 BALANCING VALVES

Along the chilled water system, balancing valves were considered to guarantee a balancing and a good distribution, as below:

- At by-passes at the end of the distribution headers;
- At the beginning of the distribution headers;

- At the process equipment inlet;
- At the chiller´s outlet.

The manual valves will be manually adjusted in the field, the valve must be adjusted to the design condition, according to the numbers of turns to be defined by manufacturer, according to the dimensioning performed in the Calculation Report.

4.15 CONSUMERS

4.15.1 LOOP 1

EQUIPMENT	TAG	FLOW RATE	INLET PRESSURE	OUTLET PRESSURE	Dp total (Note 1)
		(M3/hr)	(BARG)	(BARG)	(BAR)
250 L Media Prep Tank	TQ-5101	2.3	2.18	0.78	1.40
4500 L Media Prep Tank	TQ-5102	11.4	2.29	1.11	1.18
3800 L Media Hold Tank N°1	TQ-5201	11.4	2.30	1.12	1.18
3800 L Media Hold Tank N°2	TQ-5202	11.4	2.27	1.05	1.22
3800 L Media Hold Tank N°3	TQ-5203	11.4	2.30	1.13	1.17
3400 L Collection Vessel N°1	TQ-5701	11.4	2.25	0.93	1.32
3400 L Collection Vessel N°2	TQ-5702	11.4	2.21	0.89	1.32
4200 L Harvest Vessel N°1	TQ-5901	11.4	2.24	0.88	1.36
4200 L Harvest Vessel N°2	TQ-5902	11.4	2.20	0.85	1.35
500 L Buffer Prep Tank N°1	TQ-3701	4.6	2.16	0.75	1.41
3000 L Buffer Prep Tank N°2	TQ-3702	11.4	2.28	1.07	1.21
3000 L Buffer Prep Tank N°3	TQ-3703	11.4	2.22	0.92	1.31
320 L Bioreactor (Intermediate)	BRE-5501	0.5	2.27	1.11	1.16
2500 L Bioreactor (Chemostat) N° 1	BRE-5601	0.96	2.24	1.03	1.21
2500 L Bioreactor (Chemostat) N° 2	BRE-5602	0.96	2.27	1.07	1.20
2500 L Bioreactor (Chemostat) N° 3	BRE-5603	0.96	2.31	1.17	1.14
320 L Bioreactor Utility Panel	UP-5500	2.3	2.24	1.03	1.21
3800 L Media Hold Tank N°1 Utility Panel	UP-5201	2.3	2.22	0.93	1.29
3800 L Media Hold Tank N°2 Utility Panel	UP-5202	2.3	2.12	0.68	1.44
3800 L Media Hold Tank N°3 Utility Panel	UP-5203	2.3	2.12	0.69	1.43

Notes:

1. Total pressure drop considering 0,5 bar at the valve, 0,5 bar at the equipment, and the rest at the balancing valve, as shown at the calculation report (PRD-MEC-CLC-004 – Chilled Glycol and Chilled Water System Calculation (Process)).

4.15.2 LOOP 2

EQUIPMENT	TAG	FLOW RATE	INLET PRESSURE	OUTLET PRESSURE	Dp total (Note 1)
		(M3/hr)	(BARG)	(BARG)	(BAR)
40 L Bioreactor (Seed)	*BRE-5401*	2.8	2.02	0.10	1.92
320 L Bioreactor (Intermediate)	*BRE-5501-JL*	4.6	2.80	1.19	1.61
2500 L Bioreactor (Chemostat) N° 1	*BRE-5601-JL*	11.4	2.87	1.15	1.72
2500 L Bioreactor (Chemostat) N° 2	*BRE-5602-JL*	11.4	2.79	1.16	1.63
2500 L Bioreactor (Chemostat) N° 3	*BRE-5603-JL*	11.4	2.81	1.20	1.60
CPW Maintenance Cooler	*SK-6302 /TC-6302*	3.5	2.87	1.76	1.11
WFI Still	*MES-6401*	14.4	2.94	1.73	1.21
WFI Ambient Cooler	*SK-6401 /TC-9201*	53.4	2.56	0.89	1.67
Clean Steam Generator w/ Sample Cooler	*CSG-6501*	1.5	2.91	1.20	1.70
Clean Steam Sample Cooler (Med Prep)	*TC-6501*	0.4	2.37	0.59	1.78
Clean Steam Sample Cooler (Cell Cult)	*TC-6502*	0.4	2.38	0.63	1.75
Clean Steam Sample Cooler (DSP1)	*TC-6503*	0.4	2.42	0.76	1.66
Autoclave	*AT-9001*	3.6	2.18	0.39	1.79