BioProcess™ Modular System

2.2 Functional specification

Table of contents

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Document name	Document number	Document revision / date
2.2 Functional specification	29623228	AA / 04-Sep-2020
Product type	**Product code**	**Customer reference**
BioProcess Modular System 1 1/2 Inch	29597540	D1C1
Reference	**Product model revision**	**Page number**
20CY	N/A	1 of (18)

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1 Introduction

NOTE: This document is also valid for the following skids.

Product code	Reference	Customer reference
29597541	20CZ	D1C2
29597542	20DA	D1C3
29597543	20DB	D1C4
29597544	20DC	D2C1
29597545	20DD	D2C2
29597546	20DE	D2C3
29597547	20DF	D2C4
29597548	20DG	D3C1
29597549	20DH	D3C2
29597550	20DI	D3C3
29597551	20DK	D3C4

BioProcess Modular System is an automated liquid chromatography system built for process scale-up and large-scale biopharmaceutical manufacturing.

1.1 Purpose and scope

1.2 Purpose and scope

The purpose of this document is to specify the high-level functions included in the BioProcess Modular System, based on the P&ID [Ref ID 2].

Physical properties, utilities and environments are specified in the GS [Ref ID 3].

Only specifications with an ID are defined to be testable.

1.3 References

Ref. ID	Document name	Document number(s)
1	Terminology and Acronyms	29229457
2	Piping and Instrumentation Diagram	29616426
3	General Specification	29616428
4	Unit Design Specification	29616019

1.4 Terminology and acronyms

See [Ref ID 1].

Table 1. Product specific terminology

Term	Comment
B/E	Bind/Elute
CV	Column Volume
FT	Flow Through
HETP	Height Equivalent to a Theoretical Plate
UPS	Uninterruptible Power Supply

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2 Overview

This section specifies general functionality.

2.1 Hardware

ID	Specification
1000	The P&ID [Ref ID 2] defines piping and instrumentation on the system.
1010	The system supports redundant power supply to DeltaV controller.

2.2 Software

ID	Specification
1100	The DeltaV version used is 14.3.1.
1110	The library used is based on PCSD version 13.
1120	The resolution of the process pictures is 1920 x 1080.

2.3 Indication device

ID	Specification
1200	The cabinet is equipped with three indication lights: green, yellow, and red.
1210	Green light status: -Steady: System is powered up and ready. -Flashing: System is powered but not ready.
1220	Yellow light status: -Steady: System is running. -Flashing: System is in hold. -Off: System is not running.
1230	Red light status: -Flashing: One or more alarms are unacknowledged.
1240	The system has a buzzer which audible sound is activated when an alarm is triggered and is deactivated when the silenced button on the screen is pressed
1250	The system has a potential free remote alarm output that is active when one or more alarms are unacknowledged.

2.4 Functionality

ID	Specification
1400	Instrument ranges and digitals are set according to respective '*Range*' specified in GS [Ref ID 3].
1410	Engineering units are set according to respective '*Unit*' specified in GS [Ref ID 3].
1420	Alarm and warning levels are configurable.
1430	The system supports live trending.
1440	The system supports historical trending.
1450	CAN-instrument communication errors can be detected.
1460	The system detects if air supply is lost.
1470	The system can detect if powered from UPS.

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2.5 Critical alarms

Alarms are used by the unit to notify the user of exception conditions that have been detected by the control system and to historize those exceptions for use in electronic batch reporting.

Upon detection of a critical alarm the following occurs:

ID	Specification
1600	All pumps stop.
1610	The alarm condition is presented to the user.
1620	Valves will close in a predefined sequence.
1630	The system cannot be restarted unless alarm condition has been resolved.

2.6 Hard-wired interlocks

Hardware interlocks shall be provided where immediate response is required from the system. These interlocks are hard-wired to drive devices into a safe state and prevent them from changing state. A software feature shall redundantly disable these devices.

The system cannot be restarted unless the alarm condition has been resolved and the safety PLC has been reset by pressing the blue reset button.

The following events activate a hardware interlock:

ID	Specification
1700	Emergency stop.
1710	Post pump P-201.A system pressure > 4.4 bar (PT-115.1 or PT-115.2).
1720	Post pump P-201.B system pressure > 4.4 bar (PT-116.1 or PT-116.2).
1730	High difference between PT-115.1 and PT-115.2 (must not exceed 1/6 of the set range).
1740	High difference between PT-116.1 and PT-116.2 (must not exceed 1/6 of the set range).
1750	Electrically disconnected pressure sensor post pump P-201.A (PT-115.1 or PT-115.2).
1760	Electrically disconnected pressure sensor post pump P-201.B (PT-116.1 or PT-116.2).

2.7 Software interlocks

Software interlocks shall be provided to assure that equipment limits are not exceeded. These prevent potentially hazardous conditions from being reached on the equipment. Software interlocks are coded in the system to drive associated devices and control loops into a safe state and prevent them from changing state.

Details can be found at UDS document [Ref ID 4].

2.8 Recovery of power loss

Upon application of power to the system, the following occurs:

ID	Specification
2100	The controller initiates communication with the system.

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3 Process specifications

This section specifies process functionality.

3.1 Valve functions

The flow kits include automatic valves equipped with a pneumatic actuator and a position feedback.

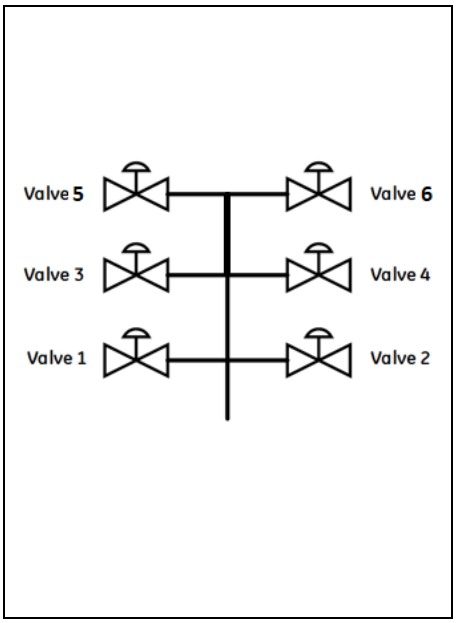
ID	Specification
2200	Valves can be set to open or close.
2210	Incorrect valve position is detected.
2220	Valves can be calibrated.
2230	The system detects if a valve is electrically disconnected.
2240	It is possible to monitor the Valve stroke times.
2250	Valve position is displayed in the process picture.

3.2 Inlet A equipment module

The Inlet A function is to provide control on liquid supply to Pump A.

ID	Specification
2400	Valves shall be set according to Table 2.
2410	Valves close after a time delay to keep an open path.

Table 2. Inlet A equipment module matrix.



1 = Open 0 = Close		State						
Valve	Equipment	Closed	Inlet A1	Inlet A2	Inlet A3	Inlet A4	Inlet A5	Inlet A6
1	XV-001	0	**1**	0	0	0	0	0
2	XV-002	0	0	**1**	0	0	0	0
3	XV-003	0	0	0	**1**	0	0	0
4	XV-004	0	0	0	0	**1**	0	0
5	XV-005	0	0	0	0	0	**1**	0
6	XV-006	0	0	0	0	0	0	**1**

3.3 Inlet B equipment module

The Inlet B function is to provide control on liquid supply to Pump B.

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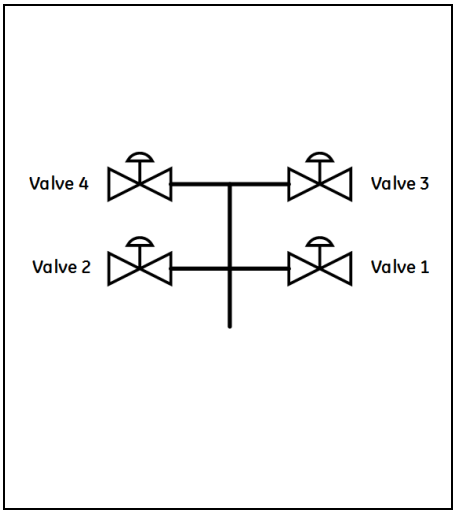
ID	Specification
2500	Valves shall be set according to Table 3.
2510	Valves close after a time delay to keep an open path.

Table 3. Inlet B equipment module matrix.



1 = Open 0 = Close		State				
		Closed	Inlet B1	Inlet B2	Inlet B3	Inlet B4
Valve	**Equipment**					
1	XV-011	0	**1**	0	0	0
2	XV-012	0	0	**1**	0	0
3	XV-013	0	0	0	**1**	0
4	XV-014	0	0	0	0	**1**

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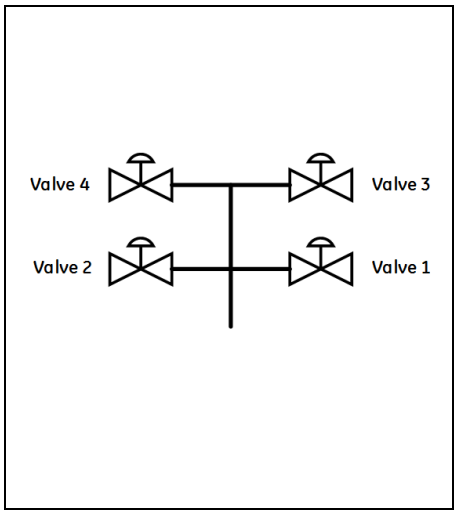
3.4 Inlet CIP equipment module

The Inlet CIP function is to provide control on liquid supply to CIP manifolds.

ID	Specification
2600	Valves shall be set according to Table 4.
2610	Valves close after a time delay to keep an open path.

Table 4. CIP inlet equipment module matrix.



1 = Open 0 = Close		State				
		Closed	CIP inlet1	CIP inlet2	CIP inlet3	CIP inlet4
Valve	**Equipment**					
1	XV-081	0	**1**	0	0	0
2	XV-082	0	0	**1**	0	0
3	XV-083	0	0	0	**1**	0
4	XV-084	0	0	0	0	**1**

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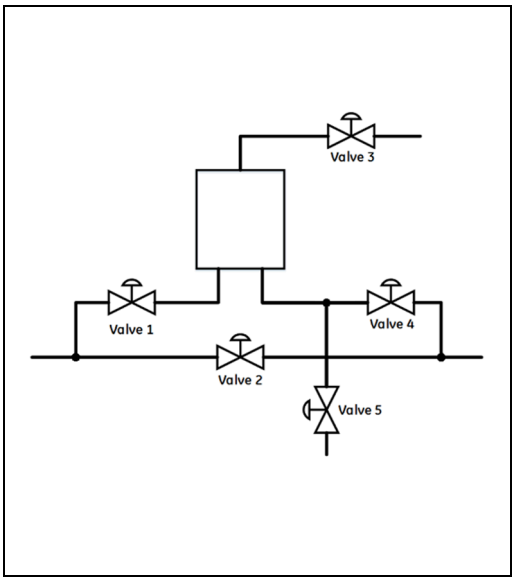
3.5 Air trap equipment module

The main purpose of the air trap is to remove air from liquid in order to prevent air to enter the column.

ID	Specification
2700	Valves shall be set according to Table 5.
2710	Valves close after a time delay to keep an open path.
2720	High liquid level is monitored.
2730	Low liquid level is monitored.
2740	Level monitors status is visible in the process picture.
2750	The system detects if a level sensor is electrically disconnected.
2760	The air trap can be automatically filled to the high level when low level is detected.
2770	It is possible to calibrate each level sensor.

Table 5. Air trap equipment module matrix.



1 = Open 0 = Close		State					
		Inline	Bypass	Fill	Fill In-line	Drain	Out Through Drain
Valve	**Equipment**						
1	XV-021	**1**	0	**1**	**1**	0	**1**
2	XV-022	0	**1**	0	0	0	0
3	XV-023	0	0	**1**	**1**	**1**	0
4	XV-024	**1**	0	0	**1**	0	0
5	XV-071	0	0	0	0	**1**	**1**

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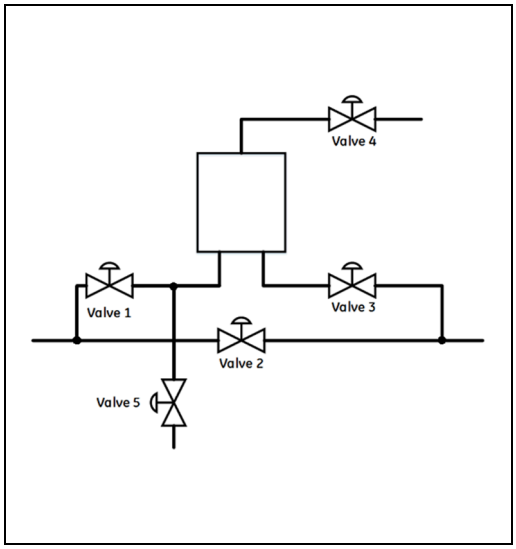
3.6 Filter equipment module

The main purpose of the filter is to remove impurity particles from liquid in order to prevent impurity particles to enter the column.

ID	Specification
2900	Valves shall be set according to Table 6.
2910	Valves close after a time delay to keep an open path.

Table 6. Filter equipment module matrix.



1 = Open 0 = Close		State					
Valve	Equipment	Inline	Bypass	Fill	Fill In-line	Drain	Out Through
1	XV-025	**1**	0	**1**	**1**	**1**	**1**
2	XV-026	0	**1**	0	0	**1**	0
3	XV-027	**1**	0	0	**1**	**1**	0
4	XV-028	0	0	**1**	**1**	**1**	0
5	XV-072	0	0	0	0	**1**	**1**

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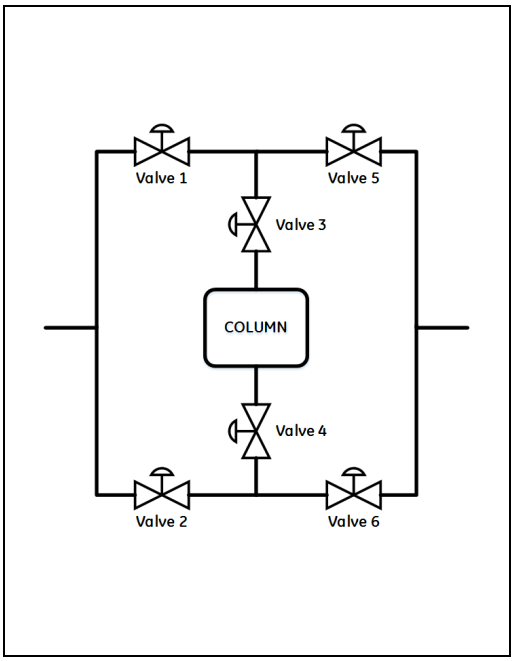
3.7 Column equipment module

There is a function controlling the flow through the column. The flow can be directed:

- Bypass(includes 3 types): the liquid travels bypass the column
- Downflow: the liquid travels from the column top to the column bottom
- Upflow: the liquid travels from the column bottom to the column top

ID	Specification
3000	Valves shall be set according to Table 7.
3010	Valves close after a time delay to keep an open path.

Table 7. Column equipment module matrix.



1 = Open 0 = Close		State				
Valve	Equipment	Bypass Both	Bypass Over	Bypass Under	Up Flow	Down Flow
1	XV-031	**1**	**1**	0	0	**1**
2	XV-032	**1**	0	**1**	**1**	0
3	XV-033	0	0	0	**1**	**1**
4	XV-034	0	0	0	**1**	**1**
5	XV-035	**1**	**1**	0	**1**	0
6	XV-036	**1**	0	**1**	0	**1**

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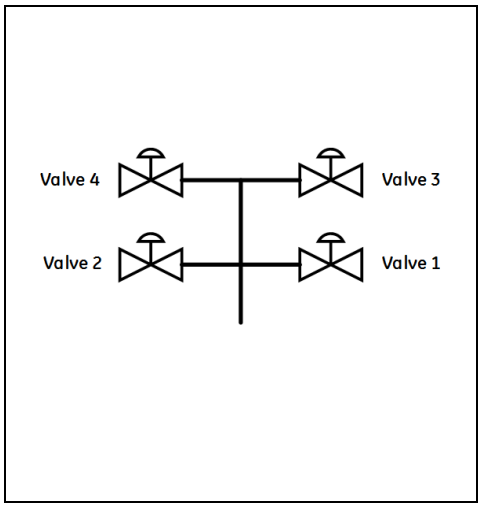
3.8 Outlet equipment module

The Outlet module provides control of the flow path and process connections/interface from the chromatography step to following steps downstream. There are four outlets on the system to collect various fractions before, during and after the separation.

ID	Specification
3100	Valves shall be set according to Table 8.
3110	Valves close after a time delay.

Table 8. Outlet equipment module matrix.



1 = Open 0 = Close		State				
		Closed	Outlet 1	Outlet 2	Outlet 3	Outlet 4
Valve	**Equipment**					
1	XV-051	0	**1**	0	0	0
2	XV-052	0	0	**1**	0	0
3	XV-053	0	0	0	**1**	0
4	XV-054	0	0	0	0	**1**

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3.9 Flow control equipment module

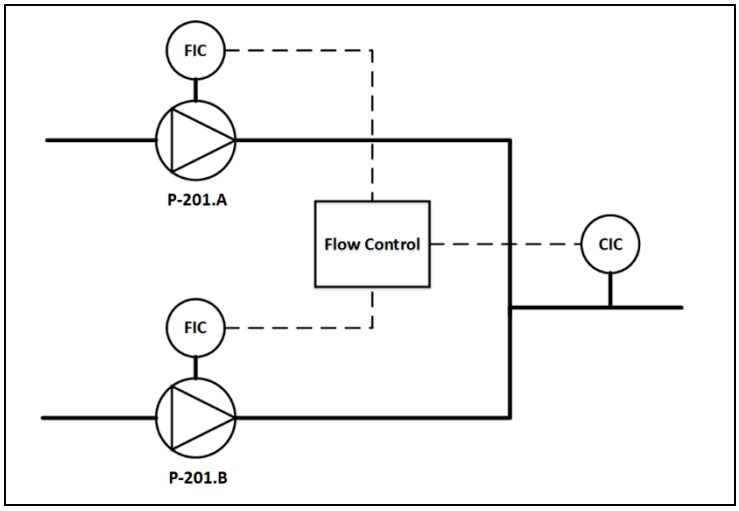
In manual flow control mode, the pump speed is set to a fixed value that is a percentage of the full pump motor speed. This mode operates without any closed-loop flow feedback control.

In flow control mode, the pump speed is regulated based on feedback from a flow meter. The user entered flow rate acts as a setpoint for the flow control system.

A simplified schematic of the flow control is shown in Figure 1.

ID	Specification
3200	There is a pump (P-201.A) post Inlet A.
3210	There is a pump (P-201.B) post Inlet B.
3220	P-201.A has higher priority than P-201.B, i.e. in a situation where the system must choose between pumps.
3230	Pump speed can be controlled manually.
3240	Pump speed can be controlled by flow feedback.
3250	To run a pump a valid flow path, from inlet through outlet or drain, must exist.

Figure 1 – Flow control



3.9.1 Gradients

Gradient flow is achieved by two pumps delivering liquid to the system flow path. The gradient flow can be operated as pump flow assigned through a calibrated flow to pump speed factor.

A simplified schematic of the gradients flow control is shown in Figure 1.

ID	Specification
3500	It is possible to run a manual gradient without feedback.
3510	It is possible to run a flow gradient with control based on flow feedback.
3520	It is possible to run a conductivity gradient with control based on conductivity feedback.
3530	It is possible to set gradient ratio in percentage.

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ID	Specification
3540	It is possible to set when target flow or conductivity gradient ratio should be reached in either time or volume.
3550	It is possible to tune flow feedback with the PID regulator for each pump.
3560	It is possible to tune conductivity feedback with the PID regulator.
3570	It is possible to set a max pre column pressure. Flow is then reduced to keep pressure below this level.

3.10 Pressure control valves

The pressure control valves are located after pumps to avoid uncontrolled liquid flow through pumps.

ID	Specification
3700	A pressure control valve is located post P-201.A to avoid uncontrolled liquid flow through P-201.A
3710	A pressure control valve is located post P-201.B to avoid uncontrolled liquid flow through P-201.B
3720	Pressure is monitored for feedback to pressure control valve, located post P-201.A
3730	Pressure is monitored for feedback to pressure control valve, located post P-201.B
3740	Pressure is displayed in the process picture.

3.11 Air detection

The system is connecting 2 air sensors, which are designed for continuous monitoring of air bubbles in the flow path.

ID	Specification
3800	Inlet air detection is monitored by a movable sensor.
3810	Air detection is monitored pre column.
3820	The system can detect if an air sensor is electrically disconnected.
3840	Air status is displayed in the process picture.
3850	It is possible to calibrate each air sensor.

3.12 Conductivity monitoring

ID	Specification
4000	Conductivity is monitored post pumps.
4010	Conductivity is monitored post column.
4020	Conductivity is displayed in the process picture.
4030	It is possible to enable/disable temperature compensation.
4040	The conductivity sensor can be calibrated.
4050	The system detects if a conductivity sensor is electrically disconnected.
4060	Conductivity is displayed in the process picture.

3.13 Flow monitoring

ID	Specification
4200	Flow is monitored post P-201.A
4210	Flow is monitored post P-201.B

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ID	Specification
4220	Flow is calculated pre column
4230	It is possible to make a zero-point adjustment.
4240	It is possible to totalize pre column accumulated volume.
4250	It is possible to totalize column up flow accumulated volume.
4260	It is possible to totalize column down flow accumulated volume.
4270	The system detects if a flow transmitter is electrically disconnected.
4280	Flow and totalizer values is displayed in the process picture.

3.14 pH monitoring

ID	Specification
4400	pH is monitored pre column.
4410	pH is monitored post column.
4420	It is possible to enable/disable temperature compensation.
4430	The pH sensor can be calibrated.
4440	The system detects if a pH sensor is electrically disconnected.
4450	pH is displayed in the process picture.

3.15 Pressure monitor

ID	Specification
4600	Pressure is monitored pre air trap.
4620	Pressure is monitored pre column.
4630	Pressure is monitored post column.
4640	Filter delta pressure is monitored (include air trap).
4650	Column delta pressure is monitored.
4660	The system detects if a pressure sensor is electrically disconnected.
4670	Pressure is displayed in the process picture.

3.16 Temperature monitoring

ID	Specification
4800	Temperature is monitored post pumps, integrated in conductivity sensor.
4810	Temperature is monitored post column, integrated in conductivity sensor.
4820	Temperature is monitored inside system cabinet.
4830	The system detects if a temperature sensor is electrically disconnected.
4840	Temperature is displayed in the process picture (except cabinet temperature).

3.17 UV monitoring

ID	Specification
4900	UV level is monitored post column.
4910	It is possible to select wavelength between 215nm, 254nm, and 280nm.
4920	It is possible to select multiple wavelengths.
4930	It is possible to set the UV averaging time.
4940	It is possible to zero the process value.

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ID	Specification
4950	It is possible to turn the UV lamp on and off.
4960	It is possible to monitor the UV lamp runtime and reset runtime value to zero.
4970	UV level is displayed in the process picture.

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4 Phase specifications

This section specifies implemented Phases.

ID	Specification
4100	System supports a Phase for INIT
4110	System supports a Phase for FILL
4120	System supports a Phase for PRIME INLET
4130	System supports a Phase for PRIME SYSTEM
4140	System supports a Phase for WASH
4150	System supports a Phase for LOAD_BE
4160	System supports a Phase for ELUTION
4170	System supports a Phase for LOAD_FT
4180	System supports a Phase for WASH_FT
4190	System supports a Phase for AxiChrom priming, packing and unpacking
4200	System supports a Phase for evaluating column performance (HETP and Asymmetry)

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