Installation and Operational Qualification Protocol no.: 01
Project 9B

Title:

Falling Film Evaporator –9B

Preparation		
Prepared by: Initials:	Date: 09.11.2020	Signature: Team 4
Examined by: Initials:	Date: 11.11.2020	Signature: Team 4

Approvals		
Approved by: **Production responsible:**		
Initials: _____	Date: 12.12.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.12.2020	Signature: _____

TABLE OF CONTENTS

1.0 OBJECTIVE

The objective of this Installation Qualification and Operational Qualification Protocol is to describe the tests and test conditions for the installation and following operational qualification of the Pharma A/S utility plant: Falling film evaporator. (Plant ID: 9B)

2.0 SCOPE

This protocol covers the IQ and OQ of the falling film evaporator, which will be used to concentrate the product from ultrafiltration 3-4 times for production of BP29F. The concentrated product from this plant is further separated in chromatographic ion in the following plant : (Plant ID: 11D). The last step is transforming the liquid into fine solid powder, which can later be used to make tablets. This transformation happens in the sprayer plant. (kilde: big pharma)

3.0 RESPONSIBILITIES

The following departments of Pharma A/S have responsibility related to this procedure:

The Engineering Dept. for:
This protocol and the associated test plans and test sheets;

The Production Dept. for:
To perform the practical qualification and decide if tests are OK or not;

The QA Dept. for:
Approval of this IQ/OQ Protocol;
Evaluate and approve possible deviation sheets from the practical qualification;

4.0 SYSTEM DESCRIPTION

The falling film evaporator is a process used for concentrating solution by evaporation. Falling film evaporators are used in the chemical and paper industry and in the food industry for e.g. in the sugar and dairy production [5]. The plants can be large and the economy very dependent upon the capacity. Regular cleaning is very important in order to minimize material buildup..

FFE works by adding the solution, which is desired to be concentrated, to the top of the evaporator and distributed by an arrangement of vertical pipes over the inlet of the heating tubes. The liquid film will then start to boil due to the external heating of the tubes by steam or hot water and is partially evaporated as a result, where it will be dragged downwards by the vacuum pump (P3). After that the concentrated solution will be collected in the bottom of the evaporator, where the centrifugal pump (P2), and the valve positions will separate the concentrated liquid in the product exit. Solvent vapour passes to the condenser unit, where the major quantity of the solvent vapour will condense by a cooling water coil. From the condenser, the condensate exits by the vacuum pump (P3). The entire process is illustrated in the P&I diagram in figure 1.
The requested evaporation capacity for FFE is 75 liter liquid product per batch and the needed evaporation capacity is 25 liter water/h. The main control parameter is the conductivity (CI2) of the concentrated product.

Main components:

- Feed tank (100 liter) (T1)
- Feed Heat exchanger (HE1)
- Feed pump (P1), Product Pump (P2), Vacuum Pump (P3)
- Evaporator Unit
- Condenser Unit

Instrumentation:

- Flowmeter evaporator entry (FI1), Flowmeter for recirculation (evaporator) (FI2), Flowmeter evaporator heat supply (FI3), Flowmeter condenser drain (FI4), Flowmeter product pump (FI5)
- Conductivity indicator product pump (CI2)
- Temperature indicator heat exchanger (TI1), Temperature indicator evaporator (TI2), Temperature indicator condenser (T3),Temperature indicator cooling water entry (TI10), Temperature indicator cooling water exit (TI11), Temperature indicator for heat supply entry (TI12), Temperature indicator for heat exchanger exit (TI13), Temperature indicator heat supply exit (TI14)
- Pressure indicator condenser (PI3), Pressure indicator product outlet (PI5), Pressure transmitter condenser (PT3)
- Level transmitter evaporator (LT1), Level indicator evaporator (LS1)

P&I diagram for the unit:

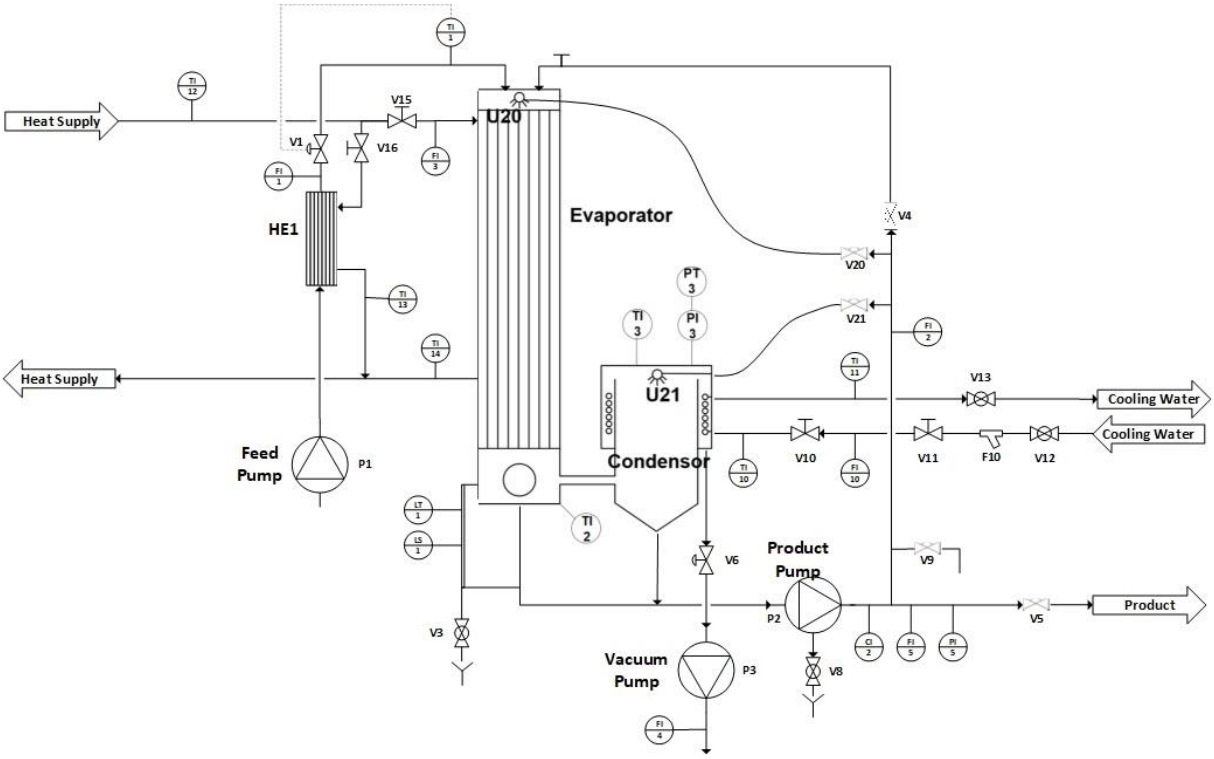


Figure 1. P&I Diagram.

5.0 REFERENCE DOCUMENTS

[1] Validation Master Plan for Pharma A/S version XX, date YY (Imaginary document)

[2] User Requirement Specification for Reverse Osmosis plant, version XX, date: YY (Your URS document)

[3] Pharma A/S Instruction no. 21, Performing of Installation and Operation Qualification, version XX.*(Imaginary document)*
[4] Pharma A/S Deviation Sheet, latest version.

[5] *Larsen*, Sten, *Plant description 9B - Falling film evaporator*, Course 28855 - GMP in pharma, biotech and food industry, DTU chemical engineering Pilot Plant, PDF, Accessed: 24.09.2020

6.0 TEST PLANS

The Installation and Operational Qualification shall take place at Pharma A/S new plant at Lyngby Denmark.
The following test plans with accompanying test sheets are to be generated and practically performed after the completed installation on the site:

Test plan no. IQ1 General requirements

Scope:
This test plan is used for Installation Qualification tests at Pharma A/S.
This test plan belongs to the IO/OQ Protocol no.: 01 (Ref. [1]) and is prepared and approved as a part of that document.
Practical qualification work shall follow the specific Validation Master Plan for this project Ref. [1], and the general directions of the Pharma A/S Instruction no. 21, Ref. [3]

Test purpose:
The Installation Qualification tests specified in this test plan shall ensure that the installation of the equipment specified in the URS Ref. [2] has been done correctly.

Test procedure:
The control of the assembly and installation of the equipment and components are performed by using the test sheet no. IQ1-xx and is to verify the following subjects:

Test	Description of test scope and test procedure	Test sheet	Test for URS requirement *1)*
1	Compliance between P&I diagram and physical plant Use a copy of a PI-diagram and check by marking (√ or ÷) on the diagram for every controlled component / instrument.	IQ1-01 P&I diagram to be used	5.1.1.2
2	All components are physically marked with TAG number according to P&I diagram, Use a copy of a PI-diagram and check by marking (√ or ÷) on the diagram for every controlled component / instrument.	IQ1-02 P&I diagram to be used	5.1.1.5
3	Dead legs must be minimized. All dead legs must be noted, and the ratios must be calculated.	IQ1-03 P&I diagram to be used	5.1.3.1

4	Installations shall be self drainable. Inclination of pipes shall be > 0.5% towards drain points. Note all controlled pipes, and calculate the inclination	IQ1-04 P&I diagram to be used	5.1.3.2
5	All piping shall be marked with flow direction and fluid ID	IQ1-05 P&I diagram to be used	5.1.3.4
6	Valves to be hygienic design, preferable diaphragm valves	IQ1-06 P&I diagram to be used	5.1.3.5
7	Where piping is required to be able to separate, the following pipe connections are acceptable: Tri-clamps, flanges with O-ring gaskets.	IQ1-07 P&I diagram to be used	5.1.5.1
8	At exit drain points a distance of minimum 50 mm from exit pipe to drain is required.	IQ1-08 P&I diagram to be used	5.1.6.1

1): URS requirement numbering to follow your specific URS.

Accept criteria:
The following criteria shall be fulfilled and noted in the observation part of the test sheet.

1	All components shall be present and located as specified on the PI-diagram.
2	All components shall be TAG numbered as specified on the PI-diagram.
3	Ratio L/d <3
4	0.5% inclination of pipes towards drain point.
5	Clear indication of Flow direction and fluid type
6	Membrane valves and preferably diaphragm valves are acceptable
7	Tri-clamps and flanges with o-ring gaskets are acceptable
8	All drain points must be measured and noted to be a minimum of 50mm from pipe to drain.

The test plans with their test sheets are prepared according to Pharma A/S Instruction no. 21 Ref. [3]. They are considered to be an integral part of this protocol.

7.0 PERFORMING TEST WORK

The practical qualification test work is performed according to Pharma A/S Instruction no. 21, current version, Ref. [3]
The test work as well as the reporting must only be done by personnel qualified by the requirements listed in Instruction no. 21 and documented by test plan no. Q1.

The OQ test work according to the OQ test plans of this protocol must only be initiated after all relevant IQ requirements are fulfilled and no open relevant deviations exist.

8.0 DEVIATIONS

In case an acceptance criteria is not fulfilled for a qualification test, a deviation must be generated. Deviations are documented on the Deviation Sheet, current version (Ref. [4]), according to Instruction no. 21. Deviation sheets shall clearly identify the failed acceptance criteria and should propose a corrective measure. Deviations are numbered in succession and must be approved by a Pharma A/S QA dep. representative.

All deviations and any associated re-tests are included in the resulting IQ/OQ report.

9.0 REPORTING

The results from this Installation and Operational qualification are collected and described in an IQ/OQ Report. *(Team Work 6)*

10.0 CHANGE LOG

Date	Initials	Version	Description
12.11.2020	*Team 4*	*1.0*	*This is first version*

APPENDICES:

Only the real test plans are mentioned and attached

1. Test plan no. IQ1-01
2. Test plan no. IQ1-02
3. Test plan no. IQ1-03
4. Test plan no. IQ1-04
5. Test plan no. IQ1-05
6. Test plan no. IQ1-06
7. Test plan no. IQ1-07
8. Test plan no. IQ1-08

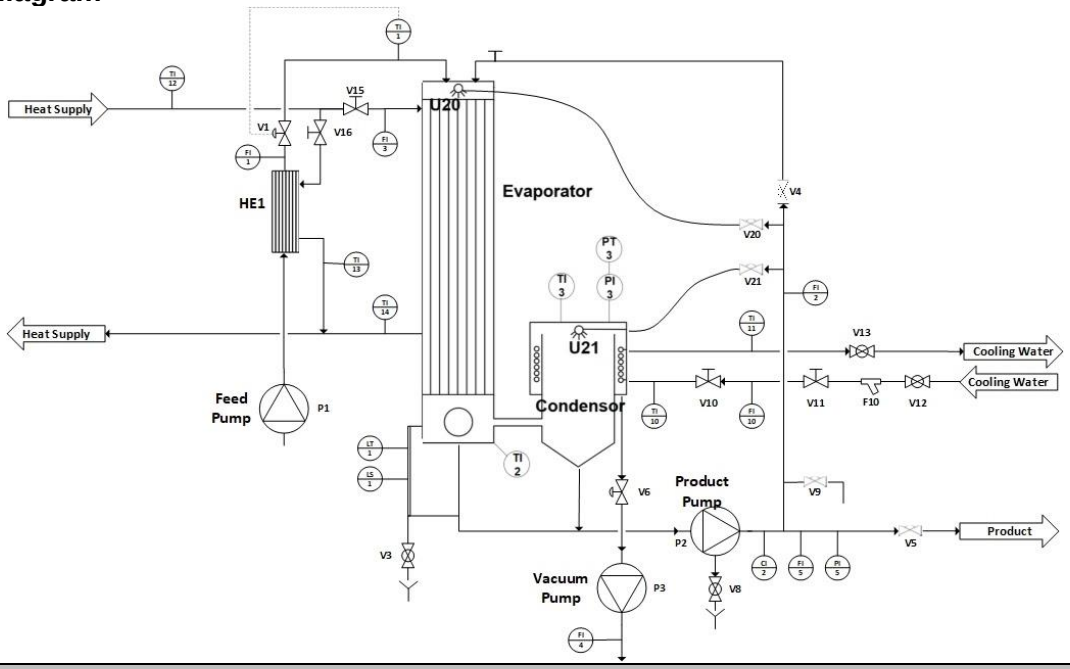
Test sheet no. IQ-01

Scope: To verify if P&I diagram and the physical plant is in compliance with each other.

Test procedure: Use a copy of a PI-diagram and check by marking (√ or ÷) on the diagram for every controlled component / instrument.

Acceptance criteria is: All components shall be present and located as specified on the PI-diagram.

P&I diagram



Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

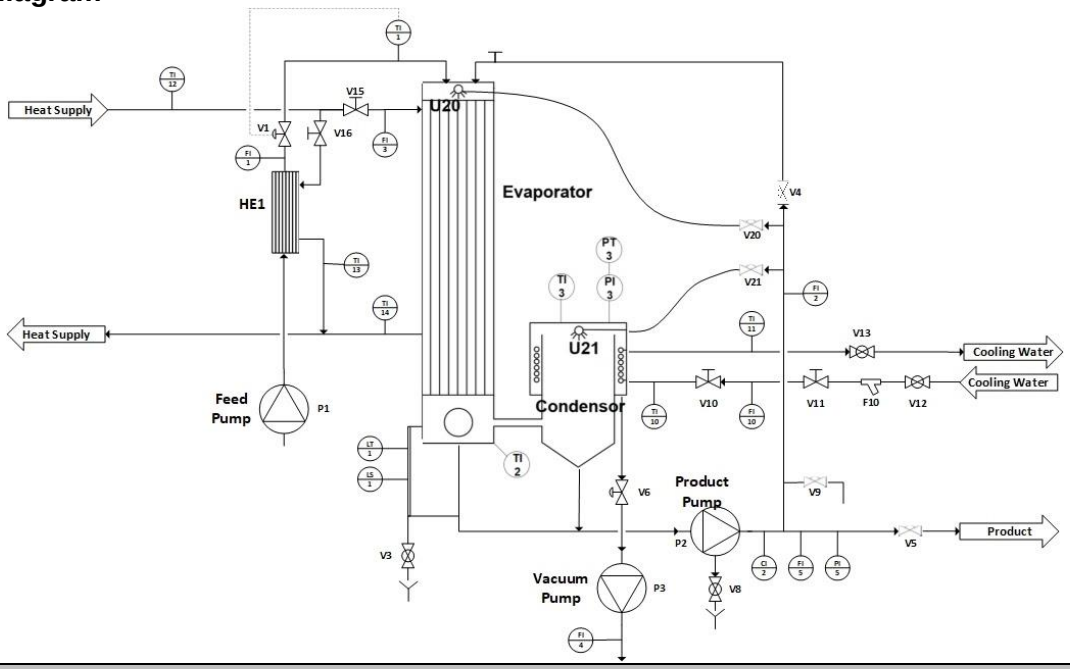
Test sheet no. IQ-02

Scope: To verify that all components are equipped with a TAG number according to P&I diagram

Test procedure: Use a copy of a PI-diagram and check by marking (√ or ÷) on the diagram for every controlled component / instrument.

Acceptance criteria is: All components shall be TAG numbered as specified on the PI-diagram.

P&I diagram



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Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

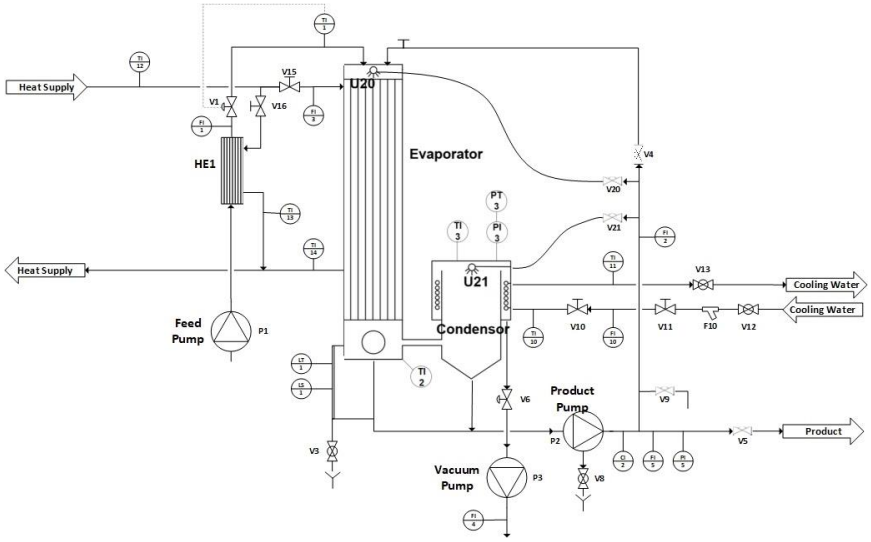
Test sheet no. IQ1-03

Scope: The scope of this test is to check that all dead legs are minimized. All dead legs must be noted, and the ratios must be calculated.

Test procedure: Measure the inner diameter (d) and the length (L) of the pipe. Calculate the ratio out of following formula:
L/d

Acceptance criteria is: That Ratio L/d < 3

P&I diagram



Dead leg	L (length)	D (diameter)	Ratio – Accepted (+ or -)

Approvals		
Approved by: **Production responsible:**		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

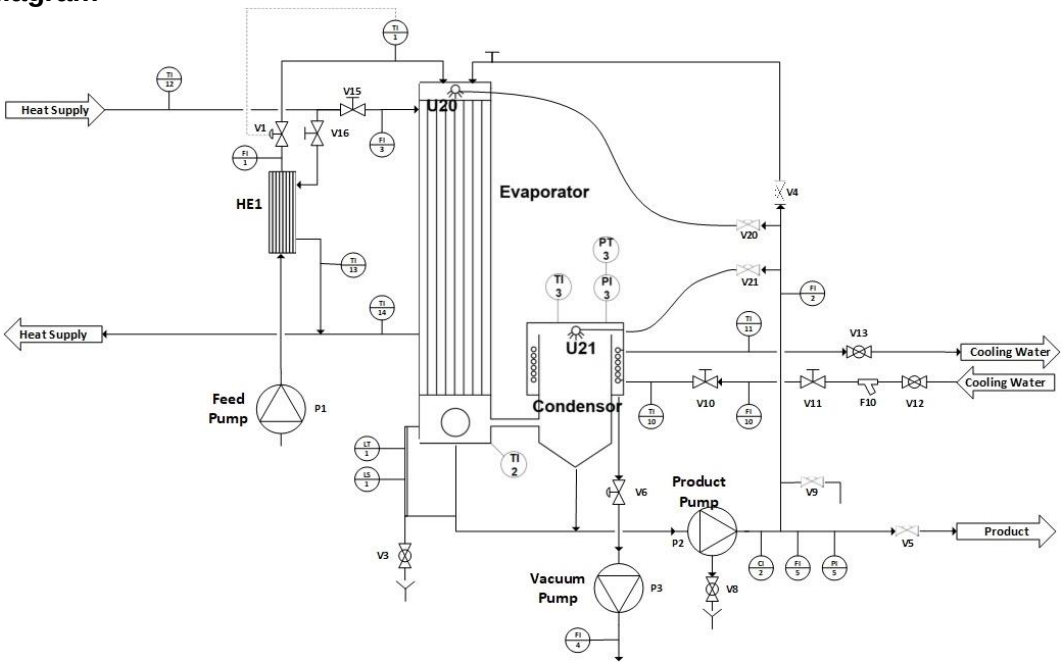
Test sheet no. IQ1-04

Scope: The scope of this test is to check that all installations are self-drainable

Test procedure: The length and height from pipe should be measured. Note all controlled pipes and calculate the inclination.

Acceptance criteria is: 0.5% inclination of pipes towards drain point.

P&I diagram



Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

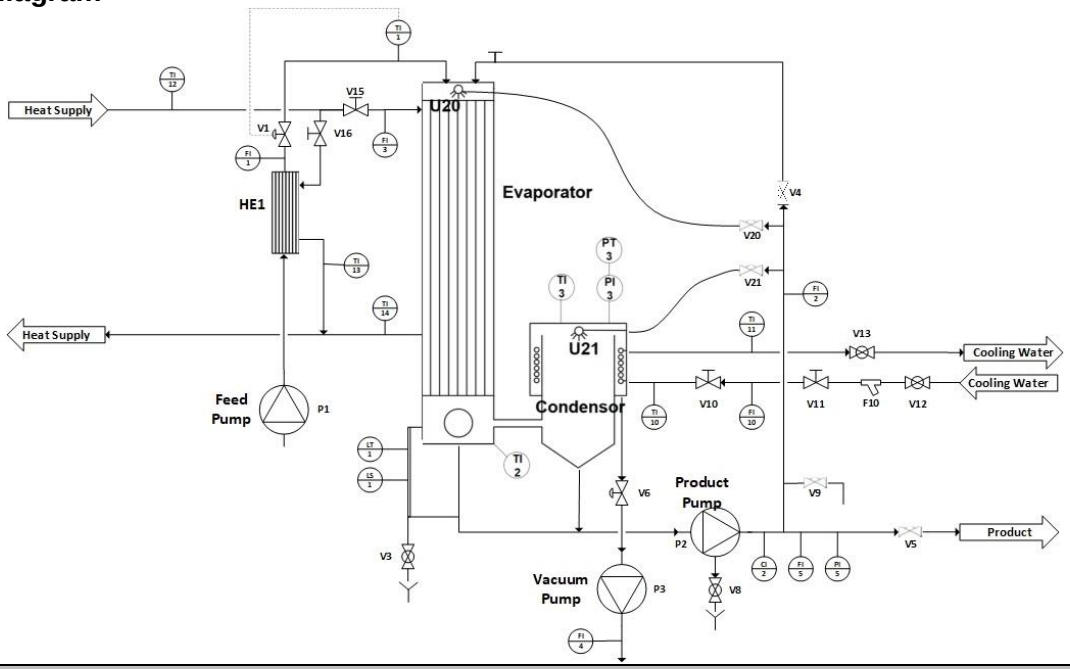
Test sheet no. IQ-05

Scope: The scope is to check that all piping are marked with flow direction and fluid ID

Test procedure: Check the P&I diagram below that all piping are marked with flow direction and fluid ID.

Acceptance criteria is: A clear indication of flow direction and fluid type

P&I diagram



Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

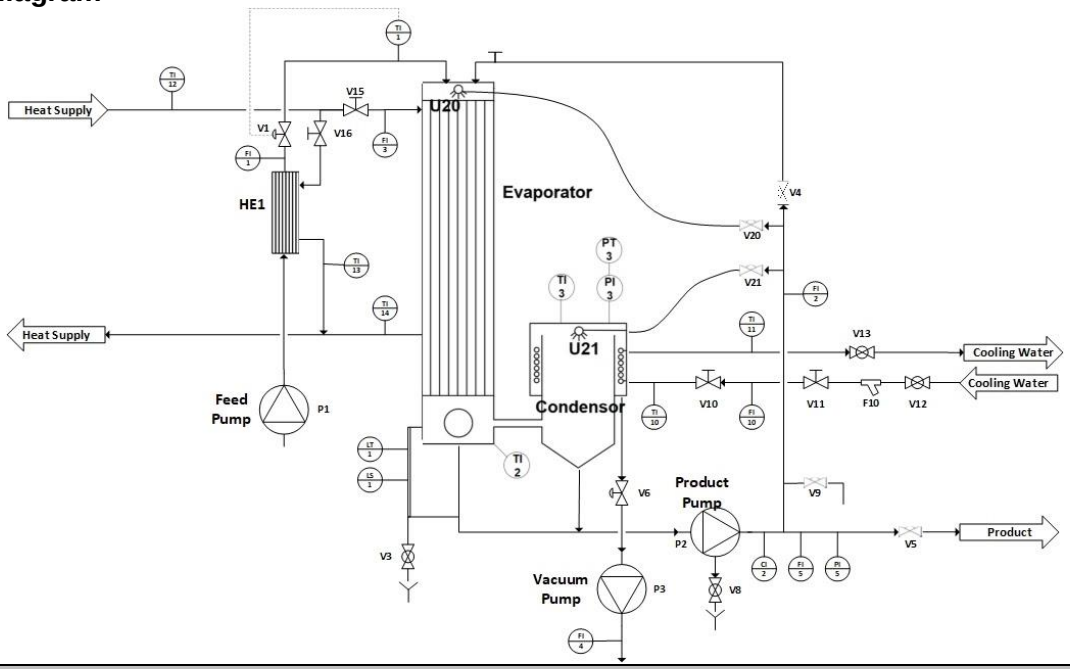
Test sheet no. IQ-06

Scope: The scope of this test sheet is to check that all the valves follow hygienic design. That all valve in contact with product are membrane valves.

Test procedure: Check the P&I diagram below that all valves follow hygienic design.

Acceptance criteria is: That membrane valves and preferably diaphragm valves are acceptable.

P&I diagram



Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

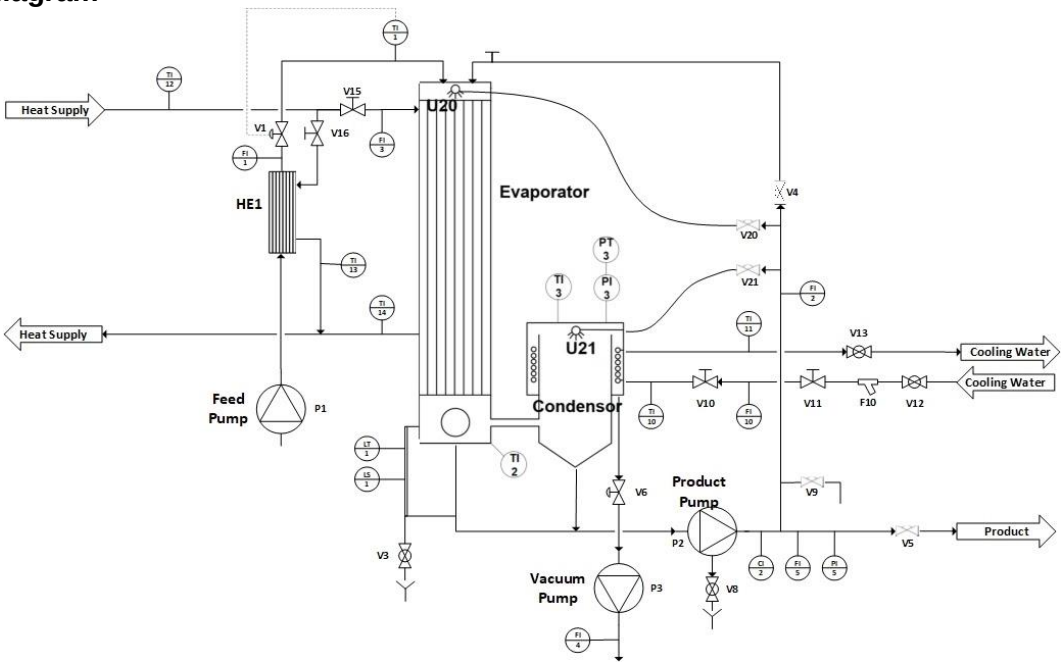
Test sheet no. IQ-07

Scope: The scope is to check that all separable pipe connections are acceptable.

Test procedure: Go through the P&I diagram, and mark ever pipe connection with “A” for accepted or “R” for rejected.

Acceptance criterium is: that pipe connections must by must be tri-clamps or flanges with O-ring gaskets.

P&I diagram



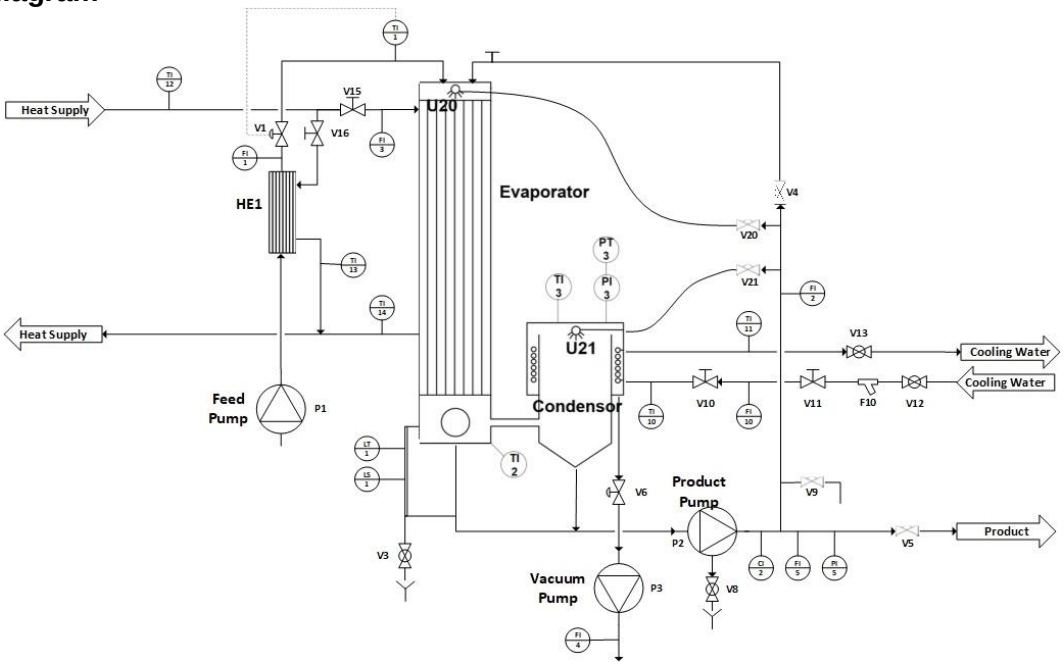
Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

Test sheet no. IQ-08

Scope:
The scope of this test sheet is to check that exit drain points are at a minimum distance of 50mm from exit pipe to drain.

Test procedure:
Locate all exit drain points on the FFE unit. Use measuring tape to measure the distance from the exit pipe to the nearest drain. If the distance is higher than 50mm, mark the exit pipe on the P&I diagram with “A” for accepted. If the distance is lower than 50mm, mark the exit pipe on the P&I diagram with “R” for rejected.

P&I diagram



Approvals		
Approved by:		
Production responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____
QA-responsible:		
Initials: _____	Date: 12.11.2020	Signature: _____

Test plan no. OQ1 Calibration of Instruments

Scope:
This test plan is used for Operation Qualification tests at Pharma A/S.
This test plan belongs to the IO/OQ Protocol no.: XX, Ref. [1], and is prepared and approved as a part of that document.
Practical qualification work shall follow the specific Validation Master Plan for this project Ref. [1], and the general directions of Pharma A/S Instruction no. 21, Ref. [3]

Test purpose:
The Operation Qualification tests specified in this test plan shall ensure that the installation and function of the equipment specified in the URS Ref. [2] has been done correctly.

Test procedure:
The tests are performed using the test sheet no. OQ7-01 and OQ7-02 and to verify the following parameters:

Test	Description of test scope and test procedure	Test sheet *2)*	URS requirement *1)*
1	Flowmeter evaporator entry (raw material) flow (FI1) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.1
2	Flowmeter for recirculation (evaporator) flow (FI2) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.2
3	Flowmeter evaporator heat supply (FI3) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.3
4	Flowmeter condenser drain (FI4) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.4
5	Flowmeter product pump (FI5) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.5
6	Flowmeter condenser cooling water (FI10) SOP XF – Calibration of flowmeters 0-1000 L/h	OQ7-01	4.7.6
7	Conductivity indicator product pump (product) (CI2) SOP XC – Calibration of inline conductivity sensor/transmitters 0-100 µS/cm	OQ7-02	4.7.7
8	Temperature indicator heat exchanger (TI1) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.8
9	Temperature indicator heat evaporator (TI2) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.9
10	Temperature indicator condenser (TI3) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.10
11	Temperature indicator cooling water entry(TI10) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.11
12	Temperature indicator cooling water exit (TI11) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.12
13	Temperature indicator heat supply entry(TI12) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.13

14	Temperature indicator heat exchanger exit (TI13) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.14
15	Temperature indicator heat supply exit (TI14) SOP XT1 – Calibration of inline temperature sensor/transmitters 0-100°C	OQ7-03	4.7.15
16	Pressure sensor condenser (PI3) SOP XP1 – Calibration of inline manometers 0-20 barg	OQ7-04	4.7.16
17	Pressure sensor product outlet (PI5) SOP XP1 – Calibration of inline manometers 0-20 barg	OQ7-04	4.7.17
18	Pressure transmitter condenser (PT3) SOP-XTm1 – Calibration of transmitters 0-20 mAmp	OQ7-05	4.7.18
19	Level transmitter evaporator SOP-XTm1 – Calibration of transmitters 0-20 mAmp	OQ7-05	4.7.19
20	Level sensor evaporator SOP XL1 – Calibration of inline manometers 0-20 barg	OQ7-06	4.7.20

1): URS requirement numbering to follow your URS.
2): You generate as many different test sheets as needed – Here is shown four.

Acceptance criteria:
The qualification shall be tested against the following criteria's, and to be noted if accepted or not in the proper part of the test sheet.

1	Accuracy: Max ± 5% at max flow
2	Accuracy: Max ± 5% at max flow
3	Accuracy: Max ± 10% at max flow
4	Accuracy: Max ± 5% at max flow
5	Accuracy: Max ± 5% at max flow
6	Accuracy: Max ± 10% at max flow
7	Accuracy: Max ± 5% at max flow
8	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
9	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
10	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
11	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
12	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
13	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
14	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
15	Accuracy: Max ± 1°C at 25°C (linearity in range 0-100°C: max ± 1°C at 0°C as well as 100°C)
16	Accuracy: Max ± 1% at max. pressure
17	Accuracy: Max ± 1% at max. pressure
18	Accuracy: Max ± 1% 0-20 mAmp
19	Accuracy: Max ± 5% 0-20 mAmp
20	Accuracy: Max ± 5% at halfway full

Deviations:

In case an acceptance criteria is not fulfilled for a qualification test, a deviation must be generated. Deviations are documented on the Deviation Sheet, current version (Ref. [4]), according to Instruction no. 21. Deviation sheets shall clearly identify the failed acceptance criteria and should propose a corrective measure. Deviations are numbered in succession and must be approved by a Pharma A/S QA dep. representative.

References:

[1] Validation Master Plan for Pharma A/S version XX, date YY *(Imaginary document)*
[2] User Requirement Specification for *Your unit, version XX, date: YY*
[3] Pharma A/S Instruction no. 21, Performing of Installation and Operation Qualification, version XX. *(Imaginary document)*
[4] Pharma A/S Deviation Sheet, latest version.

Appendices:

- Test sheet OQ1-03

Test sheet for calibration of handheld thermometer

Title: Test Sheet for evaluation of xxxx		
Done by	Signature	Document No.
Approved by:	Signature	Page 1 of 1
Version:	Date	

						Measurements by instrument						
						Cold start (0C)	Boil		Cold end (0C)	Hysteresis		
Data #	Signature	This Evaluation (date)	Next Evaluation (date)	ID for instrument to be tested	Evaluation method (ref. SOP)	Measurement	Measurement	Boiling Point	Measurement	Measurement (cold start - cold end)	Passed/Not passed	Observations
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												

DEVIATION SHEET

Deviation no.	Related to test plan no.: Test no.:
Description of the deviation: *(The same deviation sheet may be used for the same type of deviation – Say there are several TAGS missing – You only need to do one Deviation Sheet but list all the missing TAGS in the description)*	
Date and signatures: Date: Observer: _____	Date: QA Responsible:_____
Proposal for corrective measures:	
Approval. Date and signature: Proposer:	QA-responsible: