Design and implementation of CIP&SIP systems applied to isolated filling machines

Overview on the different solutions and different approaches

PDA Italy Chapter

Technology transfer in biopharma processes and operations

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IMA S.p.A. – Life division

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- Evolution in the scope of supply.
- CIP&SIP integration into Scada Supervisor.
- Differences between URS and final design, different examples.
- New hybrid systems.
- Interfacing issues with customer systems.

Evolution in the scope of supply

"Once upon a time, there were an engineering company that now becomes a process-supply company"

ASEPTIC PROCESS
For filling lines

VIAL WASHER

DEPYROGENATION TUNNEL

VIAL HANDLING

RTU

VIAL MANAGEMENT

DECONTAMINATION TECHNOLOGIES

ENVIRONMENT MANAGEMENT

ENVIRONMENT MONITORING

ISOLATION TECHNOLOGIES

LIQUID PRODUCT FILLING CIRCUIT

CFR 21 PART 11

GAMP5

LINE SUPERVISOR

AUTOMATION MANAGEMENT

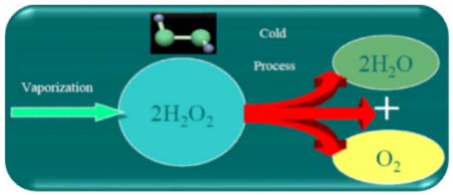
PRODUCT MANAGEMENT

FREEZE DRYING PROCESS

PROJECT MANAGEMENT

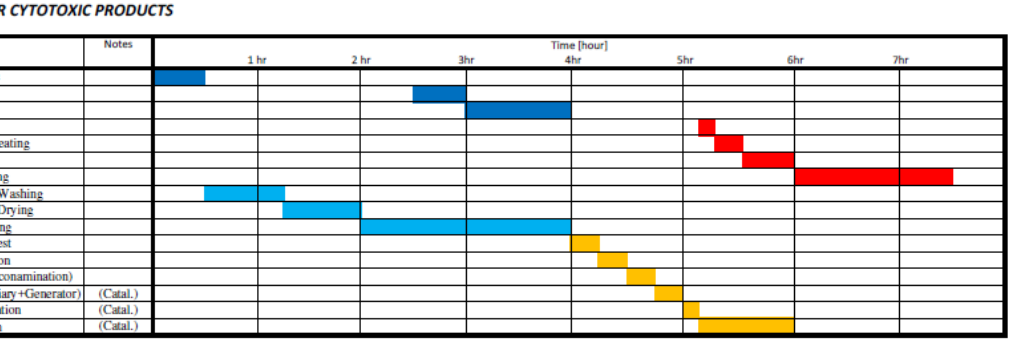
Why the interface with Isolator is different?

Process point of view
(WIP-CIP-VHP-SIP)



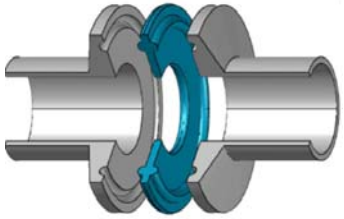
END OF CAMPAIGN PROCESS TIMING FOR CYTOTOXIC PRODUCTS

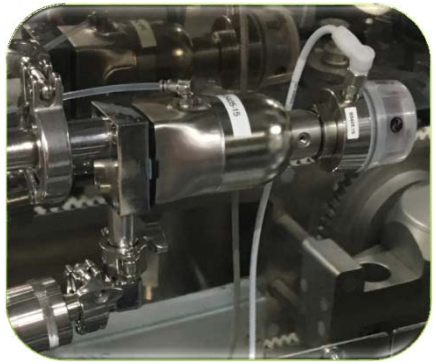
Machine	Activity	Phase	Notes
CIP&SIP skid	CIP	CIP Dynamic	
		CIP Statico	
		CIP-Cooling	
	SIP	Handling	
		Leak Test & Pre-heating	
		SIP	
		Drying&Cooling	
Isolator	WIP	Automatic + Manual Washing	
		Flushing + Manual Drying	
		Automatic Drying	
	VHP	Isolator Leak Test	
		Dehumidification	
		Iinjection (conditioning+deconamination)	
		Preliminary Aeration (Auxiliary+Generator)	(Catal.)
		Intermediate Aeration	(Catal.)
		Final Aeration	(Catal.)

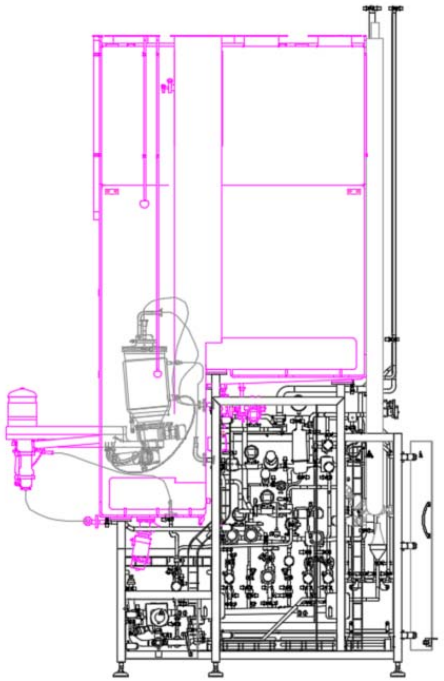


N.B. Plant dimensions and characteristics can influence the single phases time

Mechanical point of view

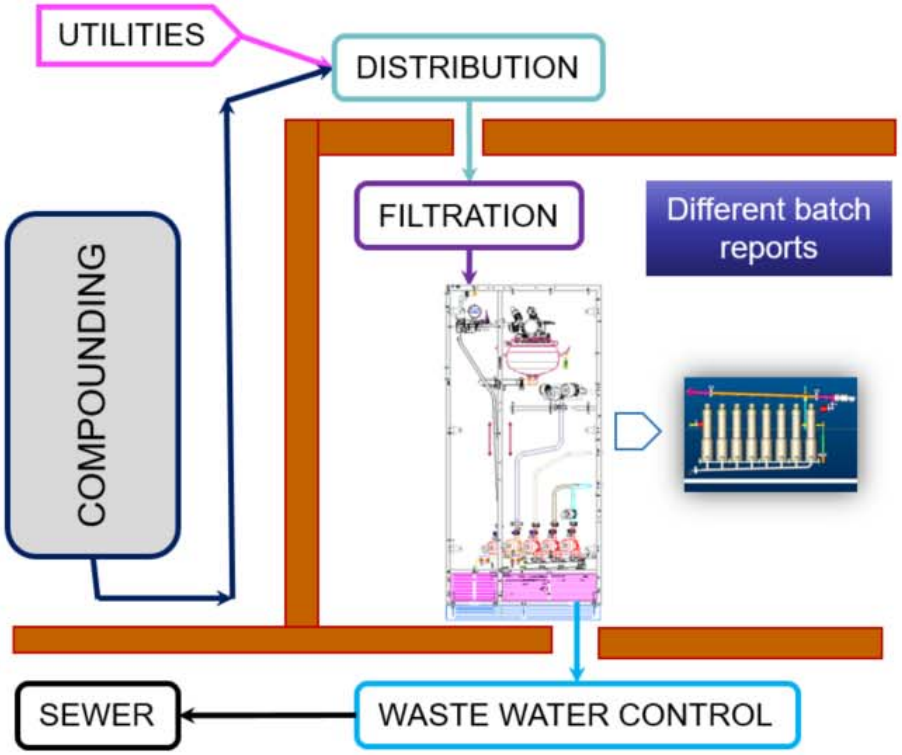




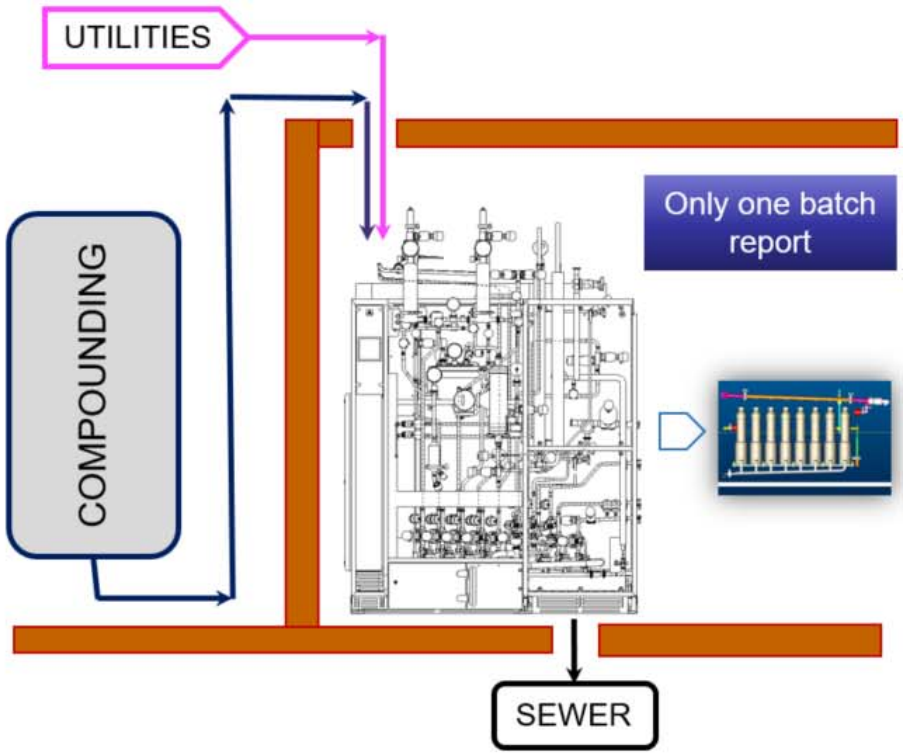


Evolution in the scope of supply

Old typical solution



Current typical solution



Increasing request to integrate the scope of supply into the filling machine CIP&SIP skid, moving also the sterility battery limit.

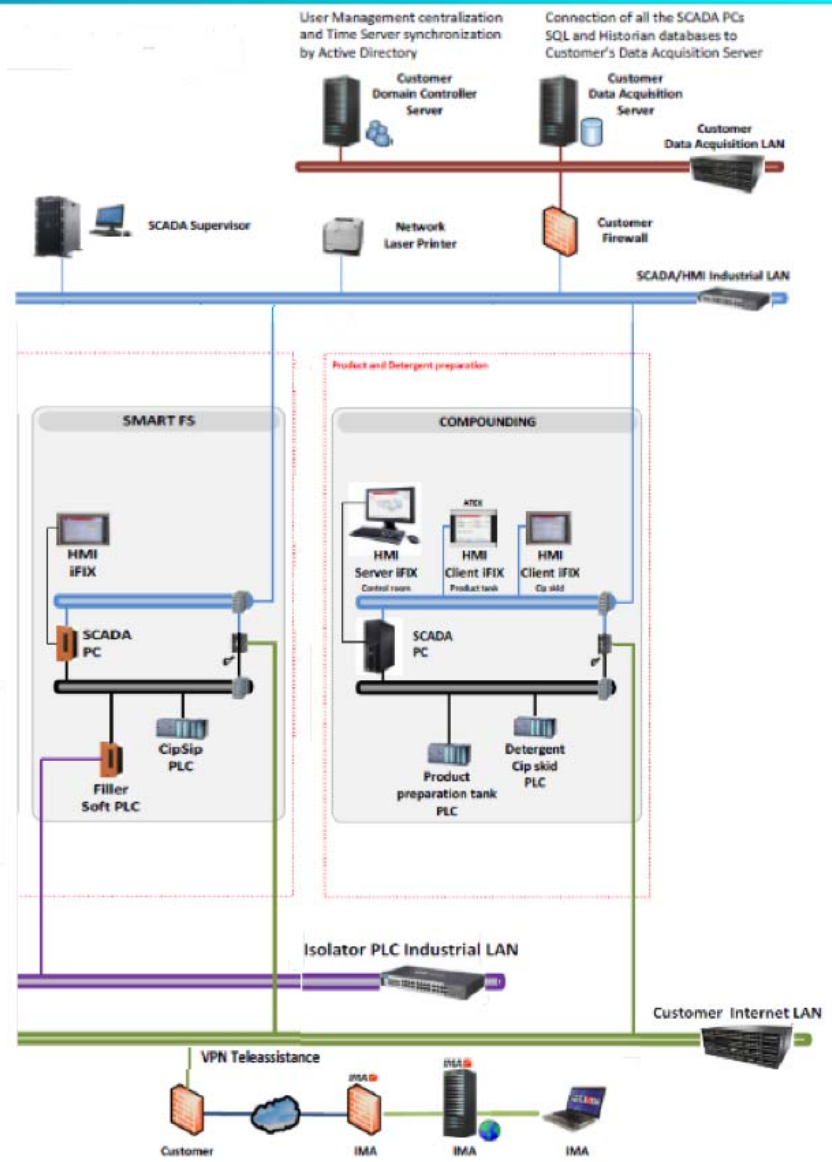
CIP&SIP integration into Scada Supervisor

CIP&SIP integrated into Scada of the filling line.

Interface with customer MES.

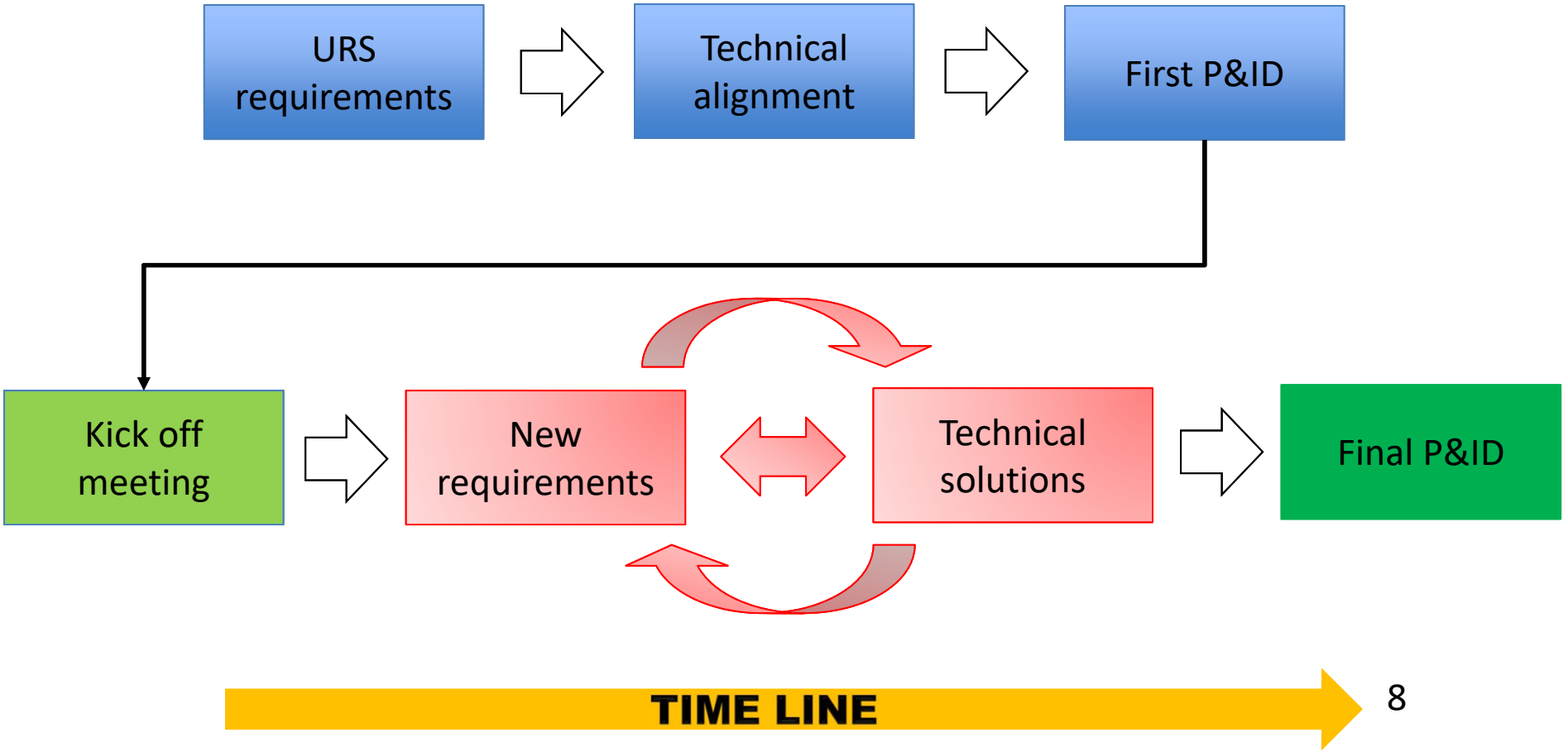
In case of supply, possibility to integrate also:

- Preparation vessels
- CIP skid



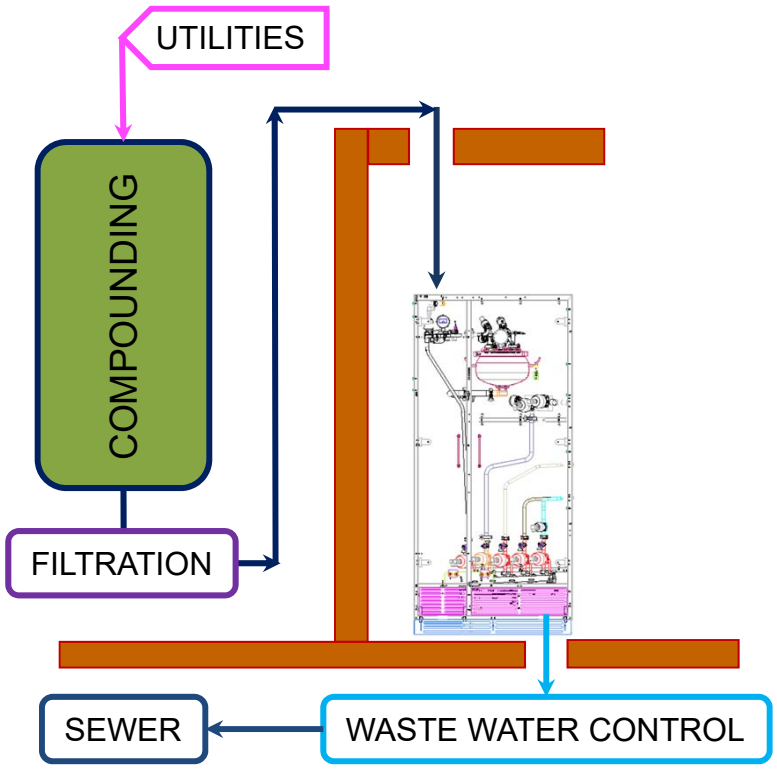
Differences between URS and final design, different examples

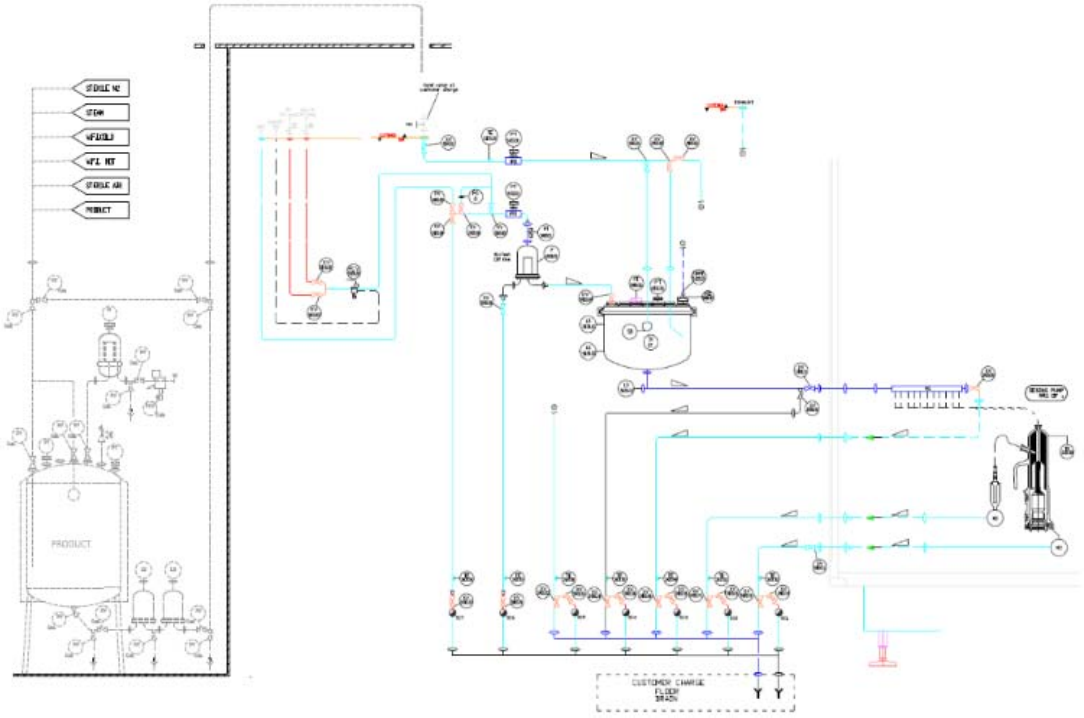
Normally what is required in URS is different from the customer need



Example 1

ID ***	The product transfer line from sterile tank to filler shall be designed for an automatic CIP and SIP process with integration with the site Sterile Filtration System. The fill design shall include the required interfaces (mechanical, electrical, plumbing) within the system boundary.





Example 1

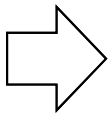
During technical alignment:

CIP&SIP of filling machine is part of compounding system CIP&SIP.

The two systems have to work together with a “strong“ software interconnection.

It‘s not possible to test it during FAT but only on site.

The compounding and utility systems have to be available for several weeks of testing.



During kick off meeting:

Compounding will not be available, the two systems have to be independent.

Utilities management at customer care.

One product filter close to filling machine.

IT pre-production and WIT.

Conductivity meter + waste water sampling valve.

Temperature probe inside tank.

Differences between URS and final design, different examples

Example 1

Flushing with product or WFI?

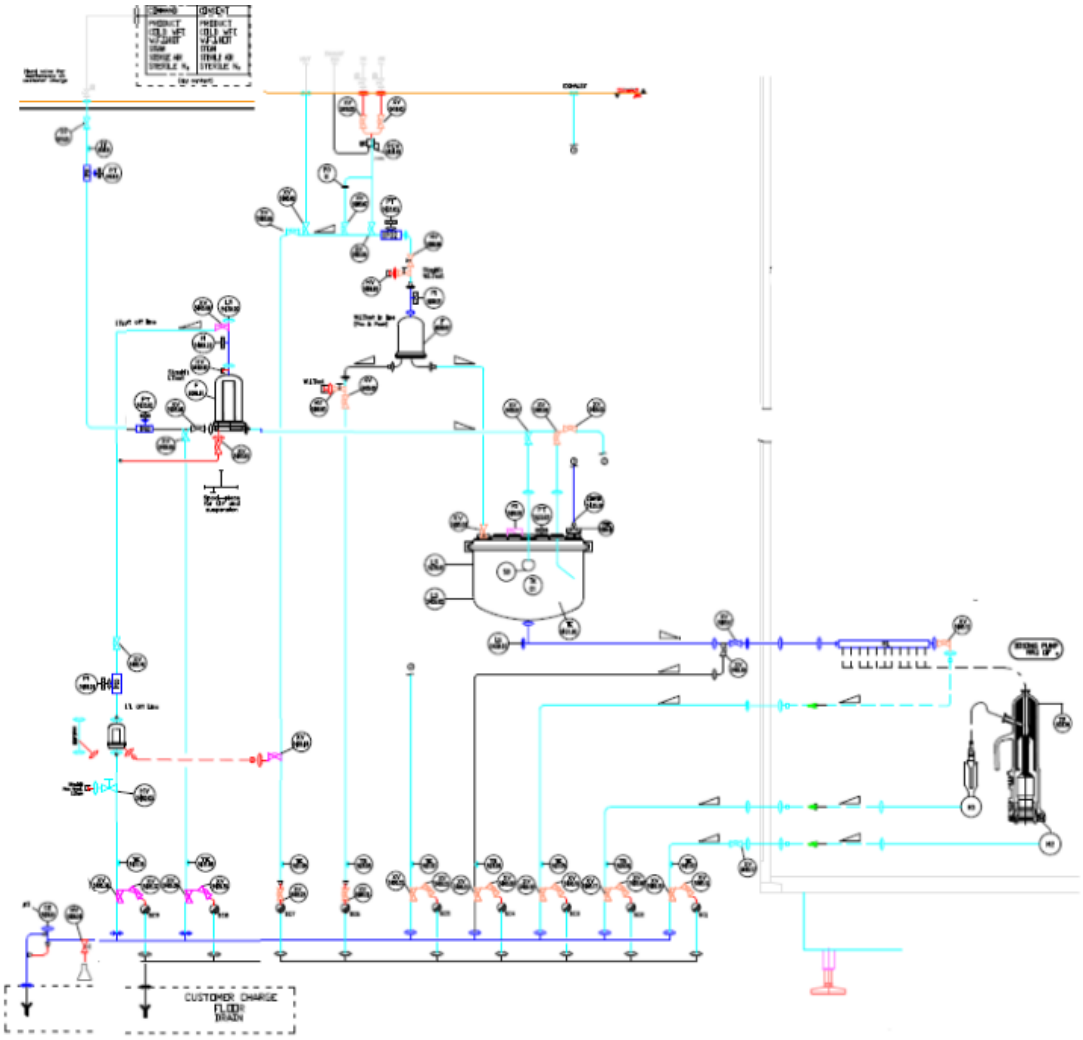
Flushing to drain or tank (E&L)?

First filter or redundant filter?

Confirmed with Product

Flush to tank (small volume)

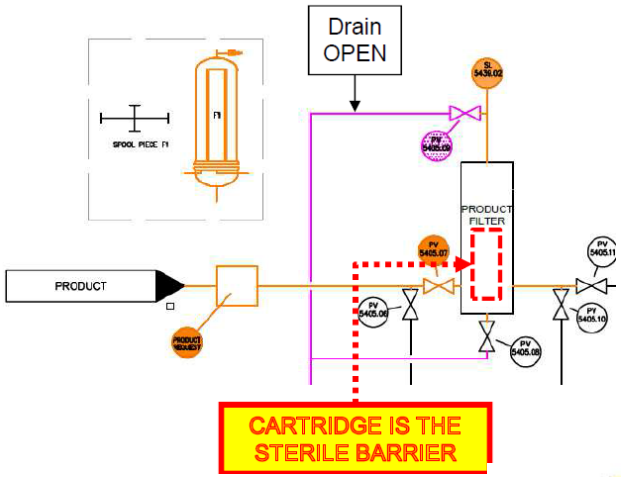
Confirmed redundant filter

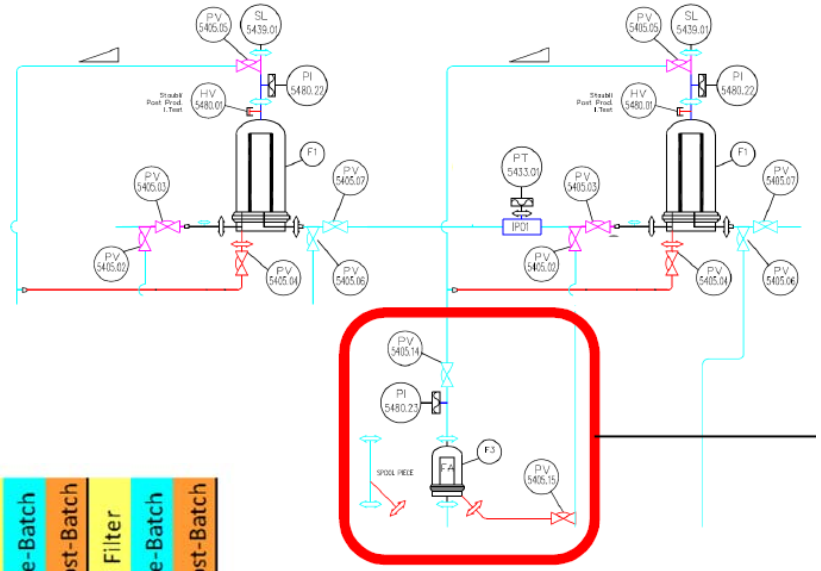


Example 1 (appendix product filter)

Unless otherwise stated in the URS, the filter cartridge is the sterile barrier.

To make a correct wetting it is necessary to ‘‘purge‘‘ from the upper side of the filter.

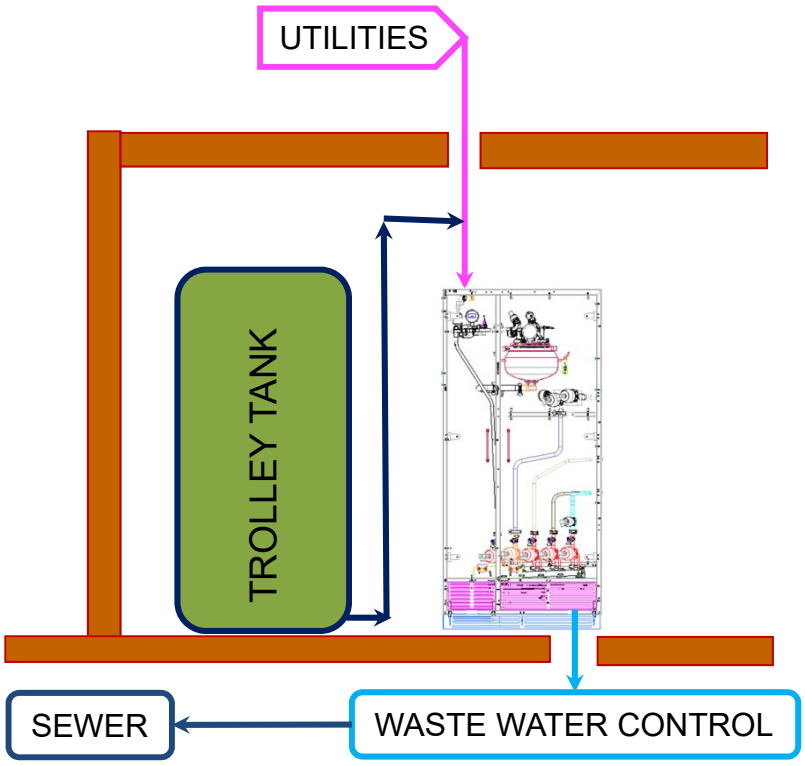


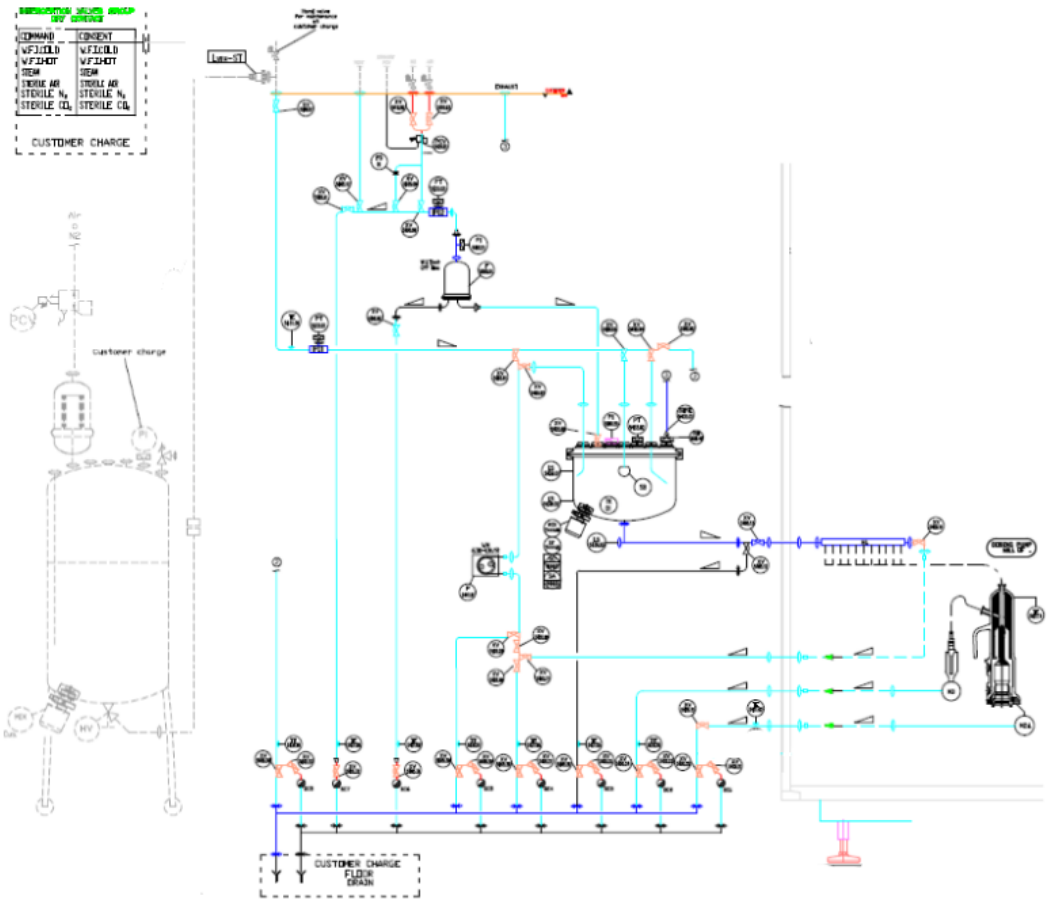


ITEM	Prod Filter	IT Pre-Batch	IT Post-Batch	Prod Filter	IT Pre-Batch	IT Post-Batch	Prod Filter	IT Pre-Batch	IT Post-Batch	Prod Filter	IT Pre-Batch	IT Post-Batch	Prod Filter	IT Pre-Batch	IT Post-Batch	
IT Pre &Post																1st Filter
	NA	NA	NA	NA	NA	NA										2nd Filter
IT Post		NA						NA			NA			NA		1st Filter
	NA	NA	NA	NA	NA	NA		NA			NA			NA		2nd Filter
IT Pre			NA						NA			NA			NA	1st Filter
	NA	NA	NA	NA	NA	NA			NA			NA			NA	2nd Filter
URS	1 Filtration			1 Redundant Filtration			Double Filtration "Bioburden"			Double Filtration "Sterile"			Double Redundant Filtration			

Example 2

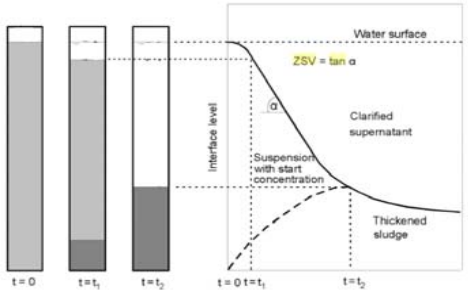
ID ***	Filler shall have the ability for continuous circulation and/or mixing of suspension products to avoid sedimentation in the product line

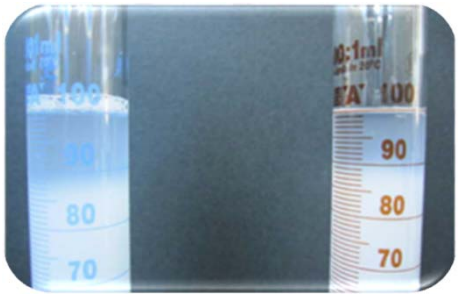




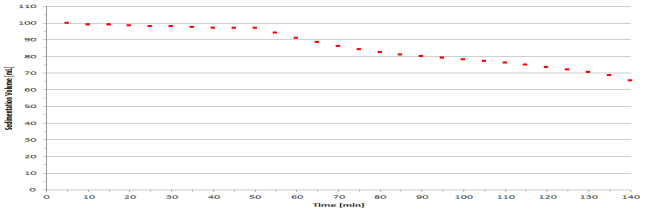
Differences between URS and final design, different examples

Example 2 (appendix suspensions)



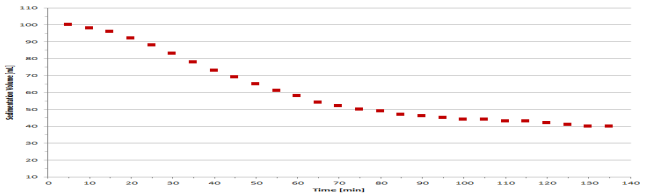


1



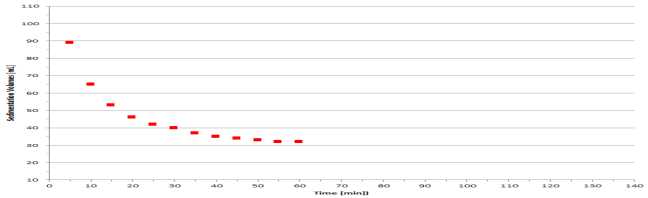
- Long sedimentation time
- «Not heavy» suspension
- Easy to re-suspend after stops
- Does not require constant turbulent flow for movement

2



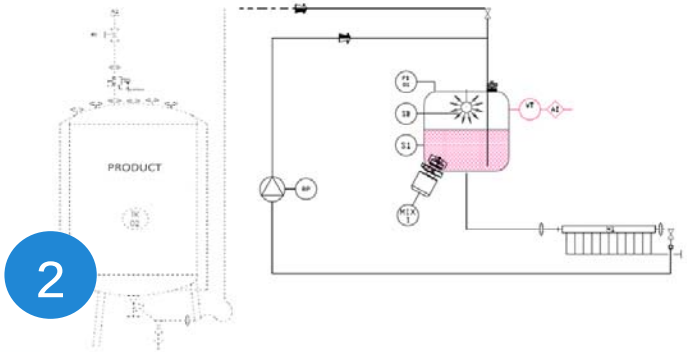
- Medium sedimentation time
- «Medium weight» suspension
- Long time to re-suspend it
- Cannot stay stop before dosing system

3

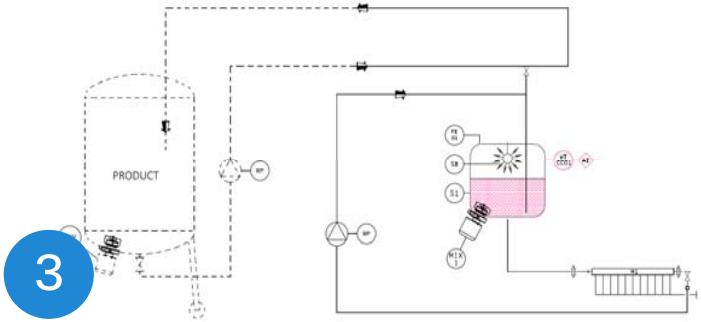


- Fast sedimentation time
- «Heavy» suspension
- The turbulent flow cannot re-suspend it
- Has to remain always in turbulent flow

2

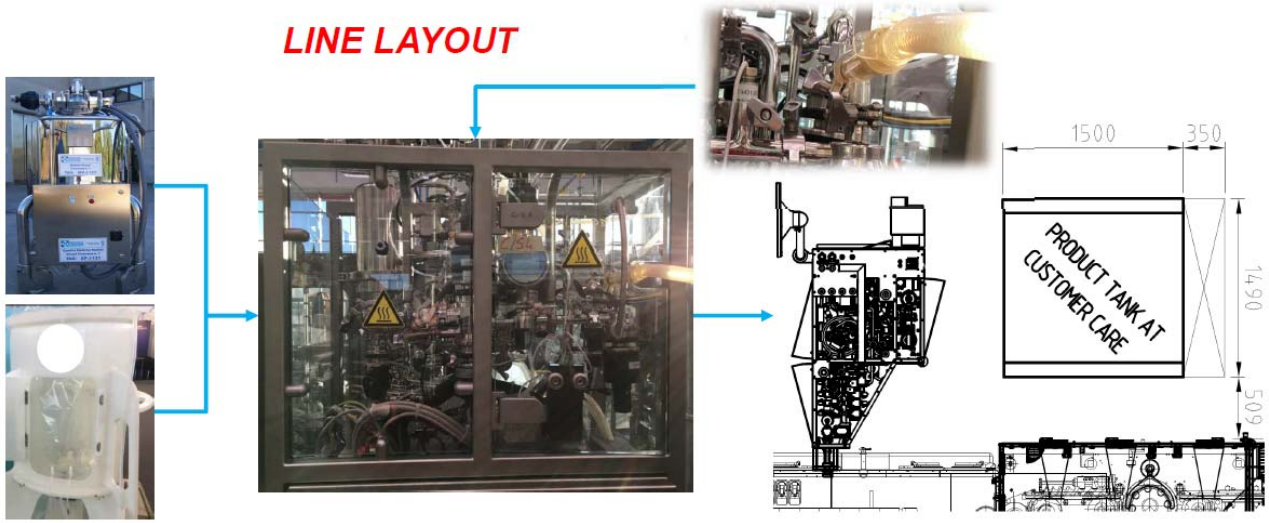


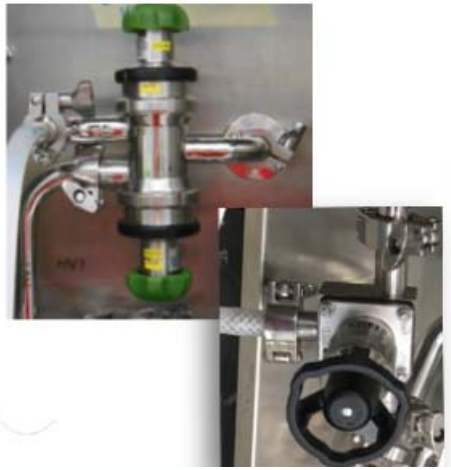
3

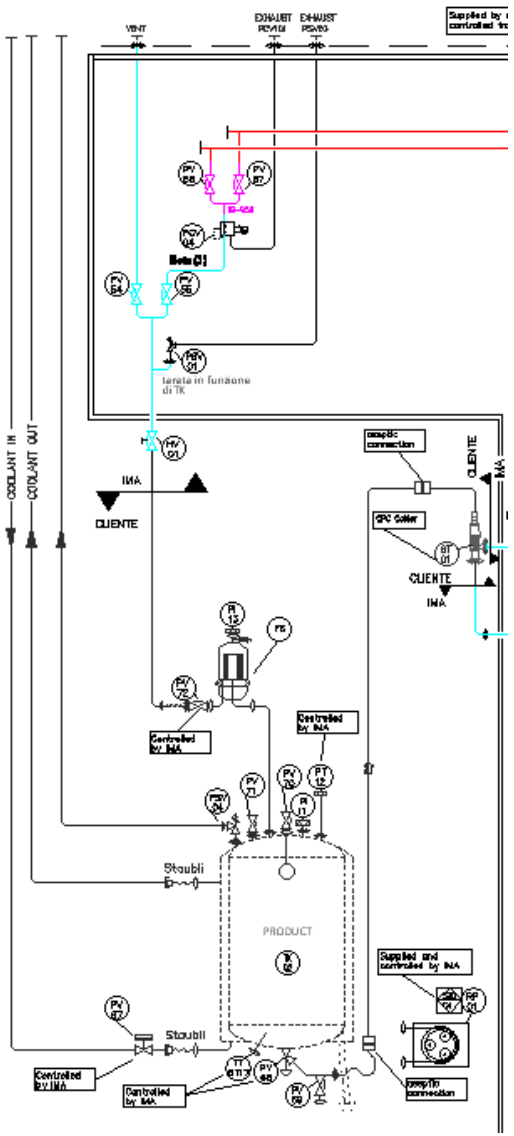


Differences between URS and final design, different examples

Example 2 (appendix trolley storage tank)







Differences between URS and final design, different examples

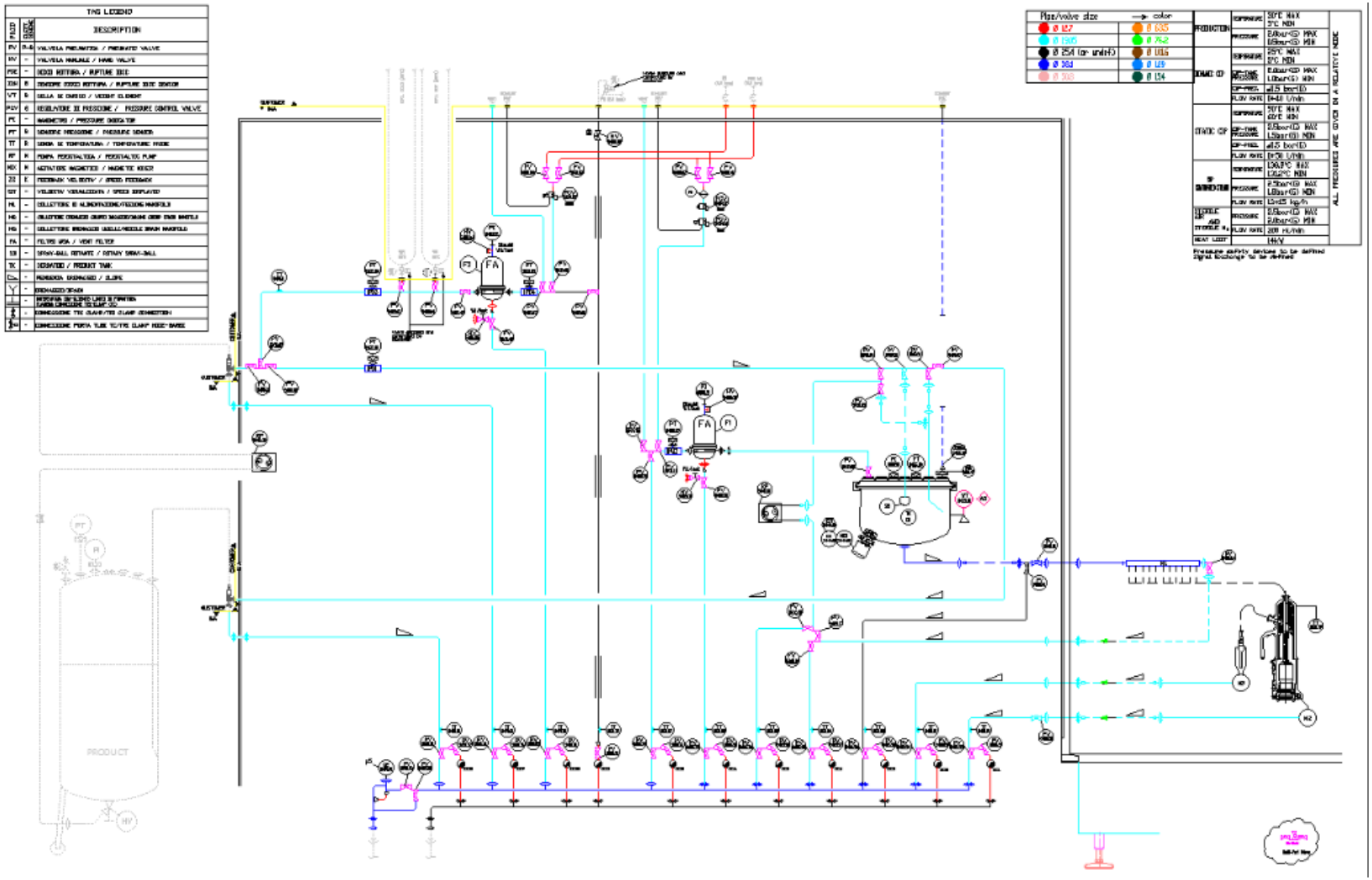
Example 2

During kick off meeting:

Heavy suspension.

Conductivity meter.

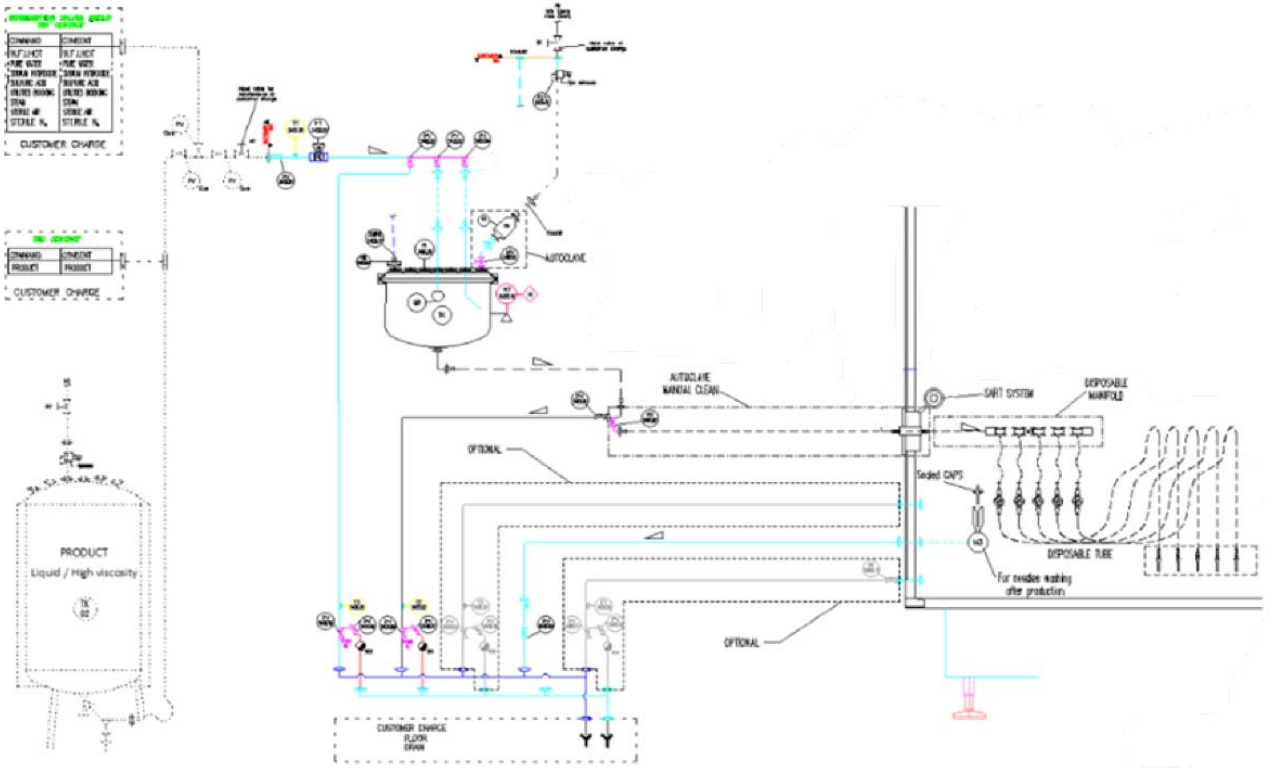
Utilities unit.



Example 1

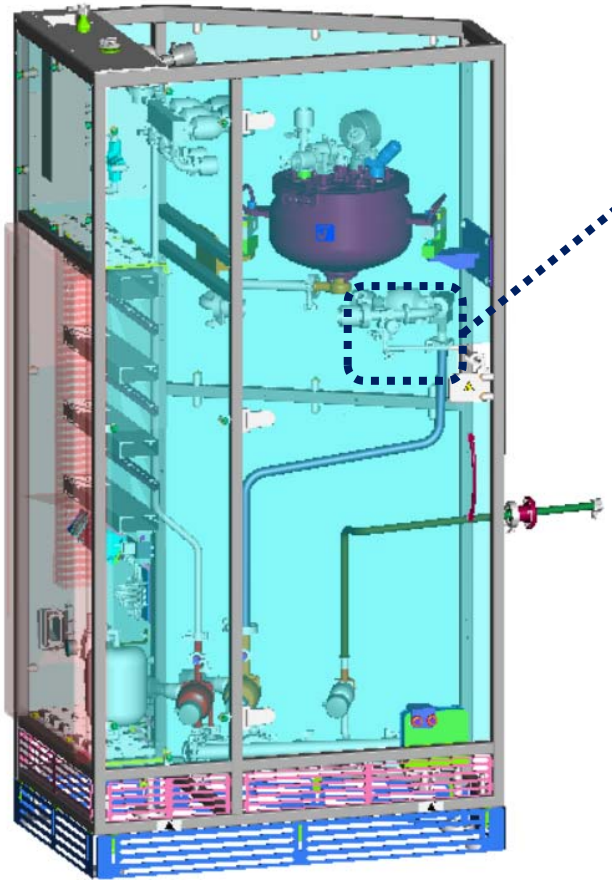
CIP&SIP system interfacing with peristaltic pump technology and predisposition for future volumetric pump technology.

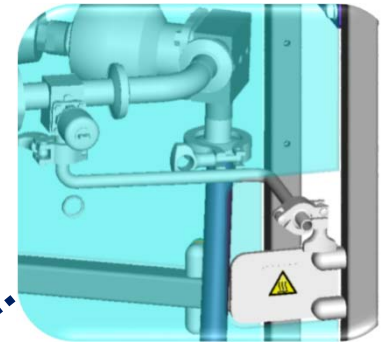
Cytotoxic products.



New hybrid system
Combination between Single Use and Multi Use

Example 1





Example 1

REASONS:

Multi-use compounding system.

Utilities distribution already present.

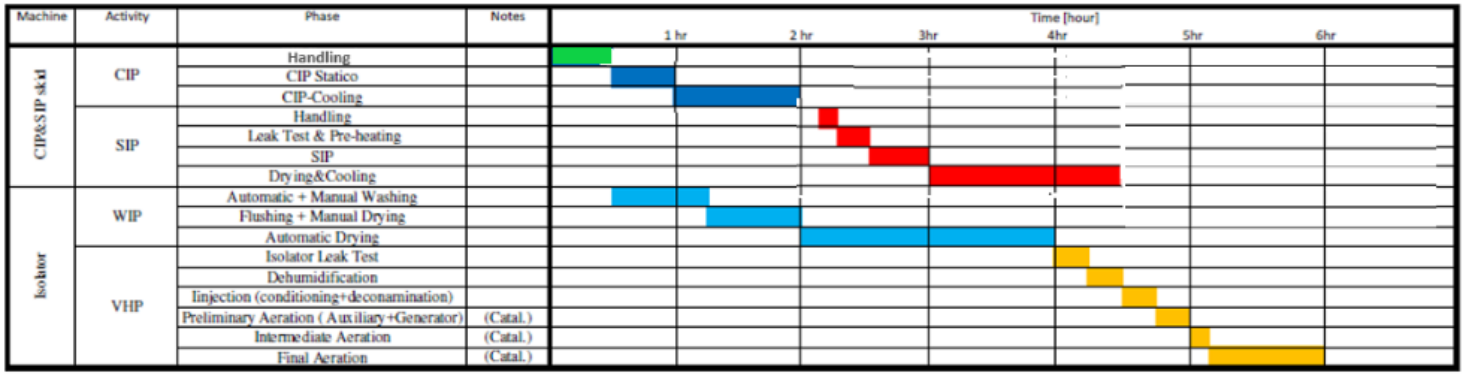
Requirement from customer to reduce SUS components.

“Shear effects“ with differential pump technology for main product.

ADVANTAGES:

CIP&SIP and Isolator Processes fully independent.

END OF CAMPAIGN PROCESS TIMING FOR CYTOTOXIC PRODUCTS



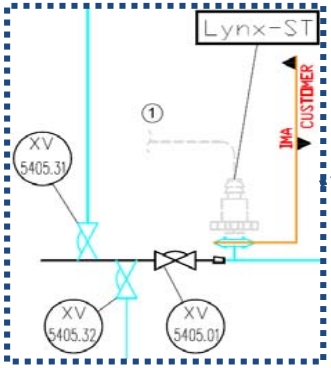
New hybrid system
Combination between Single Use and Multi Use

Example 2

- CIP&SIP system interfacing with a Single Use Redundant Filtration assembly SURF (support frame at IMA care).
- Utilities management.
- Conductivity meter.
- Toxic product.
- WIT in line.

The advantage is related to the possibility to use a single vent and utilities hydrophobic filter.

Connection required with Lynx-ST.

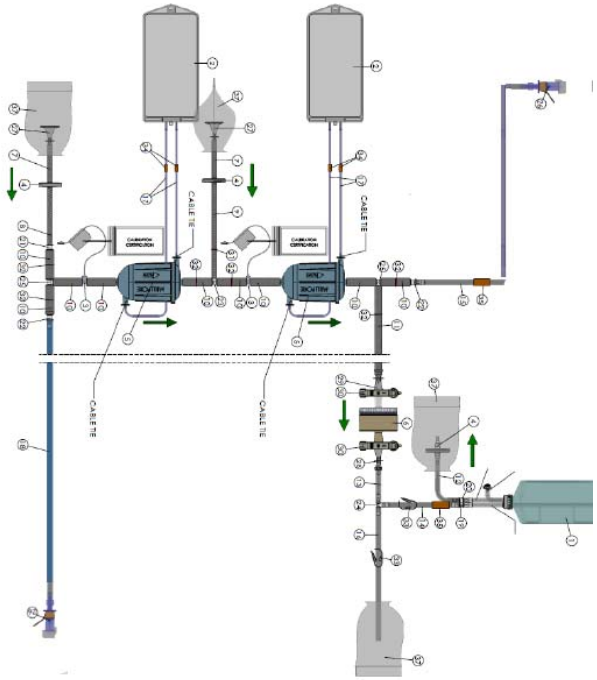


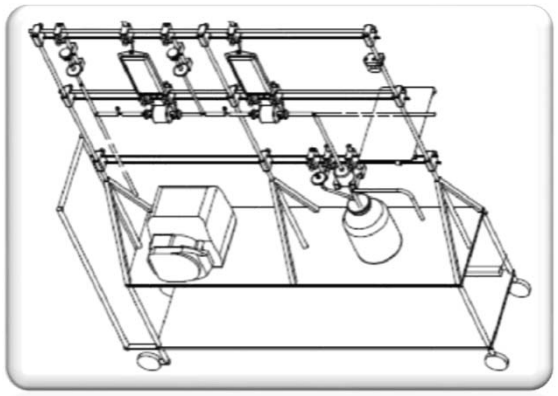
New hybrid system
Combination between Single Use and Multi Use

Example 2

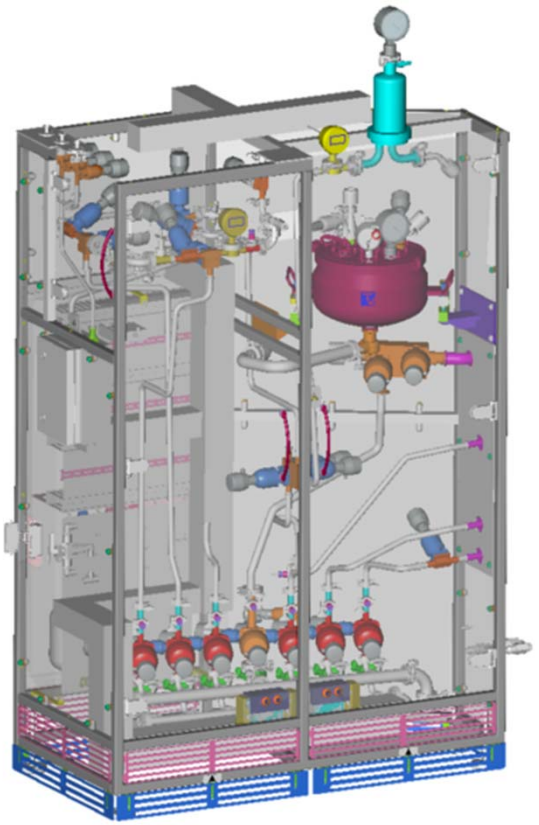
Possibility to perform IT and flushing (E&L) off line.

Possibility to connect SURF immediately before production.





UTILITIES



New hybrid system
Combination between Single Use and Multi Use

Example 1

During kick off meeting:

Single use filling system with peristaltic pump technology.

Conductivity meter with by-pass for detergents.

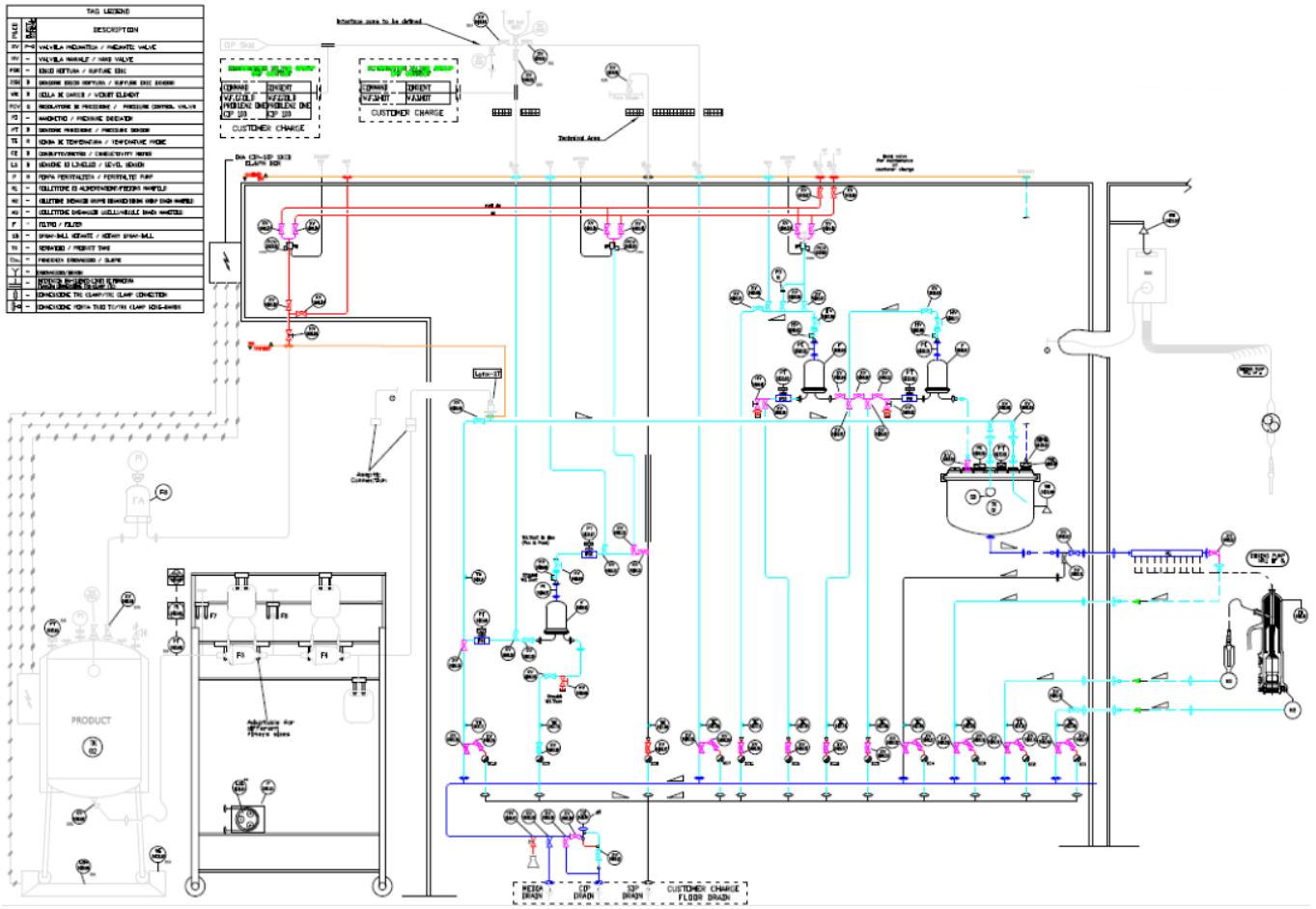
Sampling valve for waste water.

Dedicated drain first rinse.

Double venting filtration.

Management of trolley storage tank and floor scale.

Transfer by overpressure or peristaltic pump.



Example 2

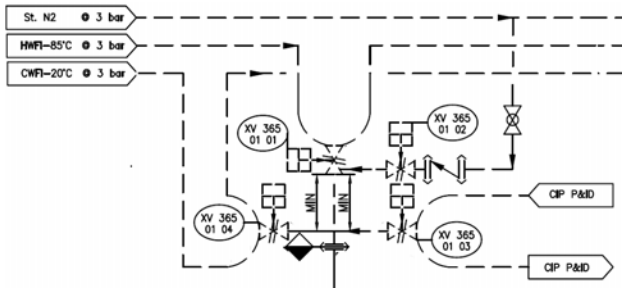
Usually customers forget the ‘‘encumbrance‘‘ of a SURF assembly in the first line layout evaluation

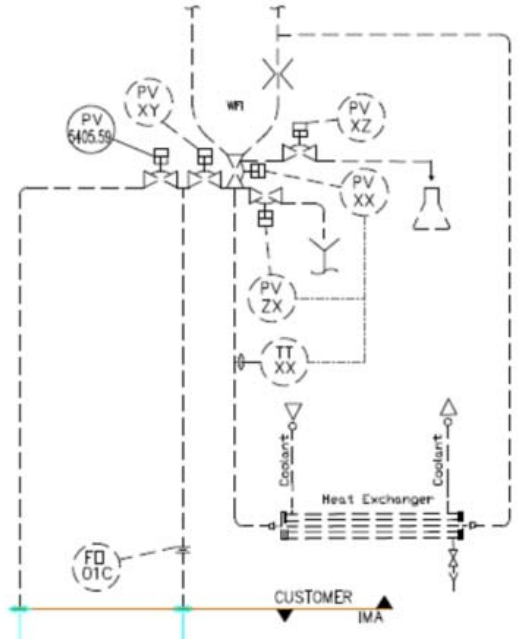
Interfacing issues with customer systems

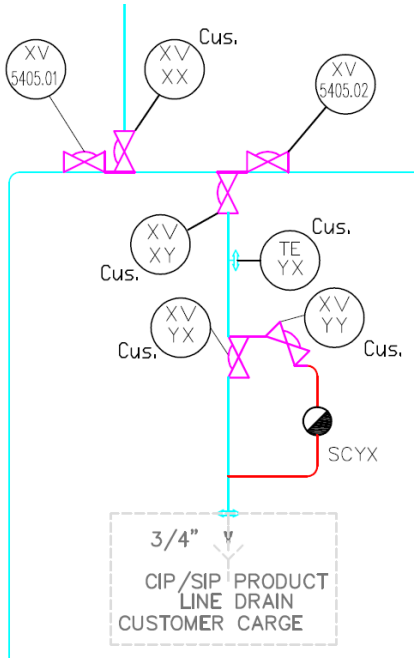
IMA needs some information when the customer is still defining them:

- DRAIN INTERFACES
- INTERFACE WITH WFI POINT OF USES
- INTERFACES WITH COMPOUNDING SYSTEM
- POINT OF USE VALVE

Air Break or pass-through?
Air flushing or SIP?
Interconnected sequences?
Managed by IMA or customer?







Thank you for your attention!

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