



# 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**

Bologna, April 11, 2019

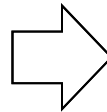
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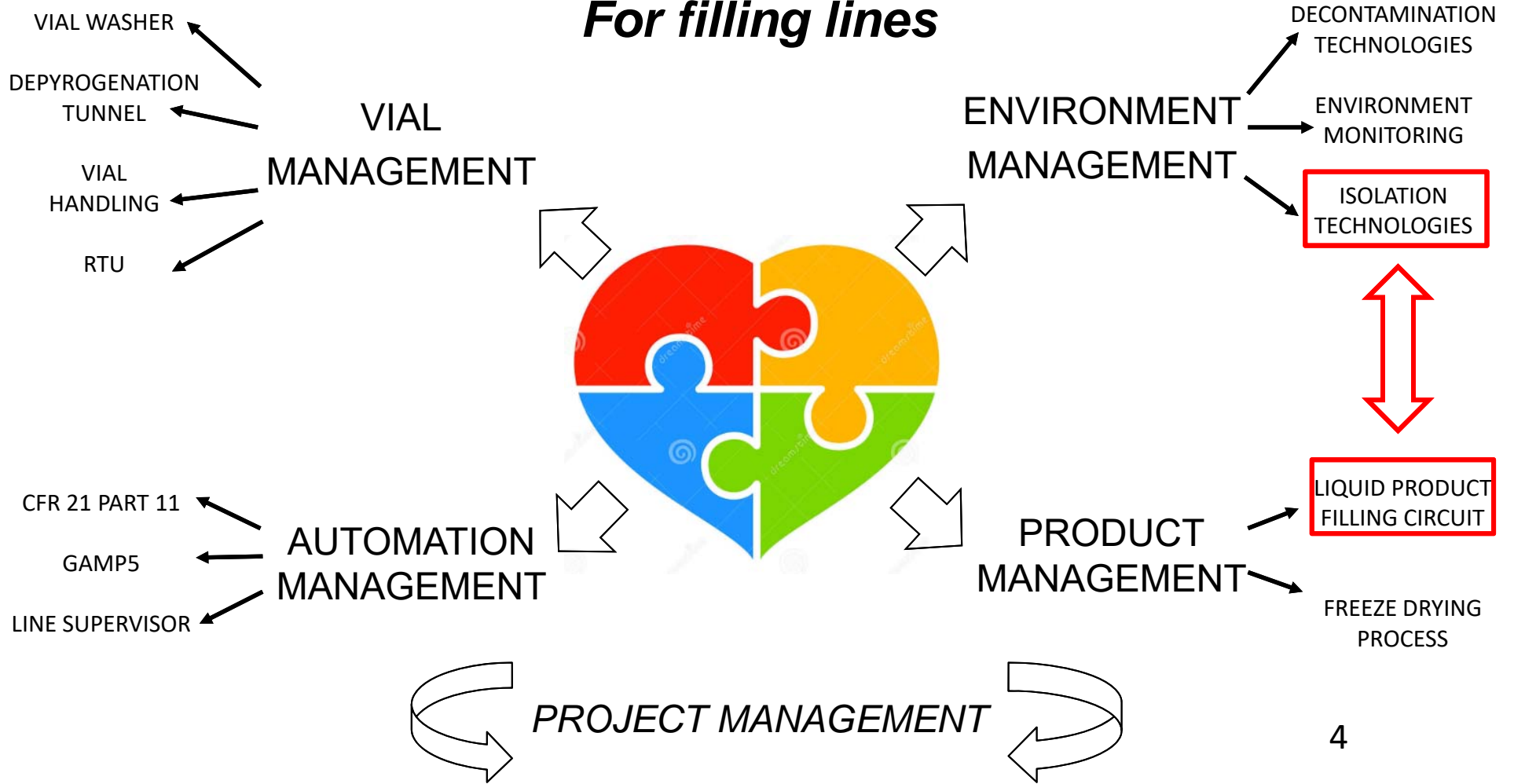
## Contents

- 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.

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



# ASEPTIC PROCESS For filling lines

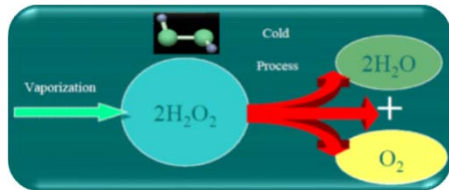




# Evolution in the scope of supply

## Why the interface with Isolator is different?

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

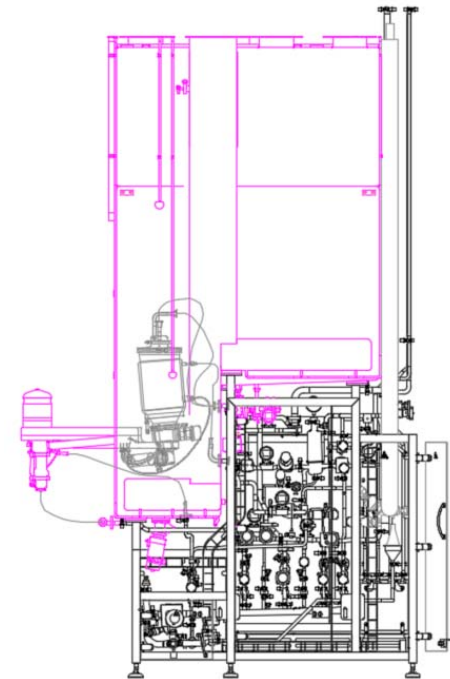
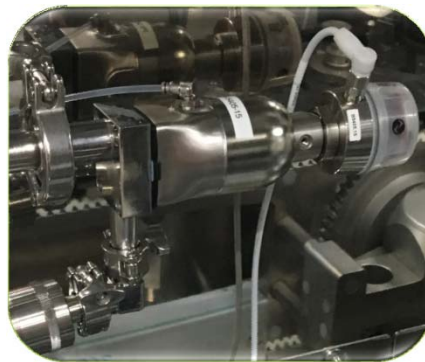
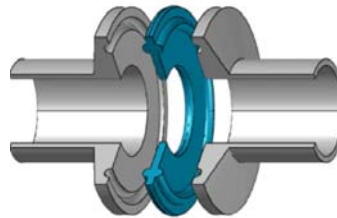


END OF CAMPAIGN PROCESS TIMING FOR CYTOTOXIC PRODUCTS

Machine	Activity	Phase	Notes	Time [hour]								
				1 hr	2 hr	3hr	4hr	5hr	6hr	7hr		
CIP&SIP skid	CIP	CIP Dynamic		█								
		CIP Static				█						
		CIP-Cooling					█					
	SIP	Handling								█		
		Leak Test & Pre-heating								█	█	
Isolator	WIP	SIP										
		Drying&Cooling										
		Automatic + Manual Washing										
	VHP	Flushing + Manual Drying			█							
		Automatic Drying				█						
		Isolator Leak Test										
		Dehumidification										
		Injection (conditioning+decontamination)										
		Preliminary Aeration ( Auxiliary+Generator)	(Catal.)									
		Intermediate Aeration	(Catal.)									
Final Aeration	(Catal.)											

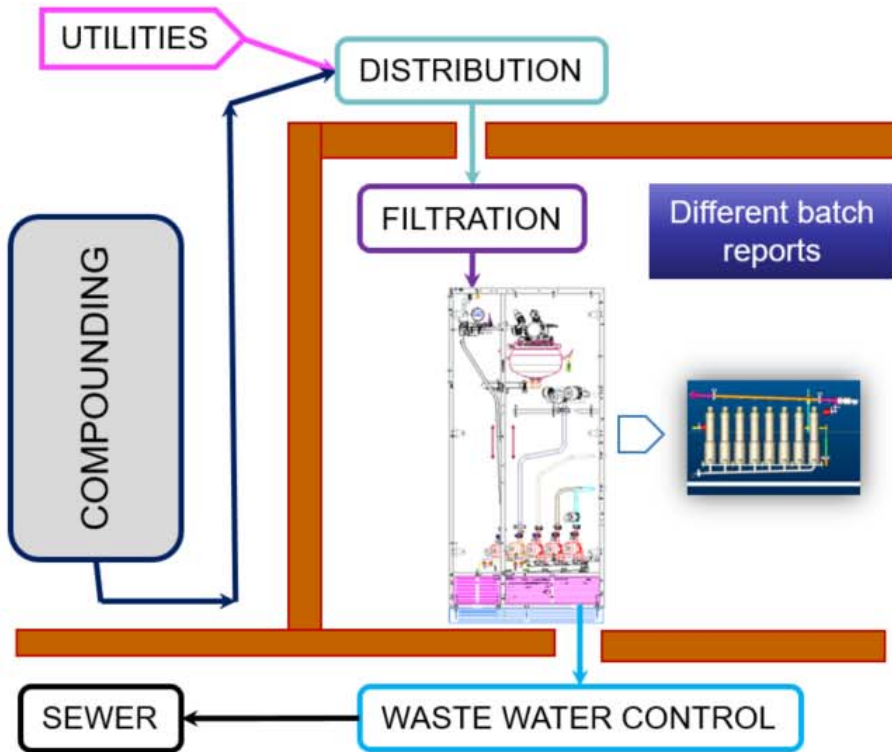
N.B. Plant dimensions and characteristics can influence the single phases time

Mechanical point of view

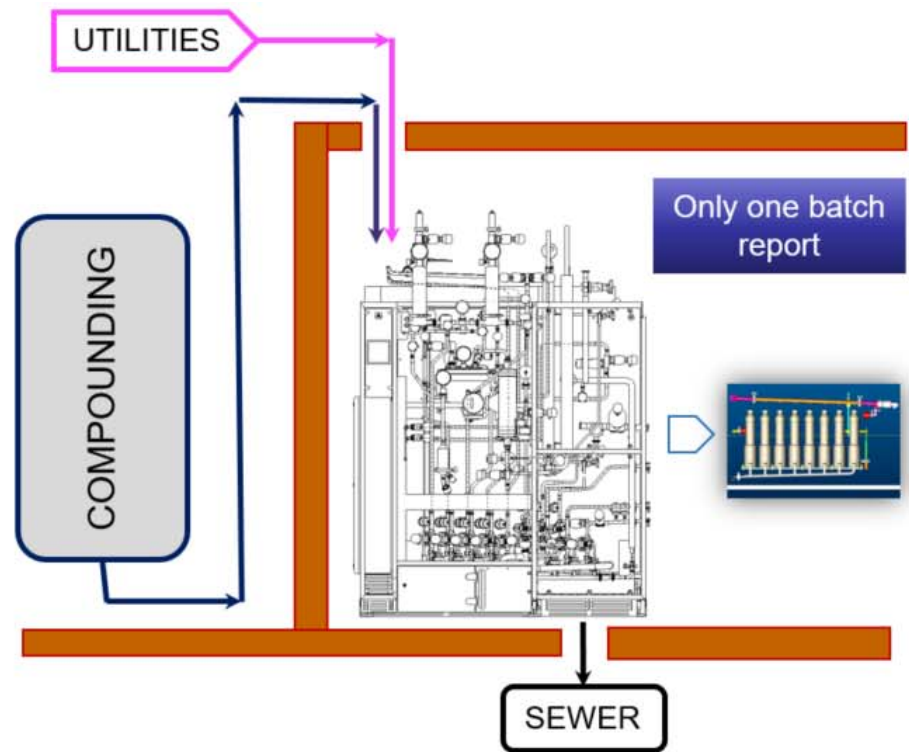




Old typical solution



Current typical solution

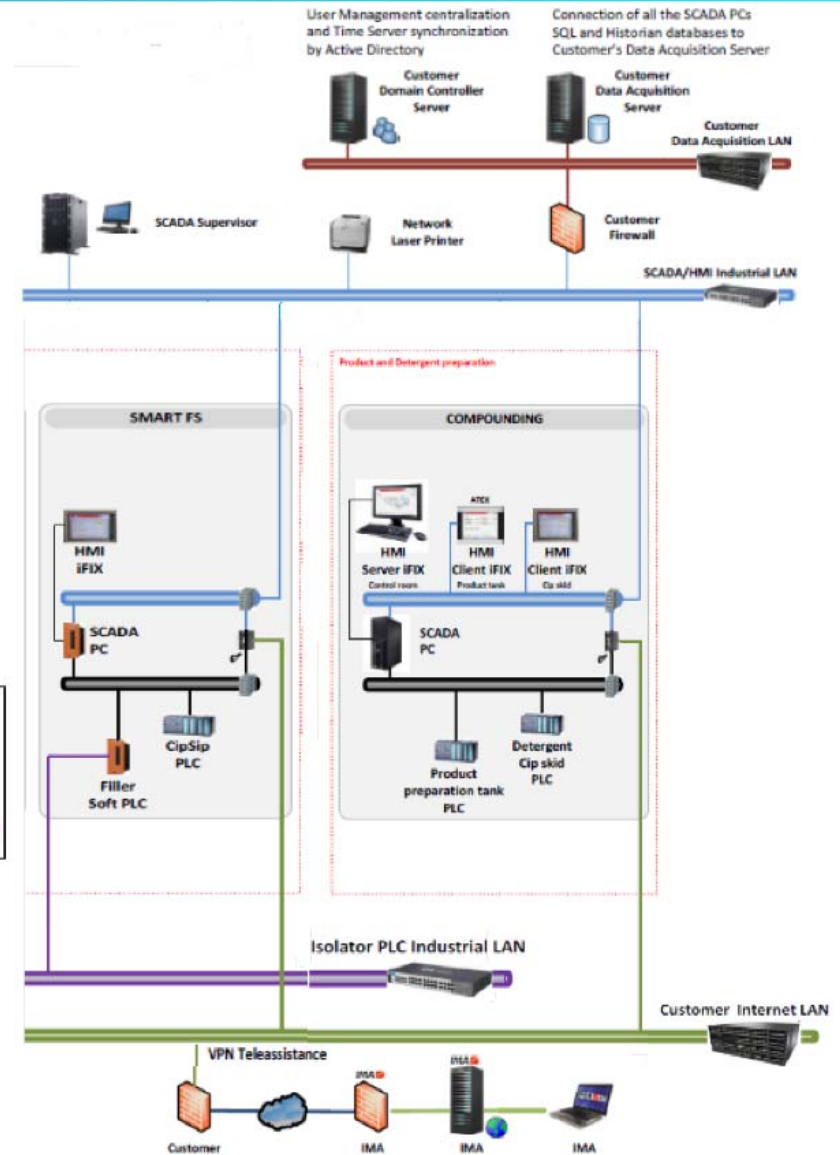


Increasing request to integrate the scope of supply into the filling machine CIP&SIP skid, moving also the sterility battery limit.

CIP&SIP integrated into Scada of the filling line.  
Interface with customer MES.

In case of supply, possibility to integrate also:

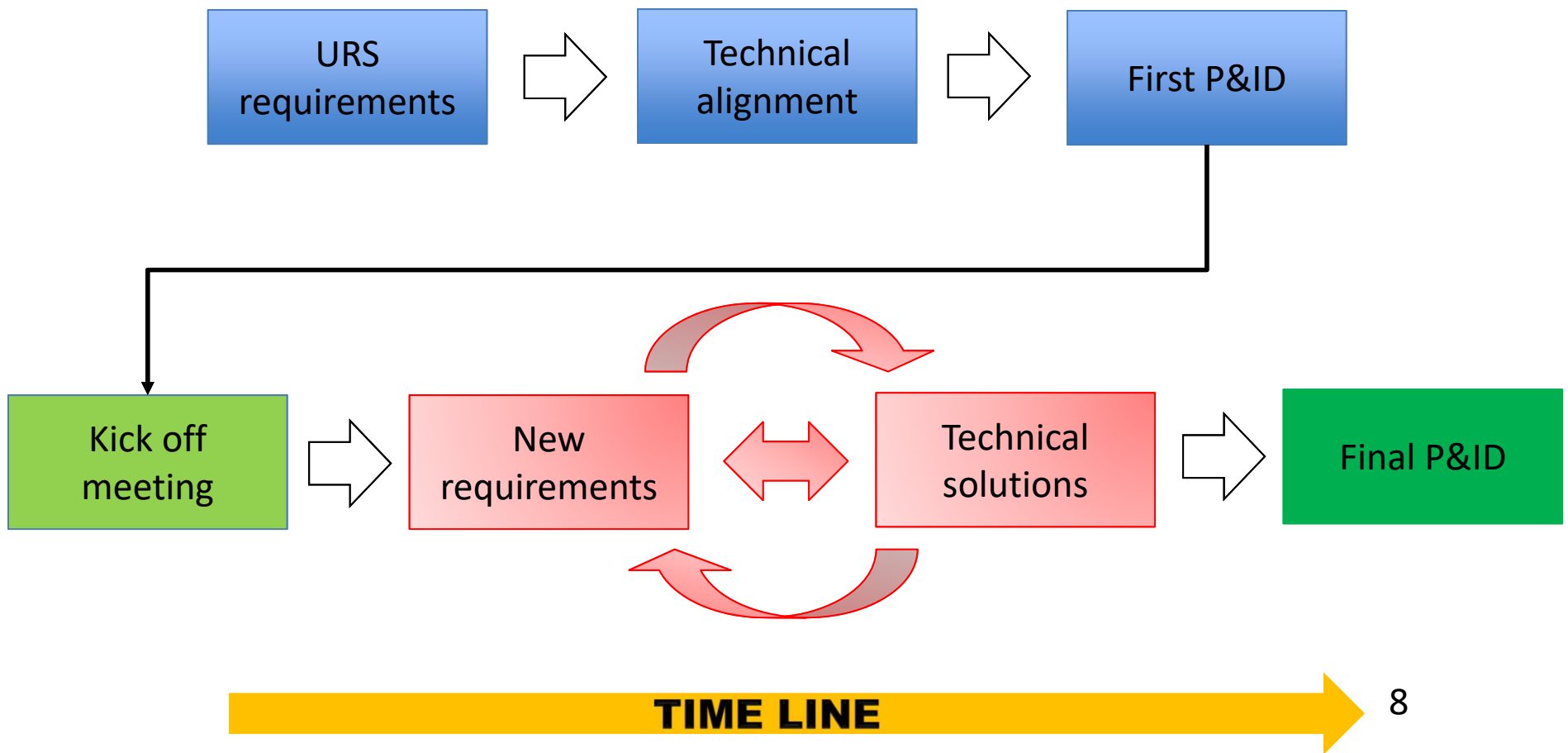
- Preparation vessels
- CIP skid



This block contains a collage of icons representing system capabilities:
 

- Three blue human figures representing users.
- A screenshot of a software interface.
- Three yellow document icons representing reports.
- A clock icon representing time or scheduling.
- An orange pill bottle icon representing a vessel or skid.
- Two line graphs and one bar chart representing data analysis.
- Icons for 'Batch reports (PDF, XLS)', 'Backups (FBK)', 'SQL', and 'HISTORIAN'.
- A screenshot of a process flow diagram.

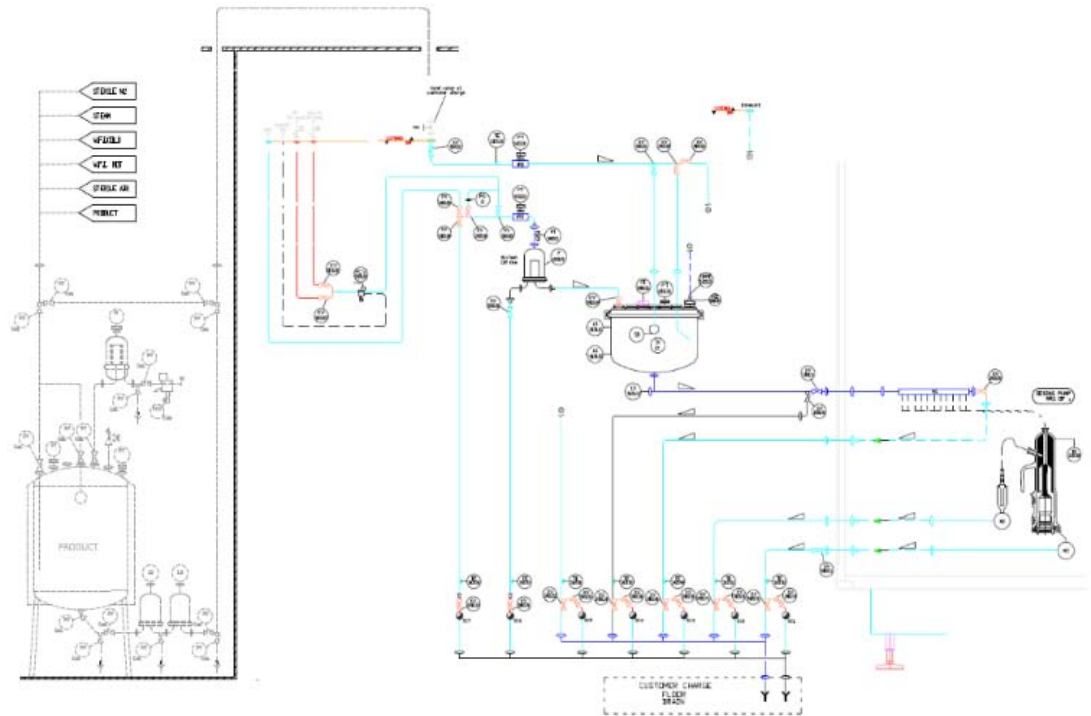
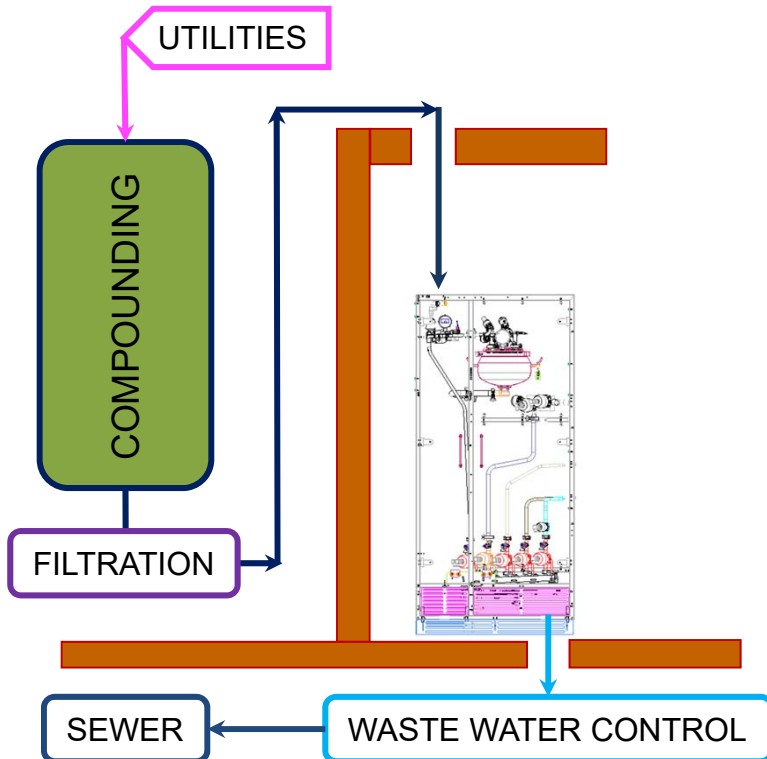
Normally what is required in URS is different from the customer need





## 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.
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## Example 1

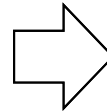
### During technical alignment:

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.

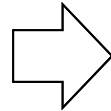
Temperature probe inside tank.

## Example 1

Flushing with product or WFI?

Flushing to drain or tank (E&L)?

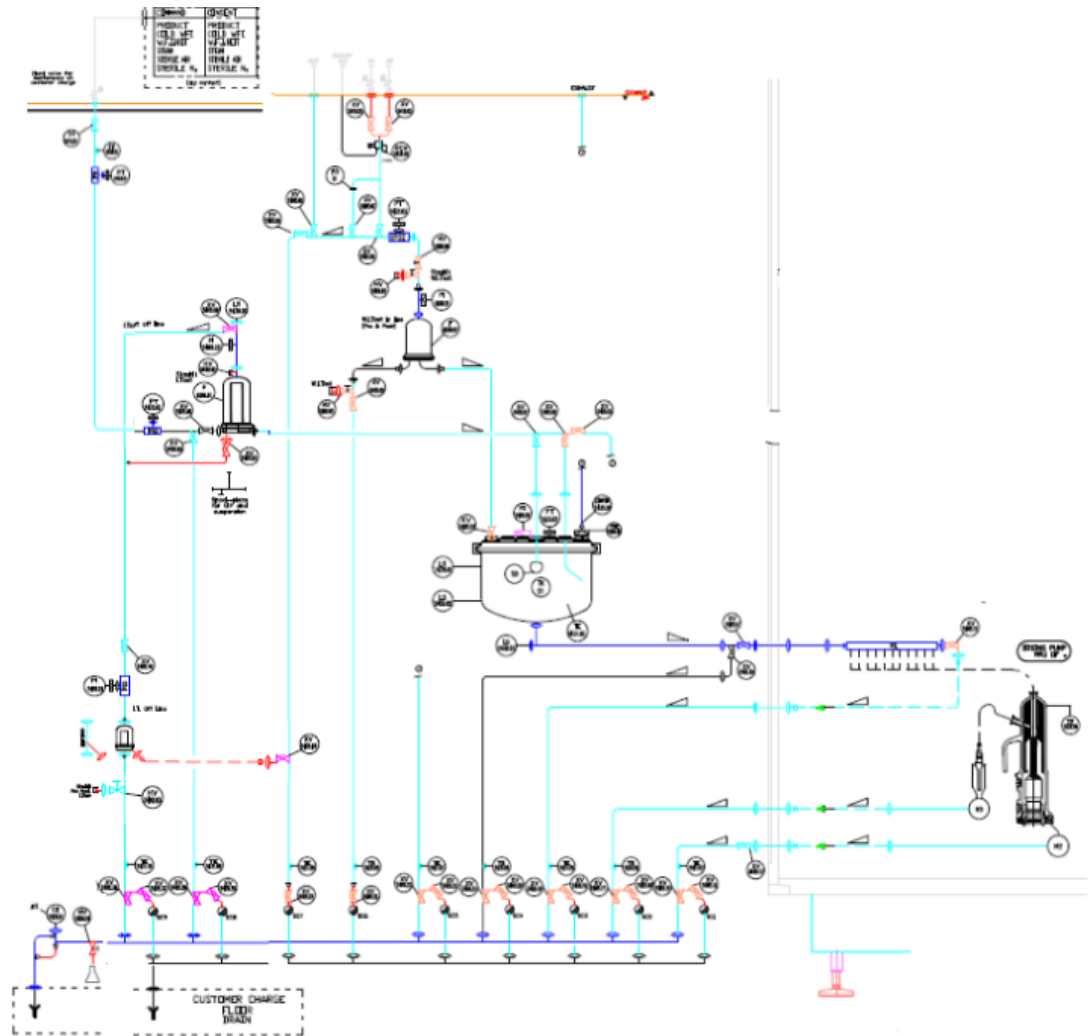
First filter or redundant filter?



Confirmed with Product

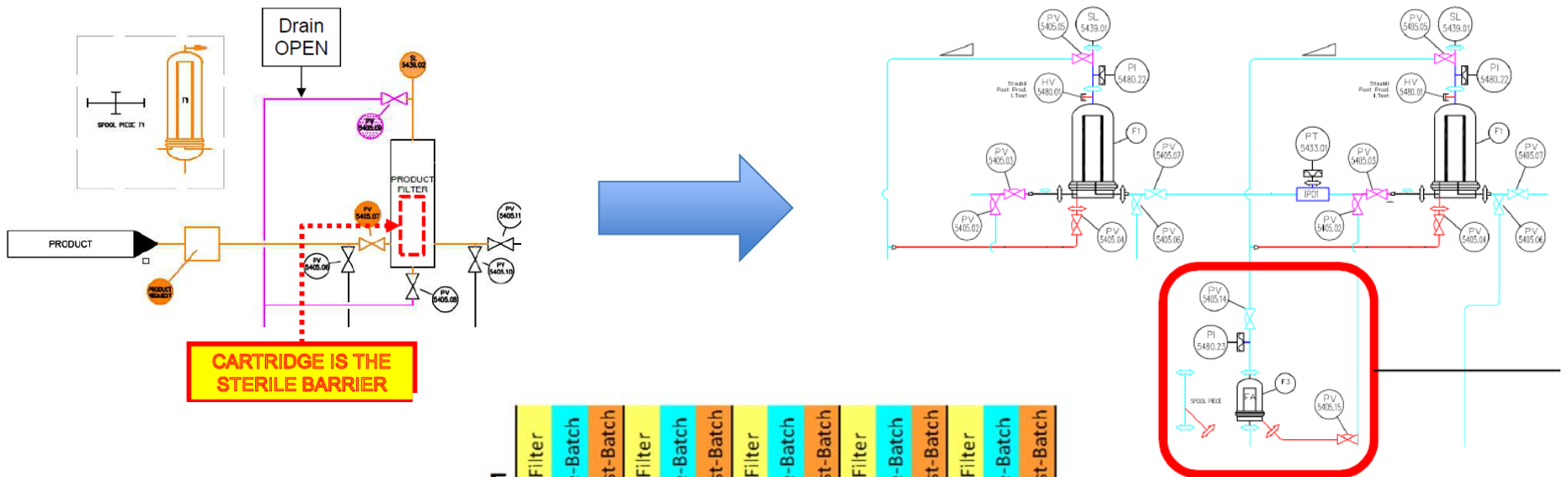
Flush to tank (small volume)

Confirmed redundant filter



## Example 1 (appendix product filter)

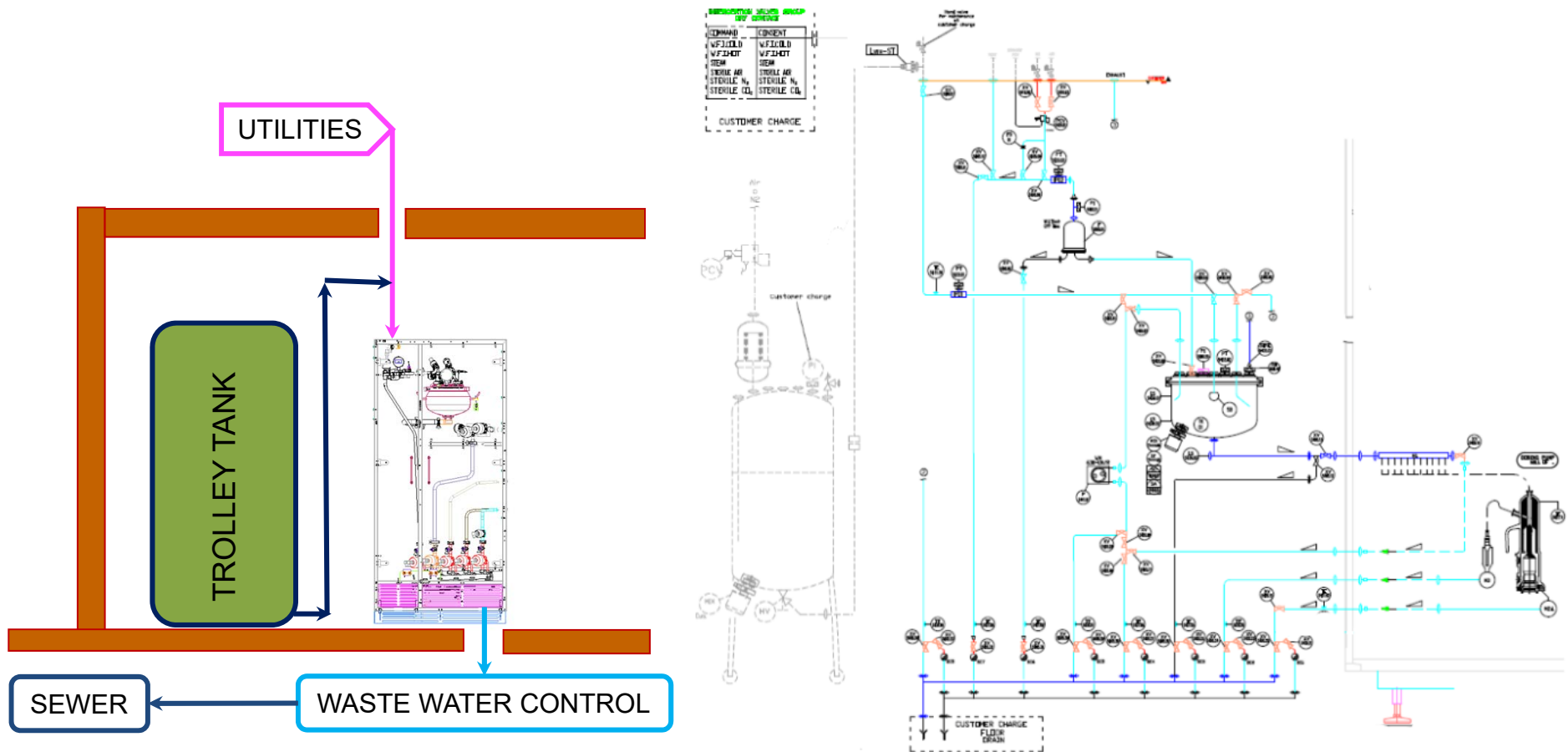
Unless otherwise stated in the URS, the filter cartridge is the sterile barrier.  
 To make a correct wetting it is necessary to “purge” from the upper side of the filter.



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	1 <sup>st</sup> Filter 2 <sup>nd</sup> Filter
	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
IT Pre & Post	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 <sup>st</sup> Filter 2 <sup>nd</sup> Filter
IT Post	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 <sup>st</sup> Filter 2 <sup>nd</sup> Filter
IT Pre	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 <sup>st</sup> Filter 2 <sup>nd</sup> Filter
URS	1 Filtration		1 Redundant Filtration		Double Filtration "Bioburden"		Double Filtration "Sterile"		Double Redundant Filtration				

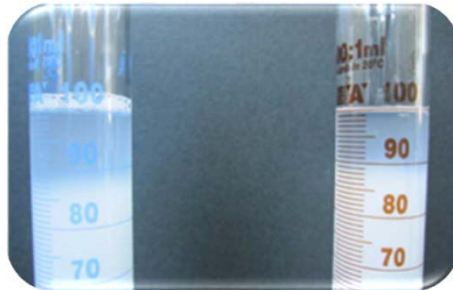
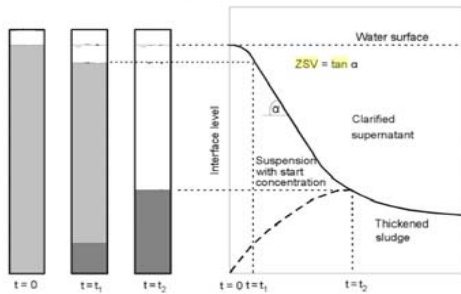
## Example 2

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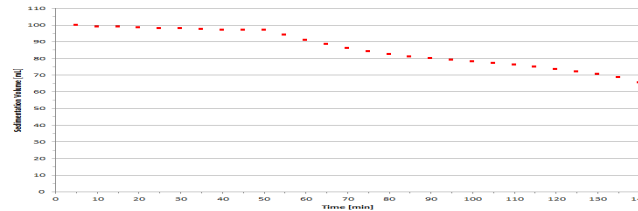




## Example 2 (appendix suspensions)

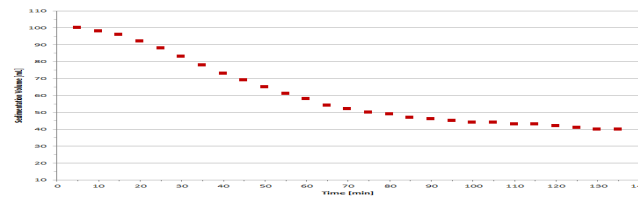


1



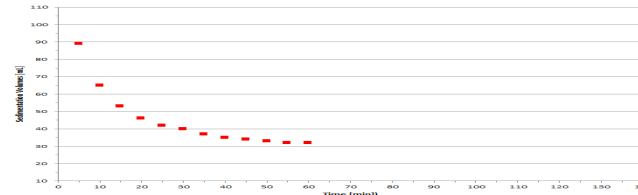
- Long sedimentation time
- «Not heavy» suspension
- Easy to re-suspend after stops
- Does not require constant turbulent flow for movement

2

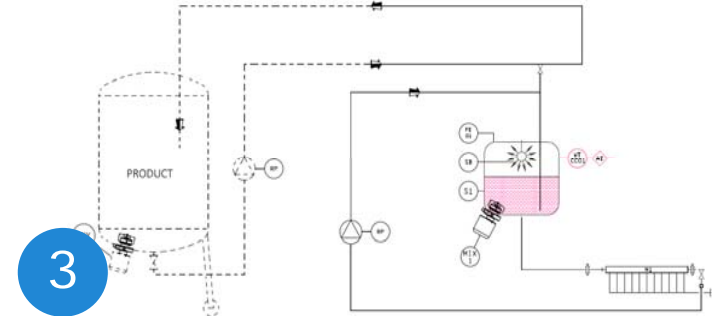
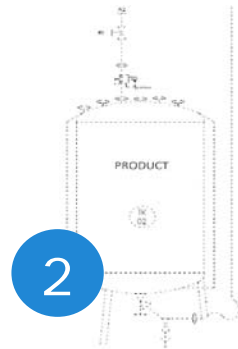


- Medium sedimentation time
- «Medium weight» suspension
- Long time to re-suspend it
- Cannot stay stop before dosing system

3

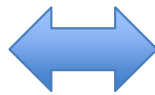
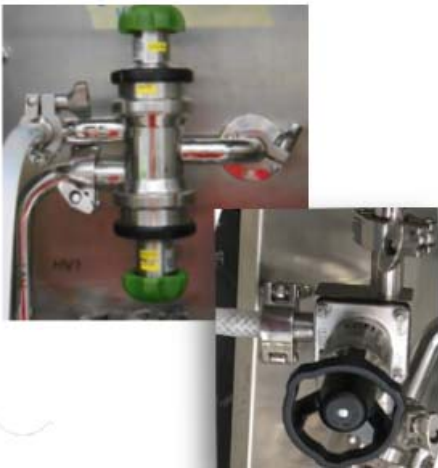
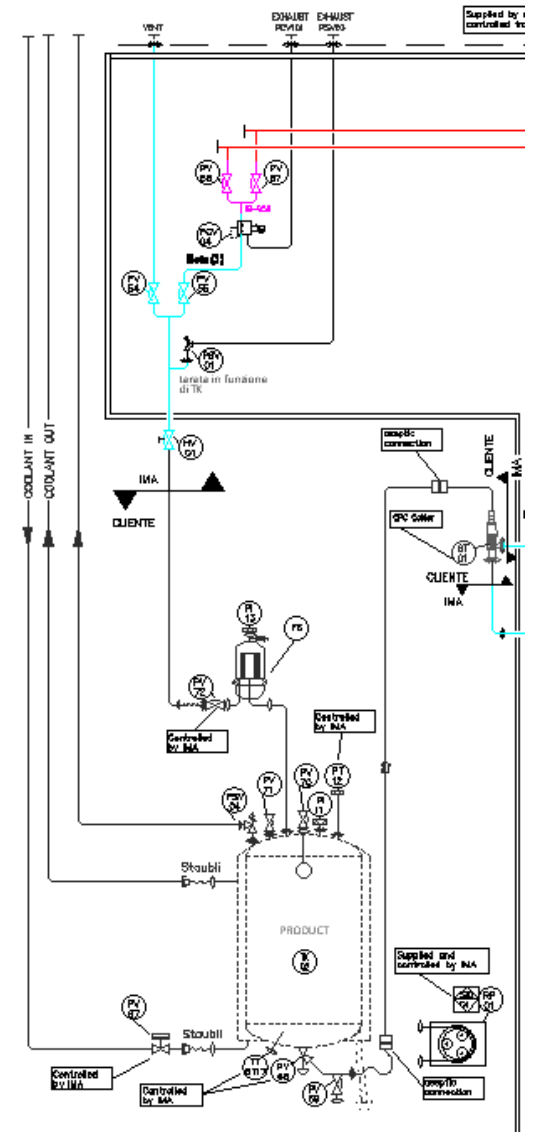
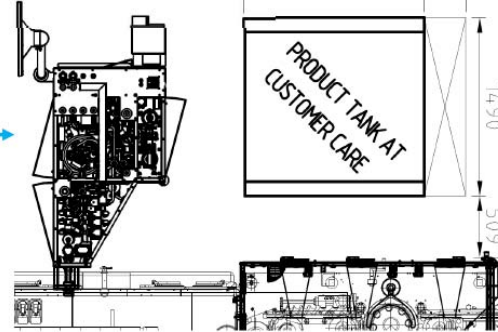


- Fast sedimentation time
- «Heavy» suspension
- The turbulent flow cannot re-suspend it
- Has to remain always in turbulent flow



Example 2 (appendix trolley storage tank)

**LINE LAYOUT**



## Example 2

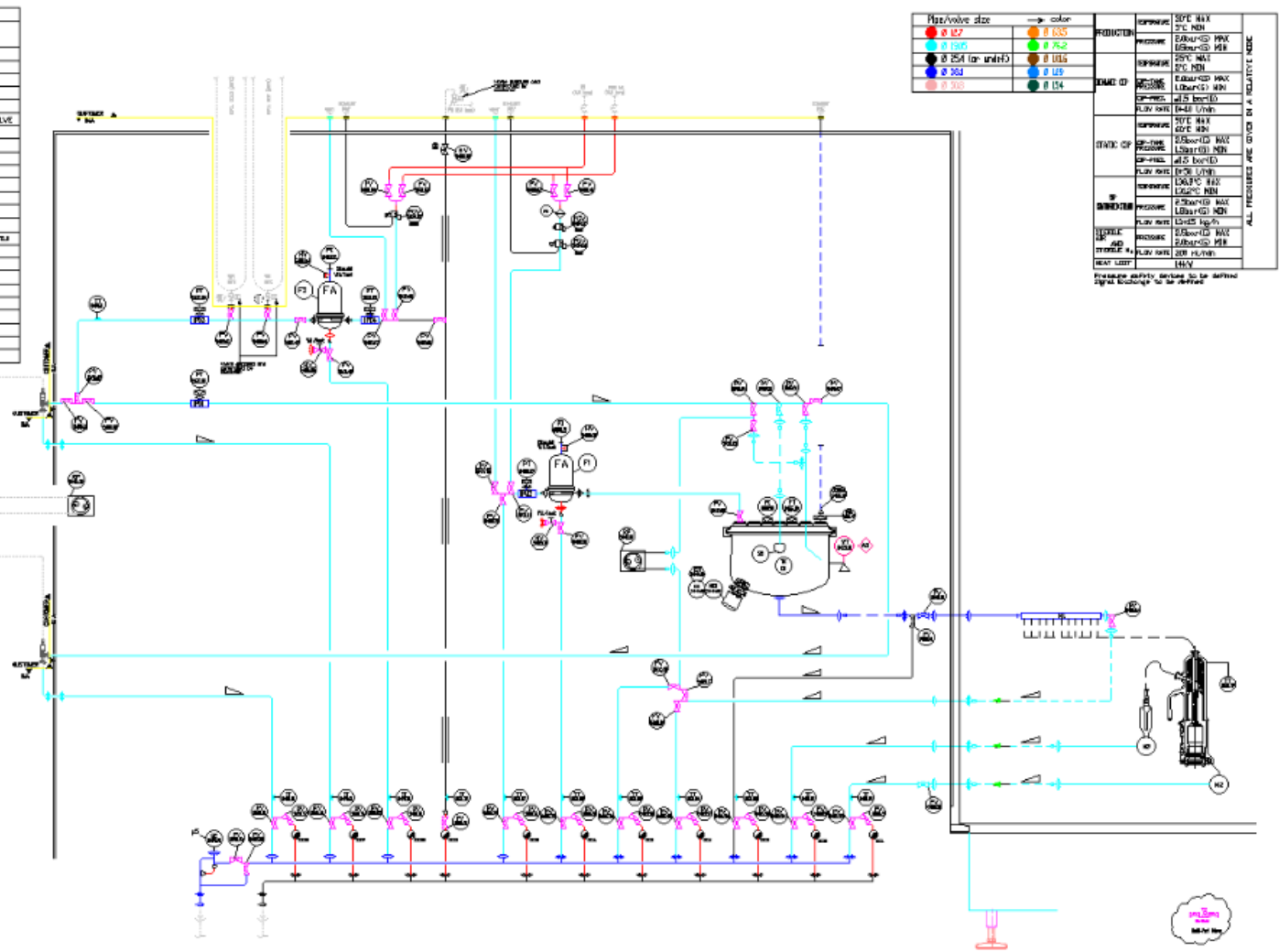
**During kick off meeting:**

Heavy suspension.

Conductivity meter.

Utilities unit.

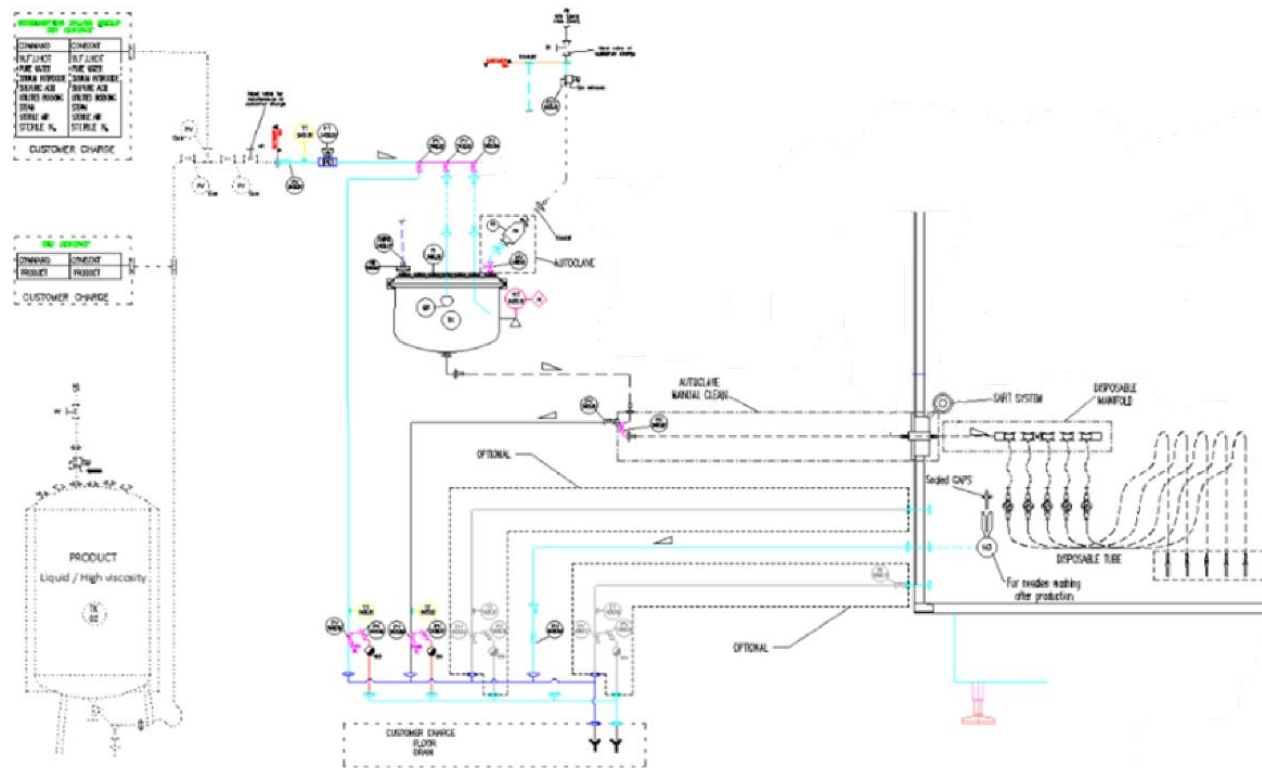
ITEM	SYMBOL	DESCRIPTION
PV	SV	VALVE (PNEUMATIC / PNEUMATIC VALVE)
SV		VALVE (MANUAL / FLARE VALVE)
HS		HEAVY SUSPENSION / MIXING TANK
TS		TEMPERATURE SENSING SYSTEM / MIXING TANK SENSOR
VT		VALVE (CHECK / CHECK VALVE)
CV		CONTROL VALVE / PRESSURE CONTROL VALVE
PL		PNEUMATIC LOGIC / PRESSURE LOGIC
SI		SENSOR (PRESSURE / PRESSURE SENSOR)
TT		TEMPERATURE TRANSDUCER / TEMPERATURE PROBE
MP		MIXING PUMP / MIXING PUMP
MK		MIXING MOTOR / MIXING MOTOR
ST		STRIP TENSION CONTROL / STRIP TENSION
ST		SURVEILLANCE SYSTEM / SPEED DISPLAY
HA		HEAVY SUSPENSION / MIXING TANK HANDLE
HA		HEAVY SUSPENSION / MIXING TANK HANDLE
HA		HEAVY SUSPENSION / MIXING TANK HANDLE
FA		FILLER AREA / VIBR. FEEDER
SB		STRIKE-BALL RETURN / RETURN STRIKE-BALL
TK		TANK / PRODUCT TANK
CA		CANISTER / PRODUCT CANISTER
VT		VALVE (CHECK / CHECK VALVE)
PT		PROBING TUBE / PROBING TUBE
PT		PROBING TUBE / PROBING TUBE
PT		PROBING TUBE / PROBING TUBE



## Example 1

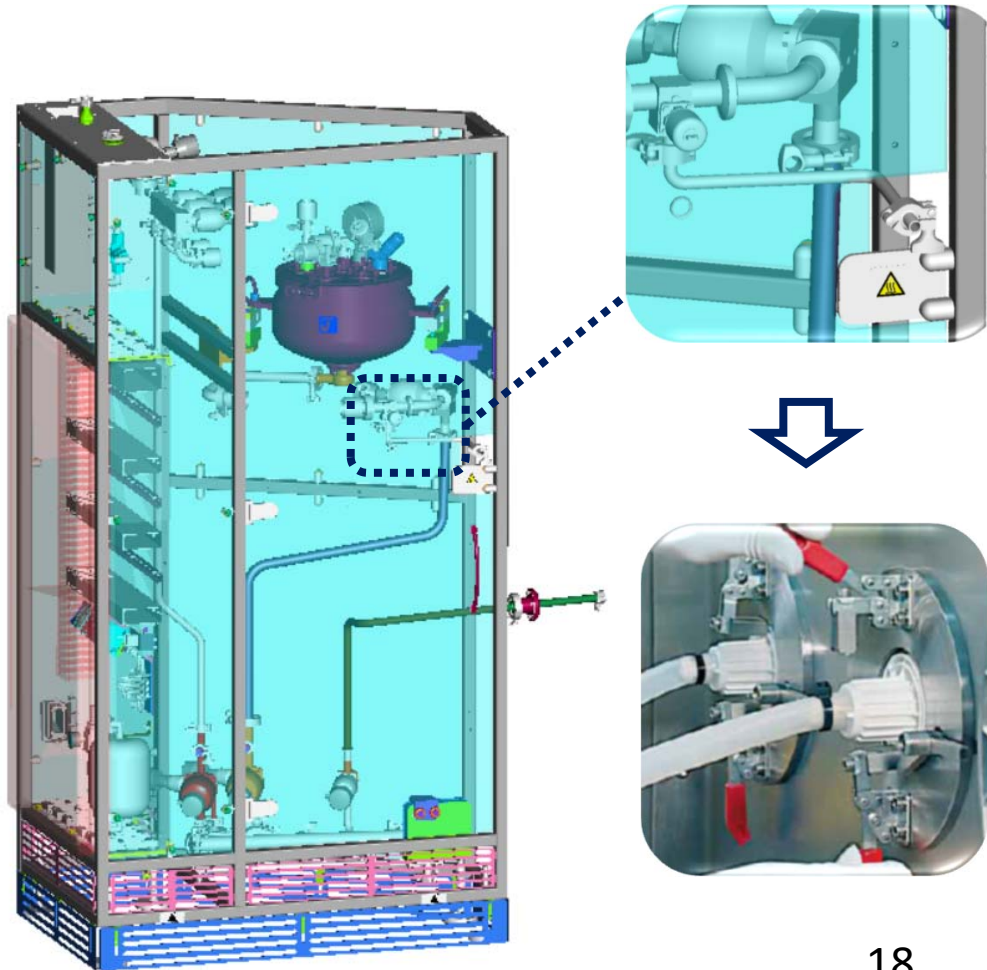
CIP&SIP system interfacing with peristaltic pump technology and predisposition for future volumetric pump technology.

Cytotoxic products.





Example 1







# New hybrid system Combination between Single Use and Multi Use

## 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

Machine	Activity	Phase	Notes	Time [hour]						
				1 hr	2 hr	3hr	4hr	5hr	6hr	
CIP&SIP skid	CIP	Handling		█						
		CIP Statico		█						
		CIP-Cooling		█	█					
	SIP	Handling				█				
		Leak Test & Pre-heating			█	█				
		SIP				█	█	█		
Isolator	WIP	Drying&Cooling					█	█		
		Automatic + Manual Washing		█						
		Flushing + Manual Drying		█	█					
		Automatic Drying		█	█	█				
	VHP	Isolator Leak Test					█			
		Dehumidification					█	█		
		Injection (conditioning+decontamination)					█	█		
		Preliminary Aeration ( Auxiliary+Generator)	(Catal.)					█	█	
		Intermediate Aeration	(Catal.)						█	█
		Final Aeration	(Catal.)							█

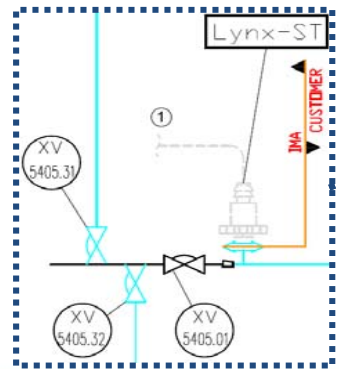
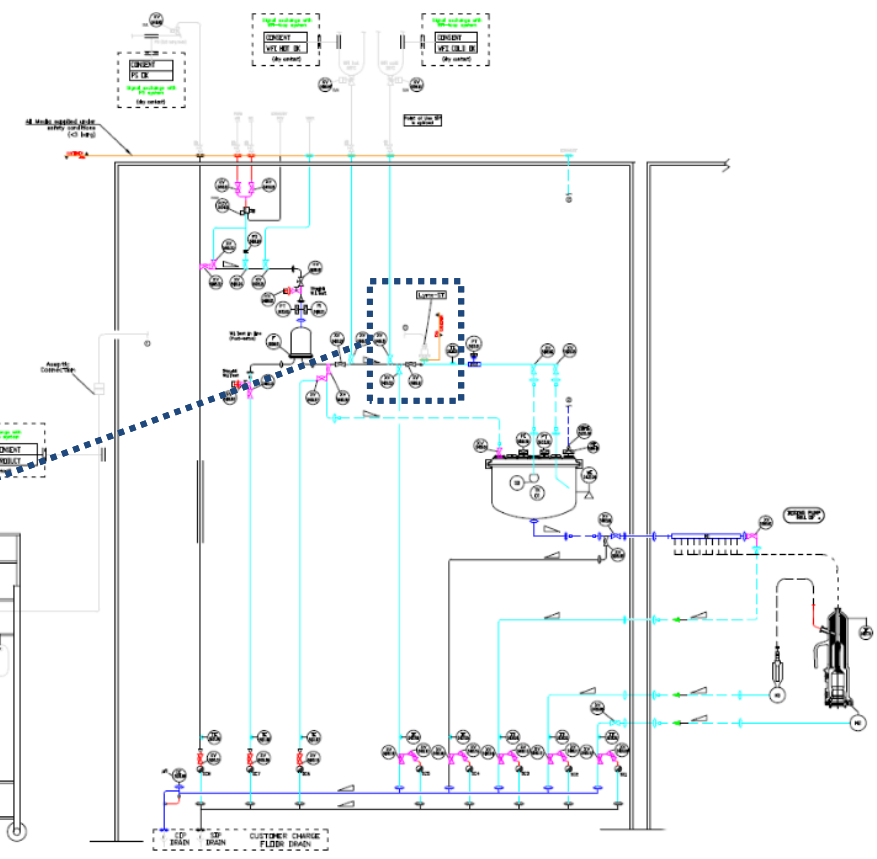
## Example 2

- 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.

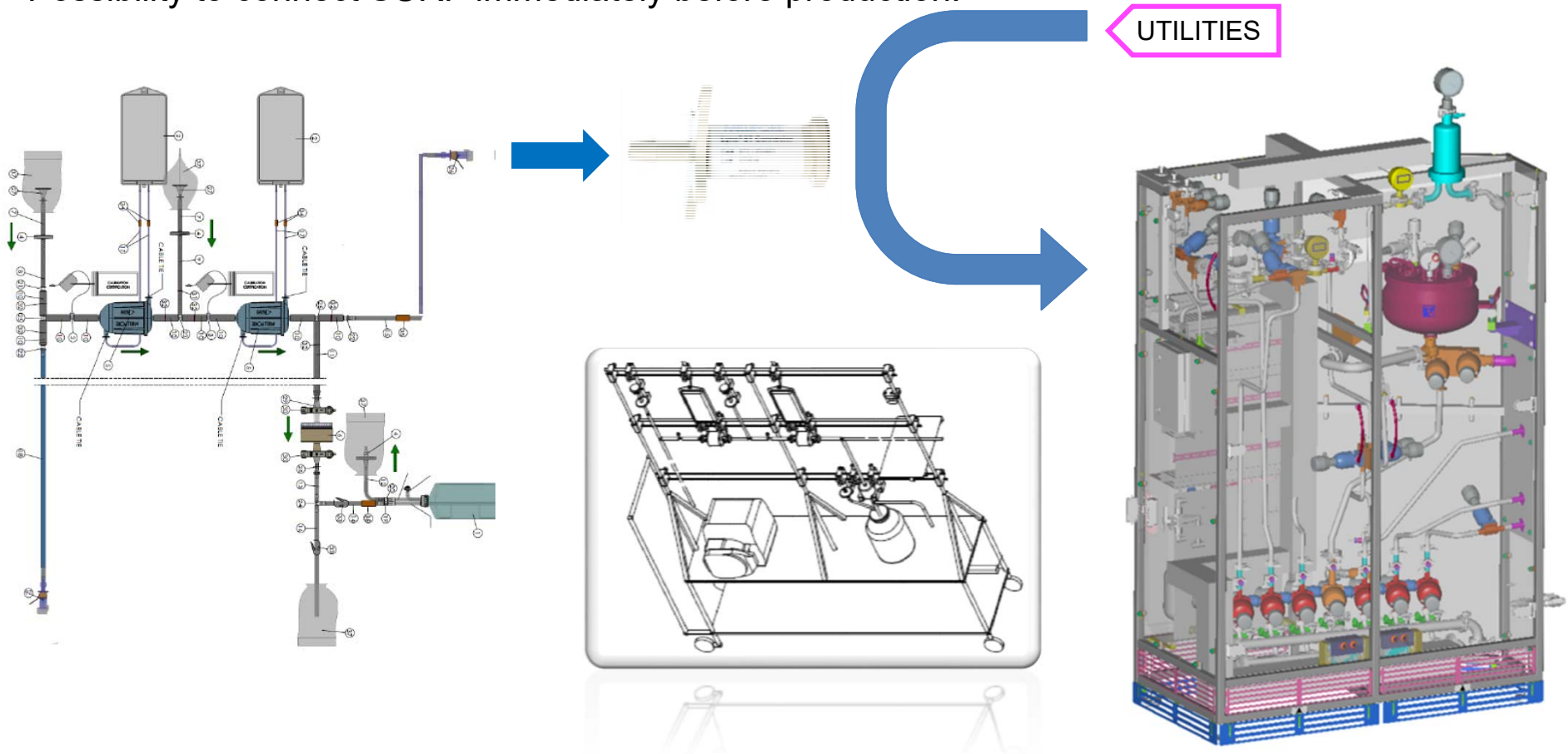
ITEM	DESCRIPTION	UNITED	FUNCTION
101	VALVE	MANUAL	STOP/START
102	VALVE	MANUAL	STOP/START
103	VALVE	MANUAL	STOP/START
104	VALVE	MANUAL	STOP/START
105	VALVE	MANUAL	STOP/START
106	VALVE	MANUAL	STOP/START
107	VALVE	MANUAL	STOP/START
108	VALVE	MANUAL	STOP/START
109	VALVE	MANUAL	STOP/START
110	VALVE	MANUAL	STOP/START
111	VALVE	MANUAL	STOP/START
112	VALVE	MANUAL	STOP/START
113	VALVE	MANUAL	STOP/START
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196	VALVE	MANUAL	STOP/START
197	VALVE	MANUAL	STOP/START
198	VALVE	MANUAL	STOP/START
199	VALVE	MANUAL	STOP/START
200	VALVE	MANUAL	STOP/START



## Example 2

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

Possibility to connect SURF immediately before production.



## Example 1

### During kick off meeting:

Single use filling system  
with peristaltic pump  
technology.

Conductivity meter with  
by-pass for detergents.

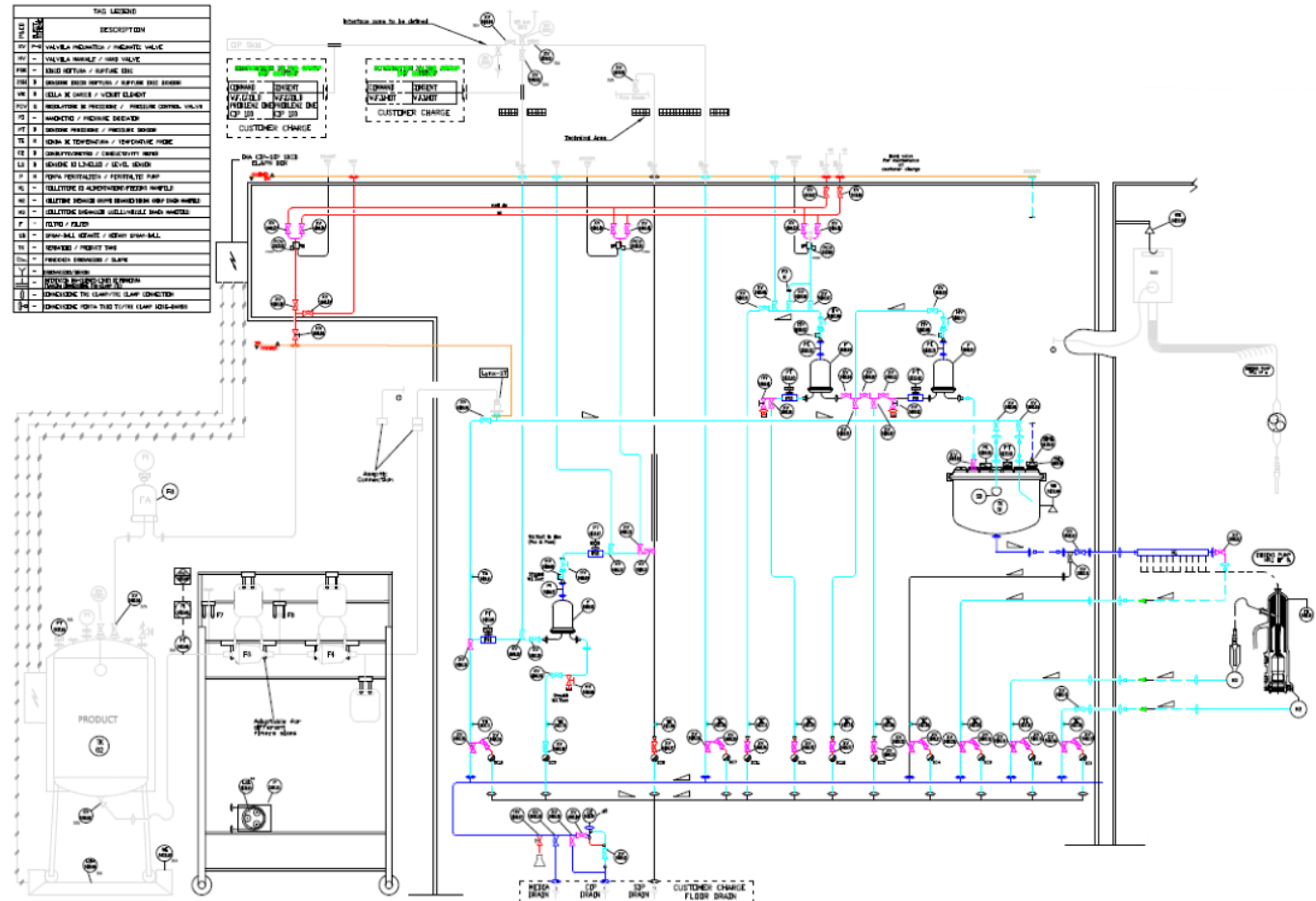
Sampling valve for waste  
water.

Dedicated drain first rinse.

Double venting filtration.

Management of trolley  
storage tank and floor scale.

Transfer by overpressure  
or peristaltic pump.





## New hybrid system Combination between Single Use and Multi Use

### Example 2

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



23



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

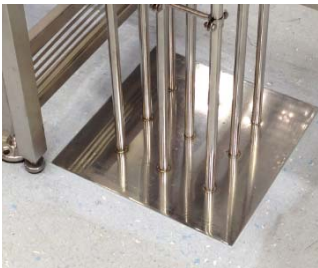
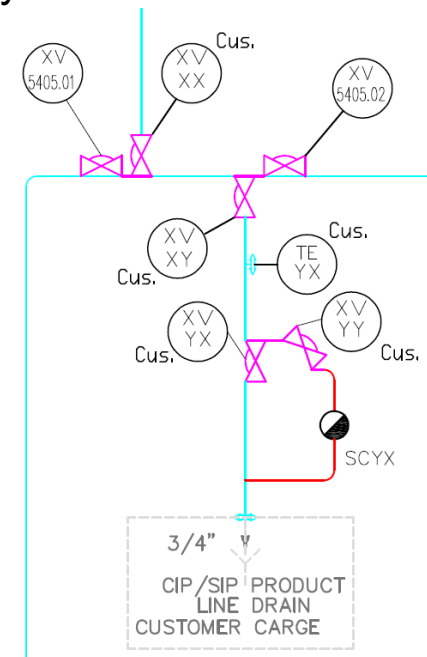
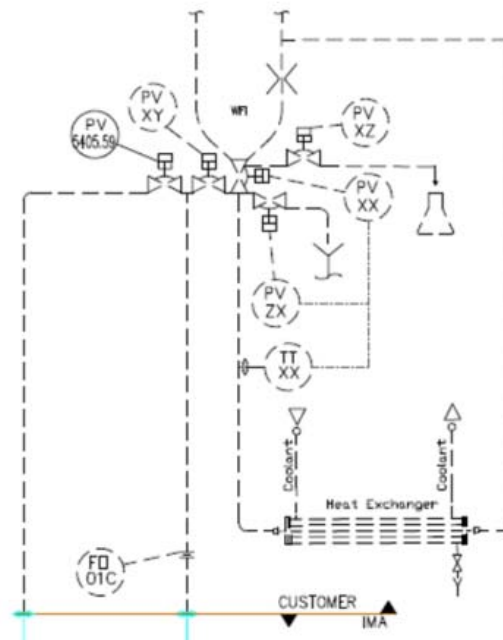
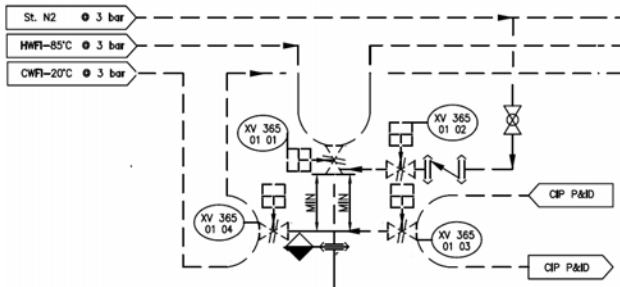
- DRAIN INTERFACES
- INTERFACE WITH WFI POINT OF USES
- INTERFACES WITH COMPOUNDING SYSTEM
- POINT OF USE VALVE

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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