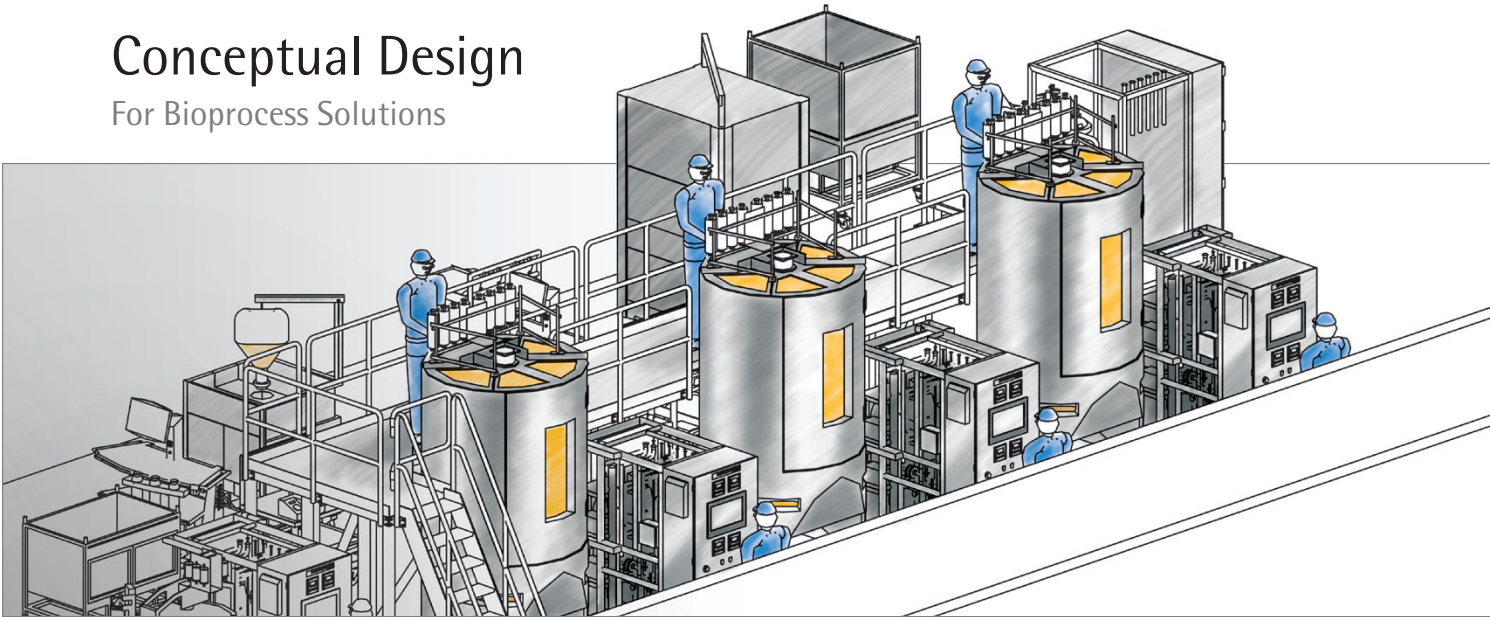




Conceptual Design

For Bioprocess Solutions



To start click here

Designing a New Manufacturing Facility for Biopharmaceuticals

The planning and designing of a new biopharmaceutical production facility is a complex process. A new facility must fulfill all regulatory requirements and the production capacity must be sufficient and flexible enough to meet ever changing demands.

At Sartorius we have extensive experience in designing facilities that fulfill all these requirements. We can help you with the creation of a facility concept and quickly find answers to fundamental questions in order to meet demanding timelines.

Our conceptual design services deliver comprehensive process reviews, process layout studies, process scale-up designs, as well as process automation concepts.

Business Drivers:

- Single or multi product facility?
- Capacity requirement ?

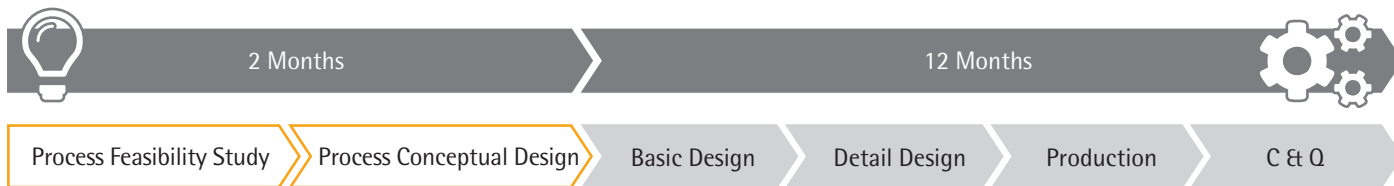
Process Drivers:

- Campaign approach?
- Fully single-use or hybrid?

Regulatory Drivers:

- Which room classification do I need in which area?
- What kind of room segregation fits best to my needs?

Conceptual Design

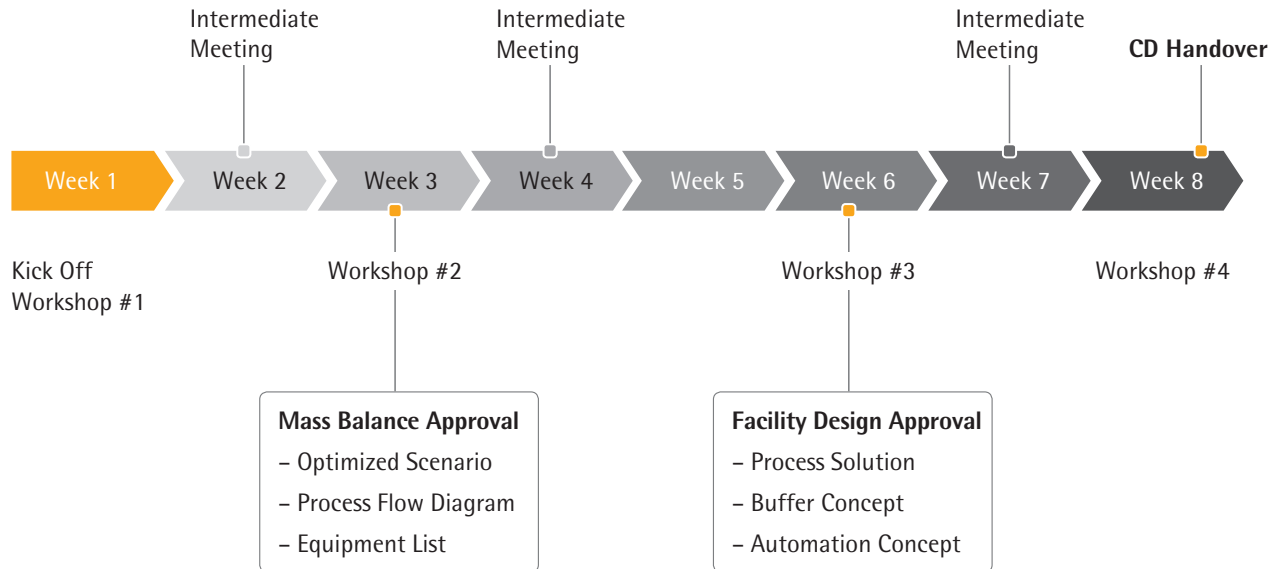


Testing of feasibility and taking key-decisions on the manufacturing strategy and design concept

- Creation of mass balances
- Process Scheduling
- Process Flow Diagram
- Equipment List
- Selection of the automation concept
- Process layout

Project Schedule | Time Schedule

Level A time schedule based on Deliverables | Activities

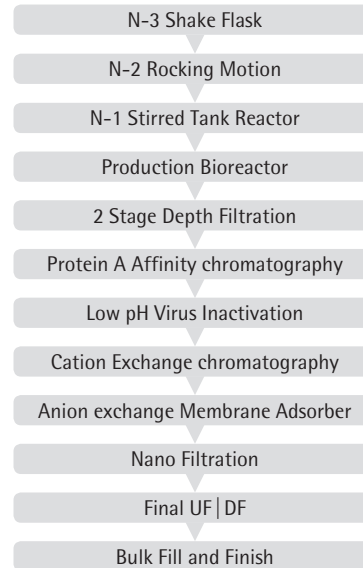


Process Modelling

Based on your process information we calculate the media and buffer requirements as well as the time scheduling of your processes.

By modelling different scenarios we can select the most optimal parameters for your facility.

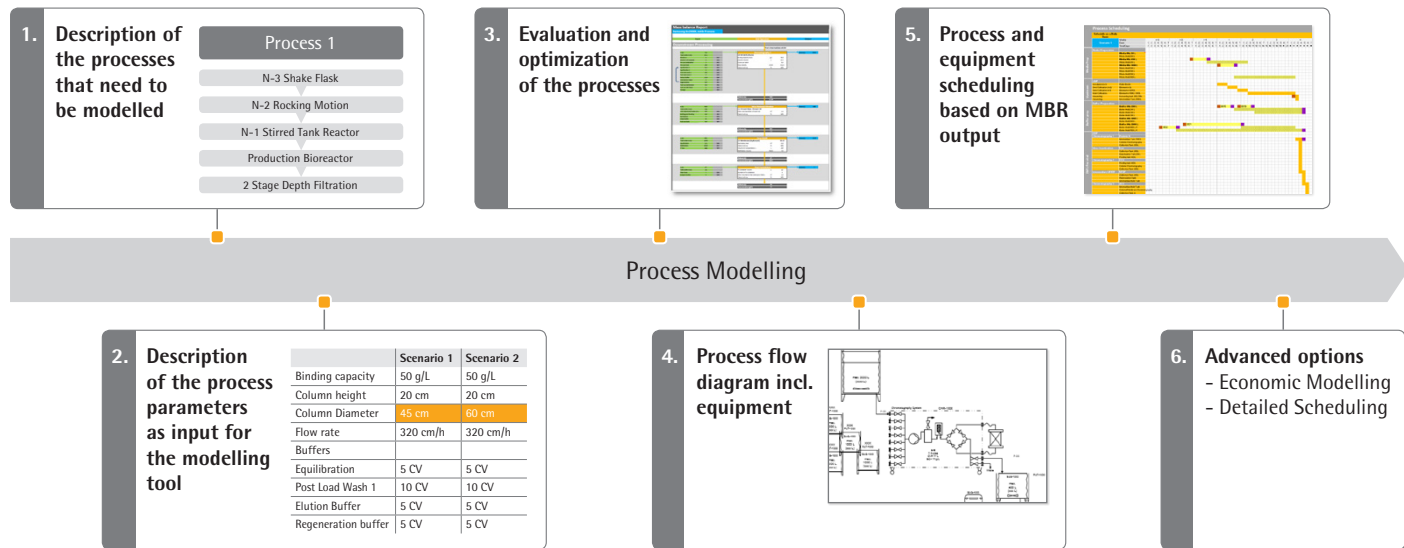
Our experiences with both single-use and stainless steel equipment will help you to find the best solution for all your processes.



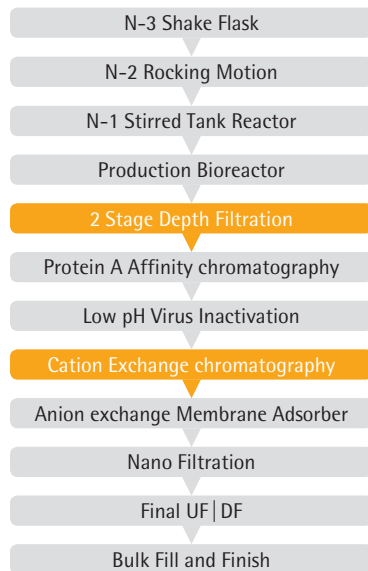
Mass Balance Review



Process Modelling



Process Description



Evaluate the impact of different technology options on your process

- Sartoclear Dynamics
 - 2 Stage Depth Filtration
 - Centrifugation + Depth Filtration
-
- IEX resin (bind and elute)
 - IEX resin (Flow through)
 - IEX membrane (bind and elute)
 - IEX membrane (flow through)

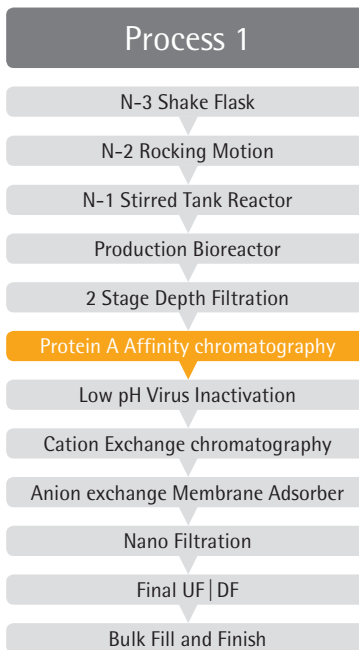
Model parameters to optimize buffer requirements and equipment sizes

	Scenario 1	Scenario 2
Binding capacity	50 g/L	50 g/L
Column height	20 cm	20 cm
Column Diameter	45 cm	60 cm
Flow rate	320 cm/h	320 cm/h



Evaluate the impact of changing parameters on important factors such as buffer demands and equipment scheduling.

	Scenario 1	Scenario 2
Binding capacity	35 g/L	35 g/L
Column height	20 cm	20 cm
Column Diameter	30 cm	45 cm
Flow rate	320 cm/h	320 cm/h
Buffers		
Equilibration	5 CV	5 CV
Post Load Wash 1	5 CV	5 CV
Elution Buffer	2 CV	2 CV
Regeneration buffer	3 CV	3 CV



Example:
Impact of Protein A column volume

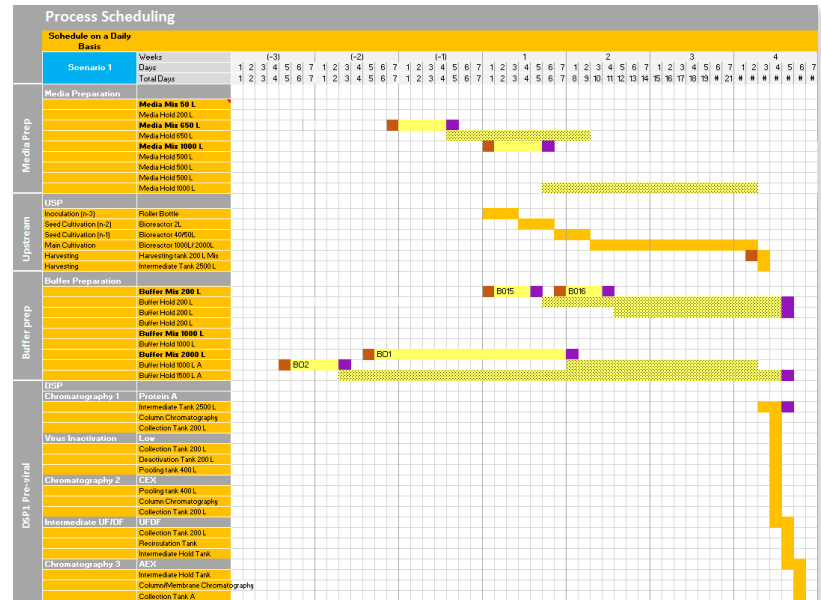
	Scenario 1	Scenario 2
Cycles per Batch	8	4
Process time	13 h	7 h
Concentration Out	14.6 g/L	12.9 g/L
Volume Out	226	254
Buffers		
Equilibration	565	636
Wash 1	565	636
Elution Buffer	226	254
Regeneration buffer	339	382

Process Scheduling

The results from the MBR and the generated PFD can be used to create detailed scheduling in order to streamline the production process.

Reasons for process scheduling:

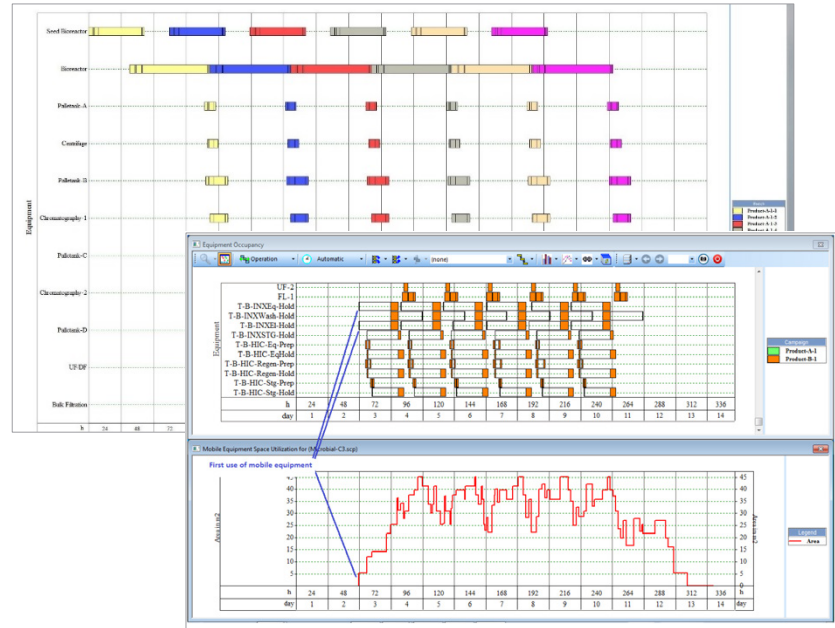
- Hourly based process scheduling considering 3 shifts
- Process debottlenecking
- Equipment capacity and availability evaluation
- Shared equipment strategy
- Media-Buffer preparation & holding concept



Advanced Process Scheduling

On request the advanced Process scheduling with Schedule Pro* can be added to the basic package.

- Process debottlenecking
- Shift modelling capabilities e.g. 2 shifts, Handles plant down-time, weekend and holiday schedules
- Multi-product campaign scheduling
- Cost engineering, optimization of media-buffer preparation and holds
- Labor, room, facility occupancy capabilities



* Schedule Pro is licensed from Intelligen Inc.

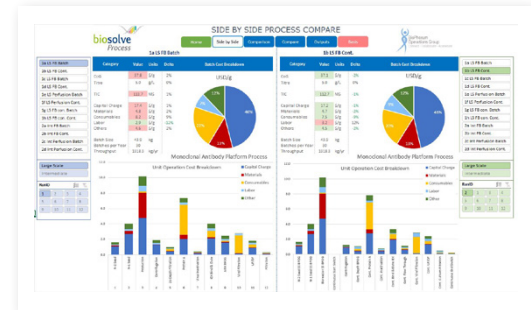
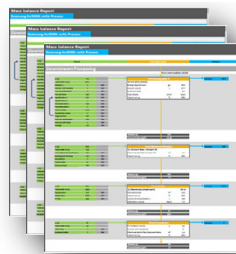
Economic Modeling

Economic modeling can help you in making better decisions for your project. Together with our partner Biosolve we can quickly evaluate the economical impact of process related factors.

Open Questions:

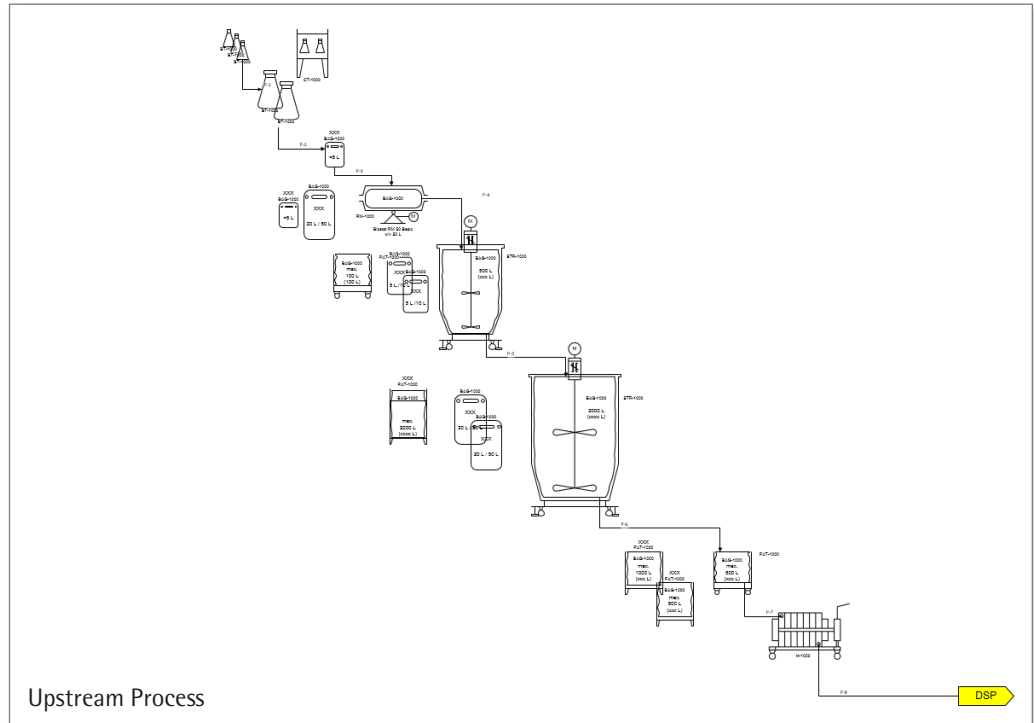
- Single-use or hybrid?
- How many bioreactors?

Mass Balance Review (MBR)



Process Flow Diagram

(PFD). This tool provides the visualization of process relationships as well as the major equipment selection based on outputs of the mass balance review.



Introduction

Mass Balance Review

Process Flow Diagram

Process Layout

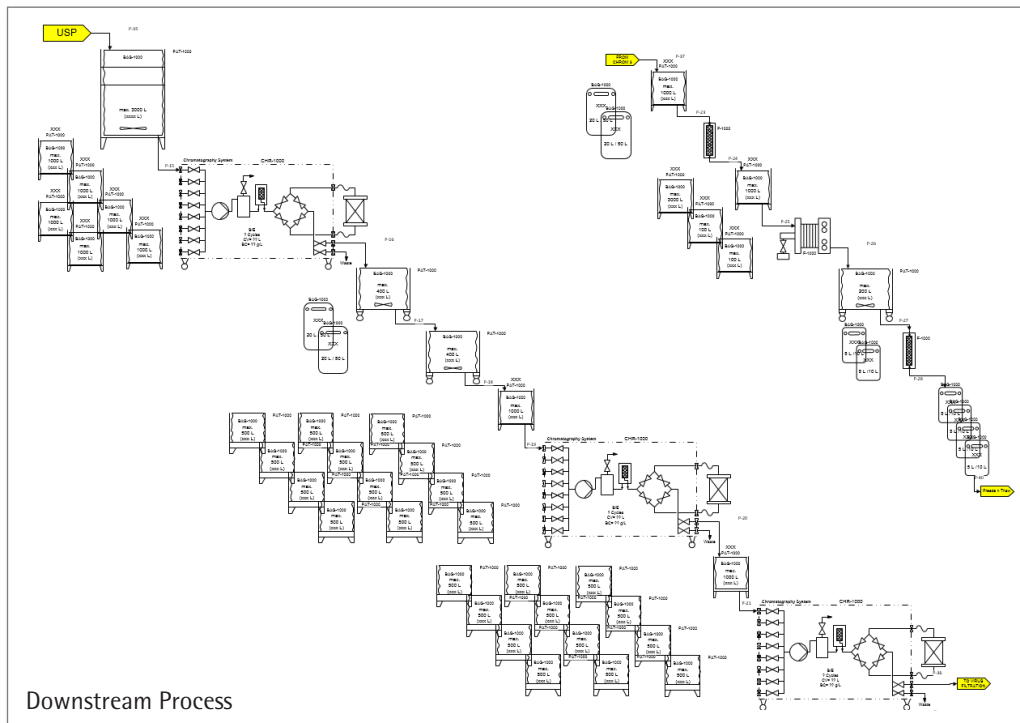
Automation

Standard CD Package



Process Flow Diagram

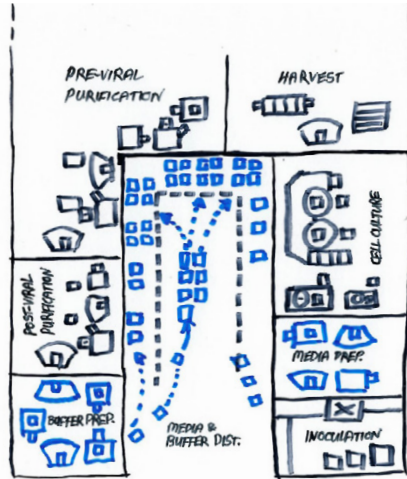
Parallel to the PFD preparation a buffer concept will be selected and visualized.



Buffer Distribution Concept

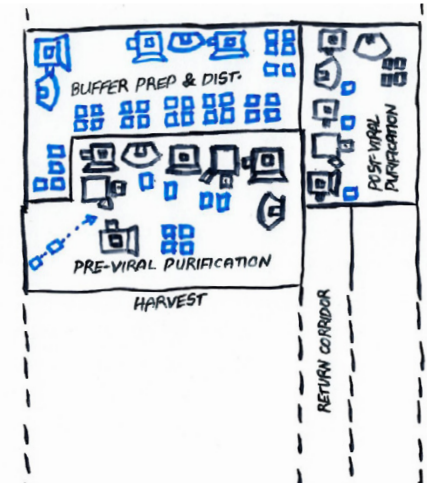
As most DSP steps require large buffer volumes, the process layout is highly impacted by the buffer preparation and distribution concept.

Single-use technology offers flexible new options for buffer concepts. Two examples can be seen on the right.



Separated preparation | ready made

- Lower room classification in distribution area
- More challenging with large buffer volumes



Combined preparation and storage

- Less trafficking
- Adjacency & wall area requirement

Concept 1: Separated Preparation | Ready Made

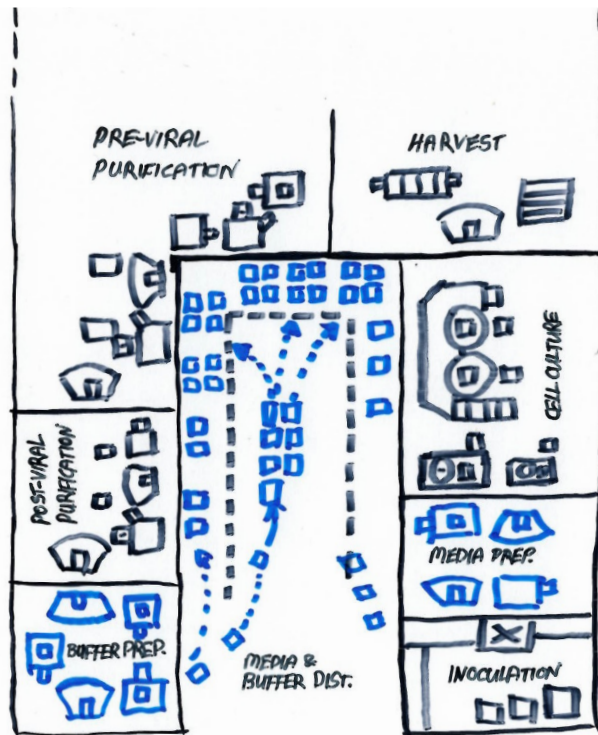
Buffer preparation is remote from the point of use

Advantages:

- High mobility and flexibility
- Distribution area can be reduced to CNC, leads to less operational cost
- Smaller Buffer Prep
- Less movement in Pre Viral & Post Viral area

Challenges:

- Adjacency & wall area required for previral and post viral room with distribution corridor
- Suitable only for low titer process, challenging for high titer process
- Fixed pallettanks
- High trafficking



Concept 2: Combined Preparation and Storage

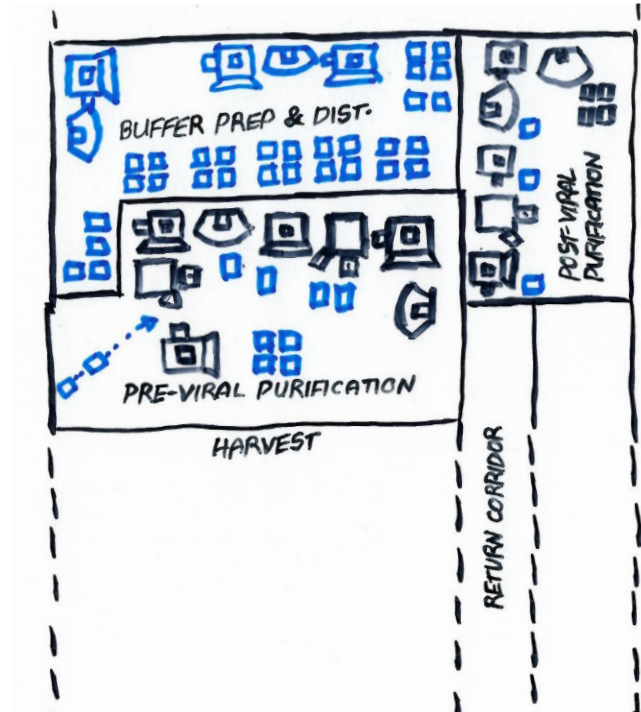
Large volume buffers are prepared and stored in proximity to the point of use.

Advantages:

- Less trafficking
- Suitable for low Et high titer process
- Less movement in Pre Viral Et Post Viral area

Challenges:

- Adjacency Et wall area required for previral and post viral room with buffer area
- Bigger space for preparation Et distribution. Extra operational area required
- Fixed high volume pallettanks
- Higher Grade D area leads to higher operational cost



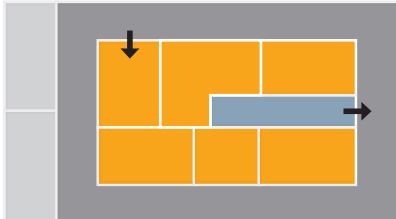
Fitting Layout Around Process Solution

Depending on the number of product, batches and flexibility requirements for the future, a process layout will be drawn. The process layout must full fill cGMP & regulatory principles and will consider personnel, material, product and waste flows.

Different concepts have been generated and optimized for common single use and hybrid projects.

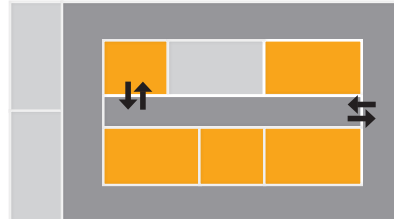
Color Codes:

- Process Area
- Supply Corridor
- Support Area
- Return Corridor



Supply to Return Concept

- Unidirectional Flow
- Less traffic



Mobile Buffer Concept

- Bidirectional flow
- High traffic



Futuristic Dance Floor | Ballroom Concept

- Reduce walls and airlocks
- Operational flexibility

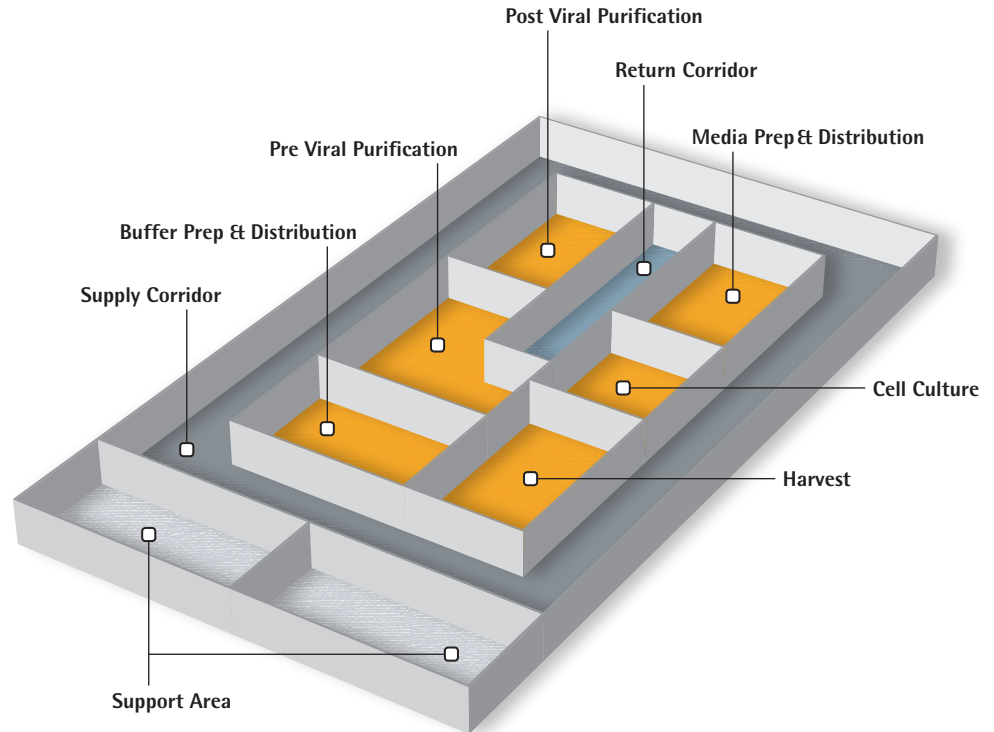
Supply to Return Concept

Characteristics of the supply to return concept:

- Unidirectional flow
- No transportation of buffers due to adjacency of buffer prep to pre and post viral purification

Guidance for 2 × 2000 L STRs:

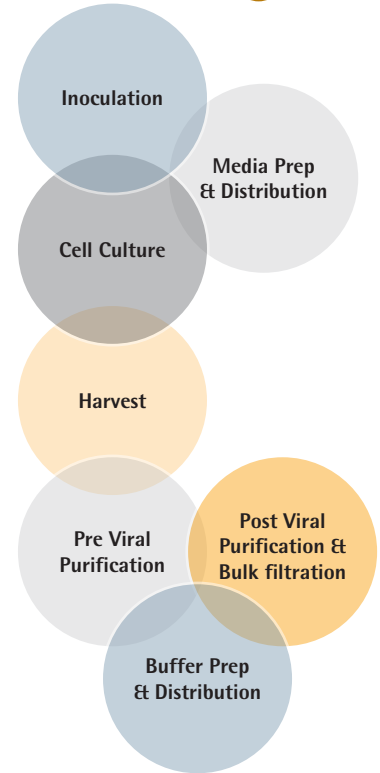
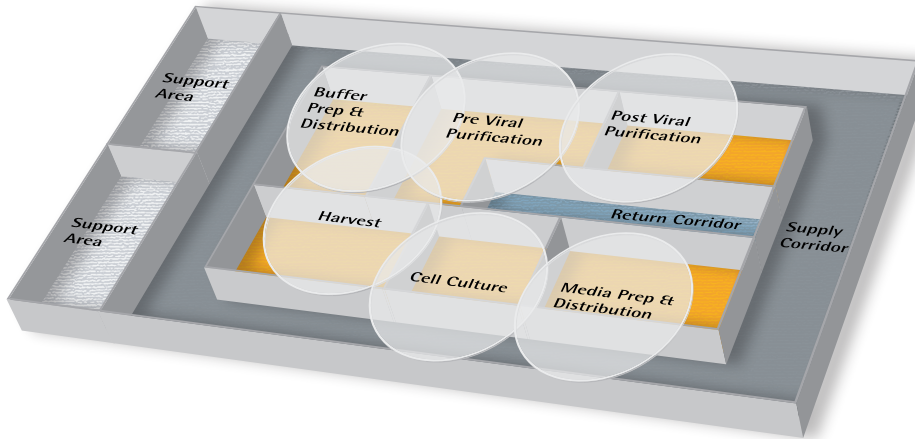
- Total process area required: 1200 – 1500 m²
- ISO8 | Grade C: 175 – 250 m²
- ISO9 | Grade D: 625 – 750 m²
- Grade NC | CNC: 400 – 500 m²



Adjacency Bubble Diagram

Adjacency of certain process areas is key for streamlined processing. Static equipment near to next process unit reduces movement of tanks and the length of tubing's.

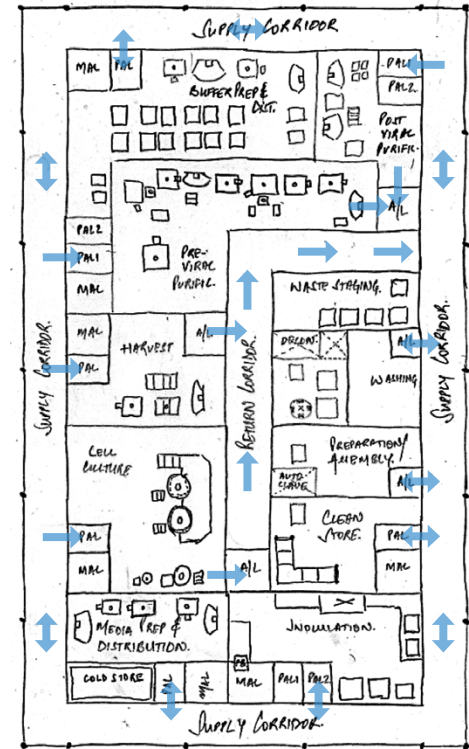
Fitting the facility around the equipment rather than the equipment around the facility



Process Layout Concept I

Personnel Flow

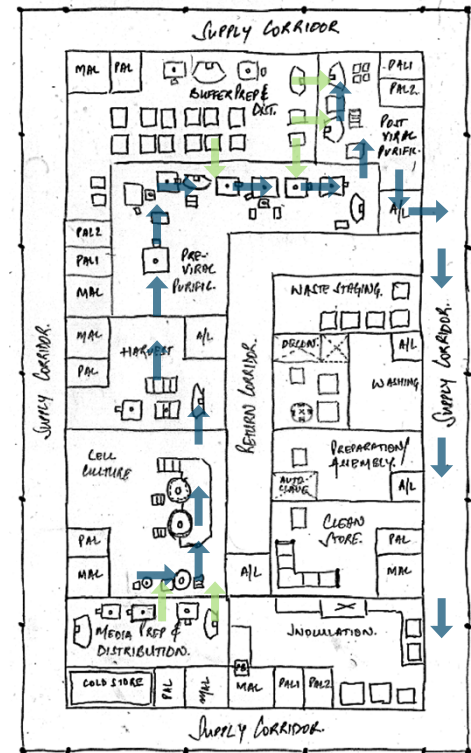
- Uni-directional flow in process areas
- Bi-directional flow for media & buffer areas with support areas



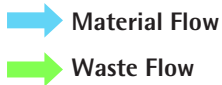
Process Layout Concept I



- Product streams incl. media and buffer transfer
- Product flow from one room to another via wall penetrations
- Planned room adjacency



Process Layout Concept I

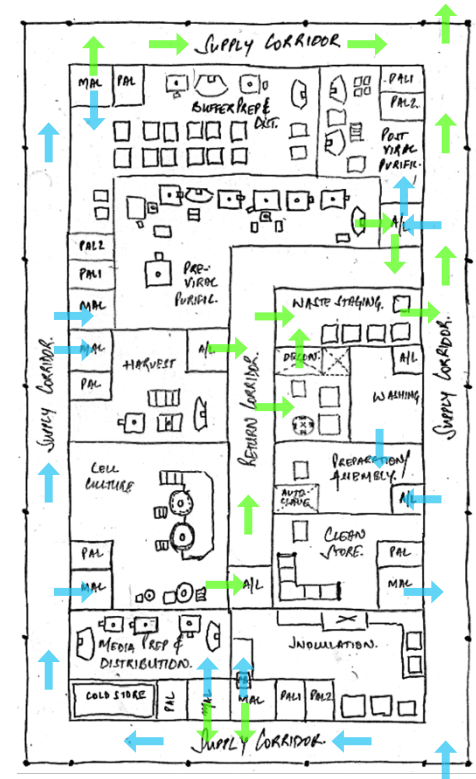


Material Flow

- Uni-directional flow in critical environments
- Risk Based Approach
- Temporal Segregation, Procedural Control

Waste Flow

- Uni-directional flow
- Decontamination of GMO soiled solid & liquid waste
- Risk Based Approach
- Temporal Segregation, Procedural Control



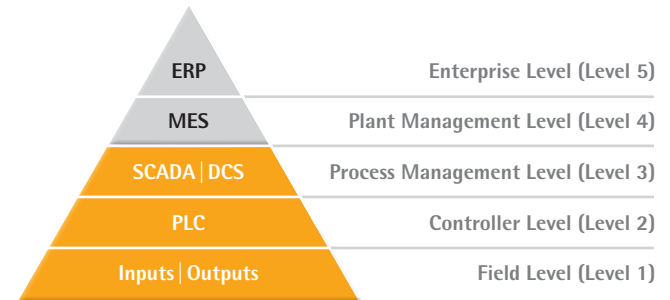
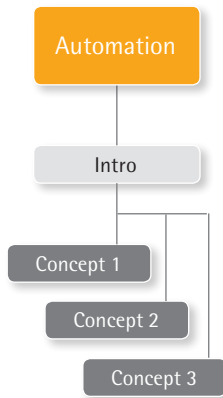
Introduction

The automation of your processes and the integration into existing networks is a key factor for a successful operation.

Unit operations such as bioreactors and DSP equipment can be implemented at different levels providing you different levels of control and flexibility.

Depending on the kind of project we can either offer proprietary solutions or partner with all major industrial players such as Siemens (PCS7) and Emerson (DeltaV).

Our automation expertise covers the full spectrum from basic stand alone units, to fully integrated systems, into DCS networks.



Introduction

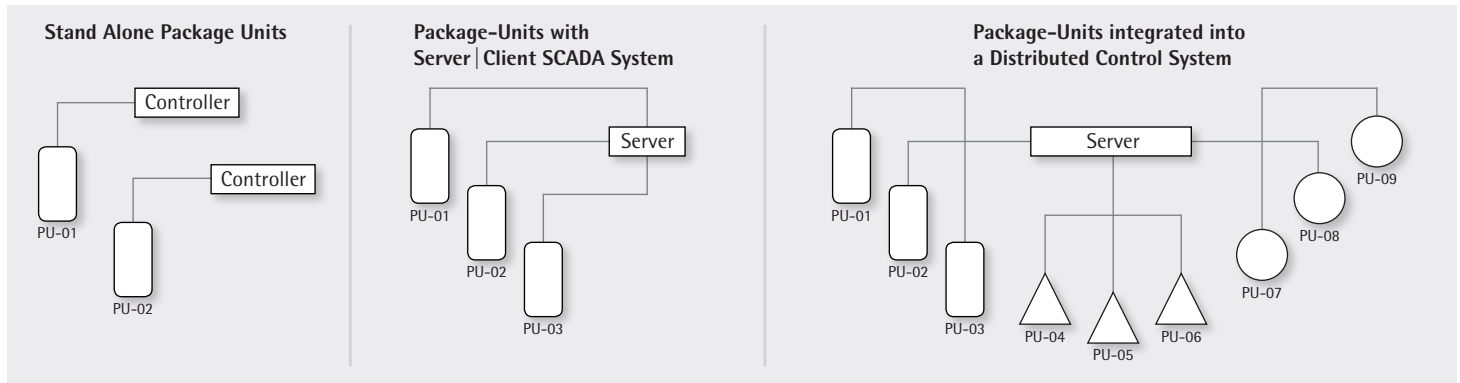
Mass Balance
ReviewProcess Flow
DiagramProcess
Layout

Automation

Standard
CD Package

Automation Concepts Overview

In general there are 3 different automation concepts that can be applied in manufacturing facilities. At Sartorius we guide you to the best approach for your unique situation.



- Individual local control
- Data transfer via OPC

- Remote control of group
- Central Unit Reports

- Plant wide process visualization with batch and recipe control
- Plug-and-Play capabilities

Introduction

Mass Balance
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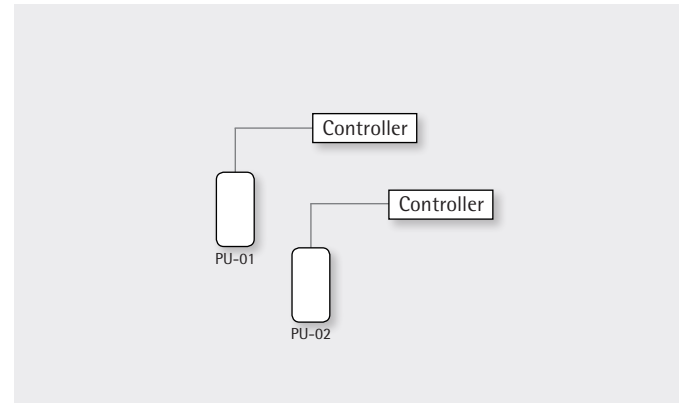
Stand Alone Package-Units

All control, reporting, recipe and unit operations are localized into one system called the "package-unit". This includes all parameter settings for unit-based control loops as well as recipes.

Acquired measurement data can be transferred to a higher level via OPC connectivity.

The autonomous process units, require individual maintenance and 21 CFR 11 reports are only possible per individual unit.

This basic approach is an ideal solution for a process with a limited set of parameters.



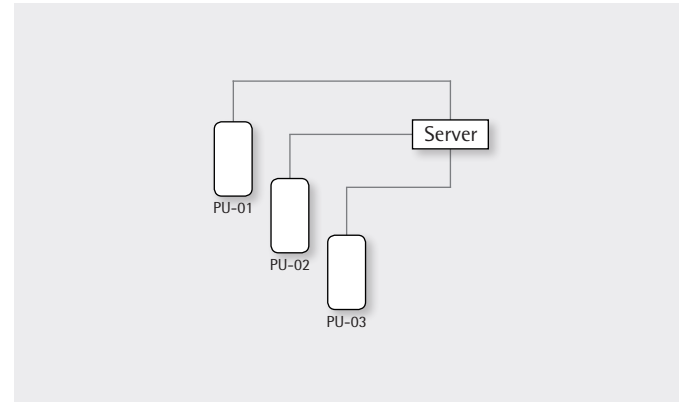
Package-Units with Server | Client SCADA System

A group of unit operations or clients (e.g. all bioreactors) is connected to a server with all control functionalities installed on it (SCADA). Control loops and recipes are used for this group only.

Additional unit operation groups may use another server system or use local package unit functionalities.

Measurement data from all individual systems can be transferred to one server which enables centralized data handling.

This classical approach has lower investment costs and is often used in pilot plants and small facilities.

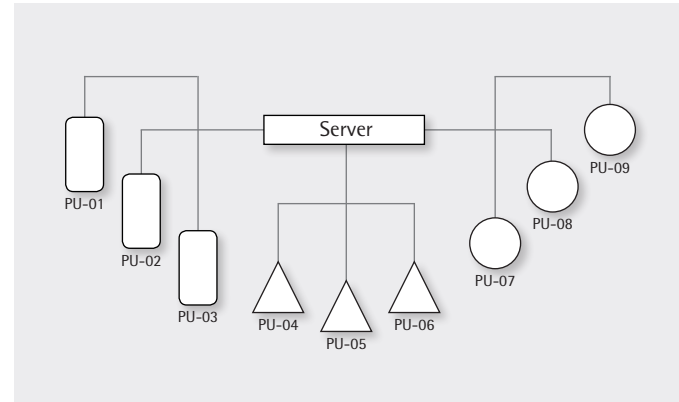


Package-Units Integrated into a Distributed Control System

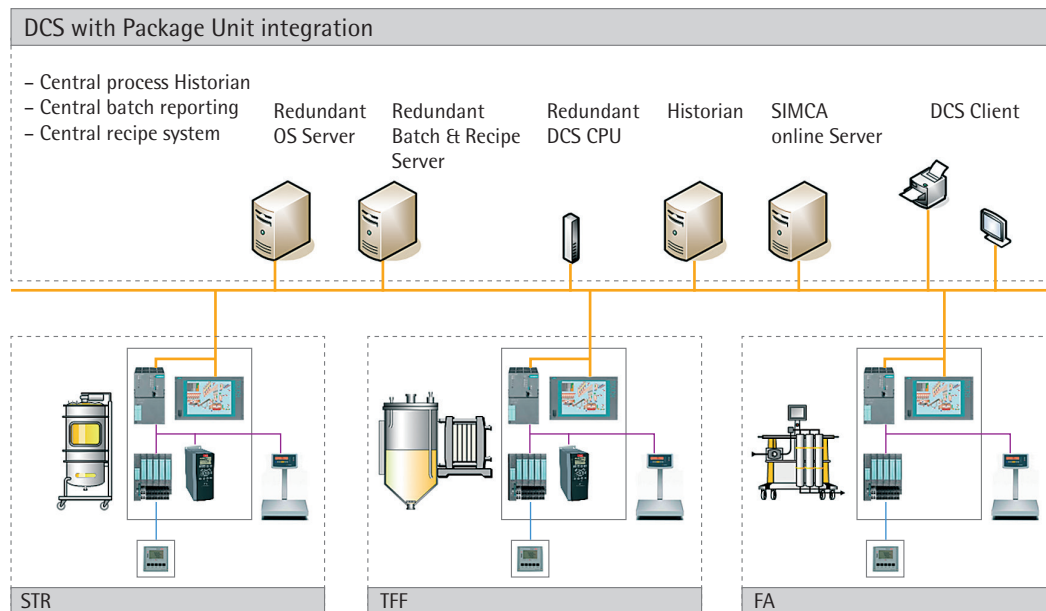
All control and data acquisition functionalities are integrated top to bottom. Parameter settings, recipes, as well as batch management control loops are distributed on a plant-wide level.

Implementing a single control platform across all plant applications provides a number of advantages, including more synchronized processes, increased reliability, reduced maintenance efforts and seamless transfer of real-time data for improved decision-making and increased manufacturing flexibility.

Distributed control systems are to those seeking a state of the art automation system driven by the process state.



Example of a DCS Network



Introduction

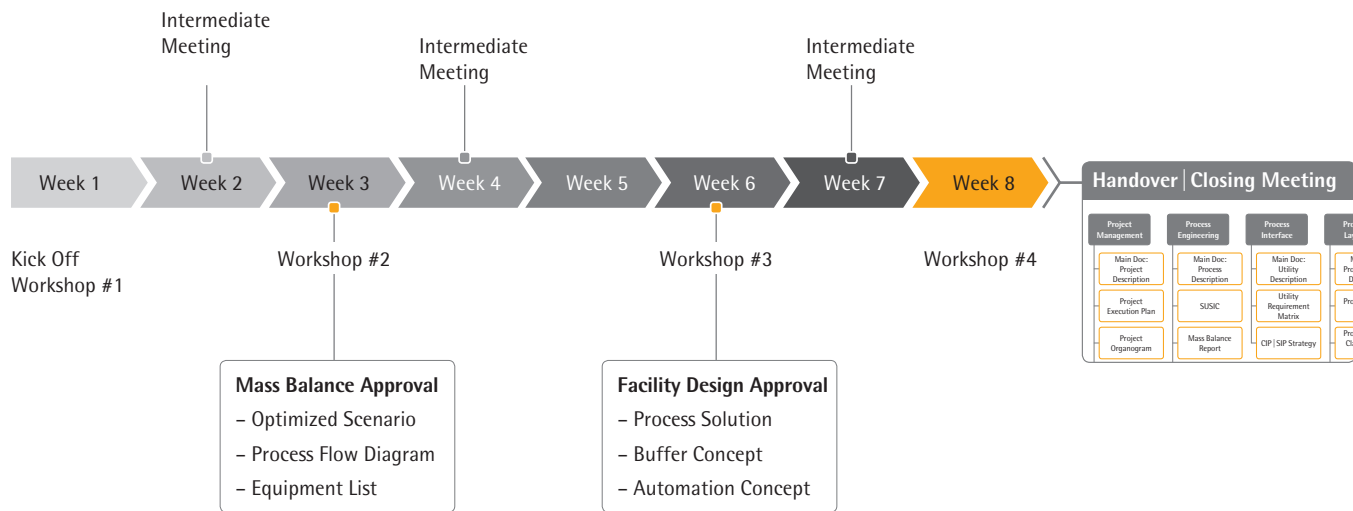
Mass Balance
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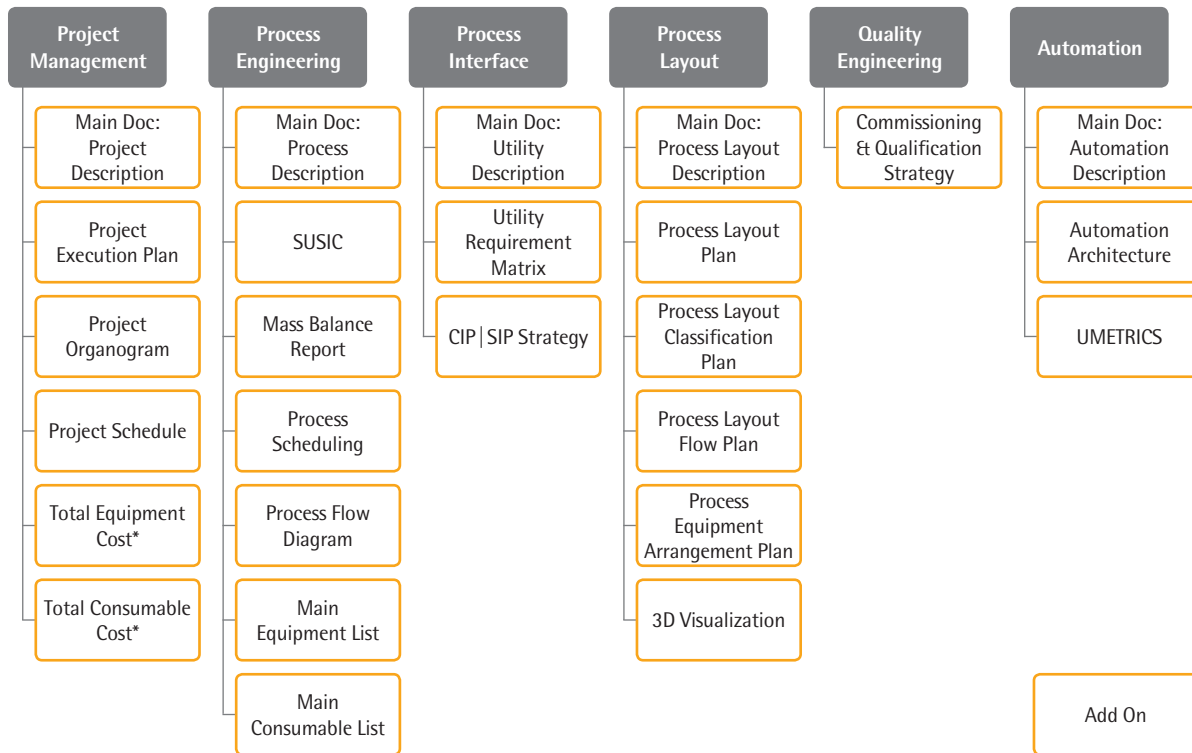
Automation

Standard
CD Package

A concept design study from Sartorius will provide insight to your process and new production facility within 8 weeks time.

At the end of the study a handover package will be generated containing all information needed for a smooth project execution.





Introduction



Mass Balance Review



Process Flow Diagram



Process Layout



Automation



Standard CD Package



For more Information:
RFQSystems@Sartorius.com

PROCESS **4** SUCCESS

Introduction

Mass Balance Review

Process Flow Diagram

Process Layout

Automation

Standard CD Package

