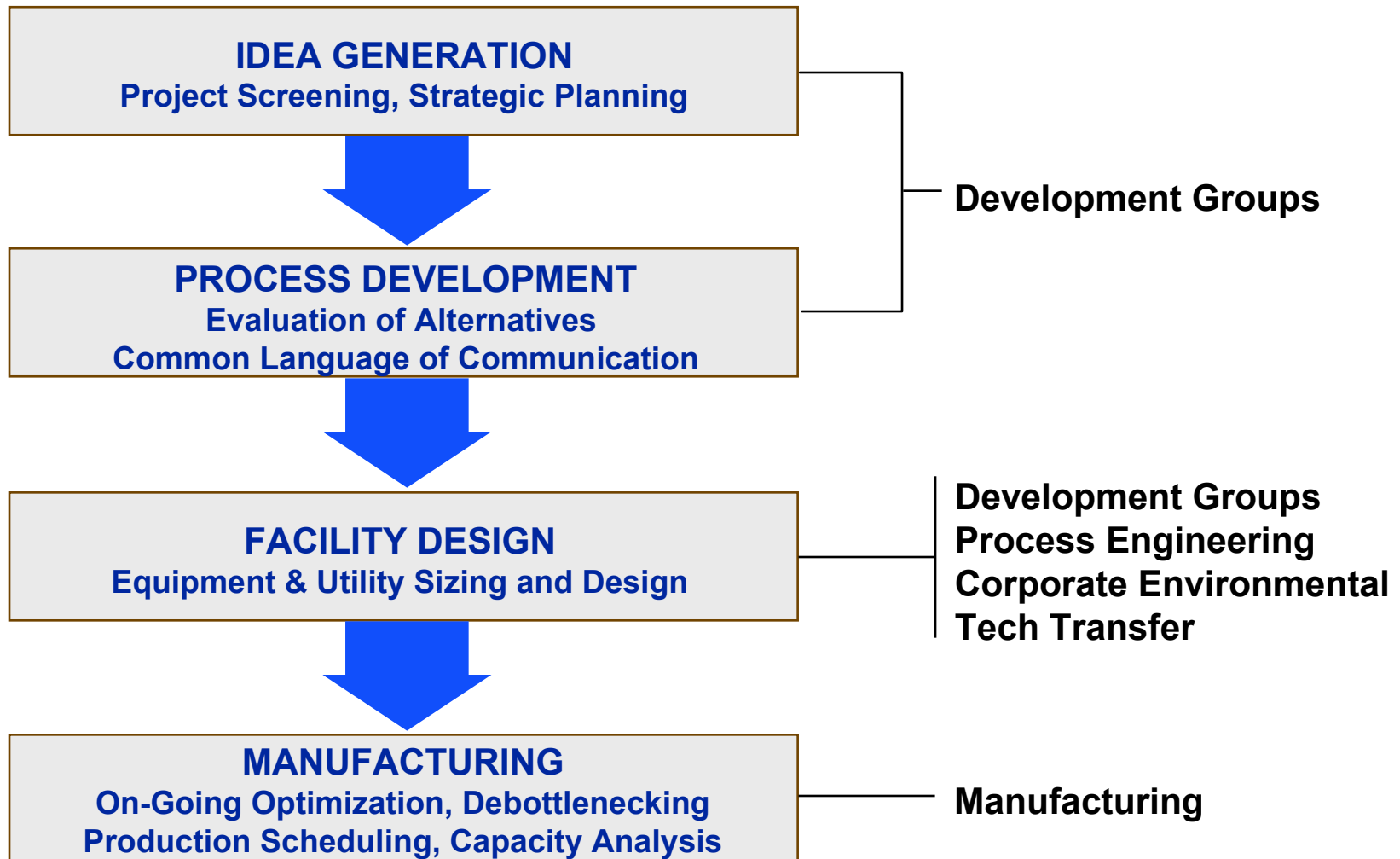


The Role of Simulation and Scheduling Tools in the Analysis and Optimization of Biochemical, Pharmaceutical, Fine Chemical, Consumer Product, Food, and Related Processes



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dpetrides@intelligen.com
www.intelligen.com

The Role of Process Simulation and Scheduling Tools in Product Development and Commercialization



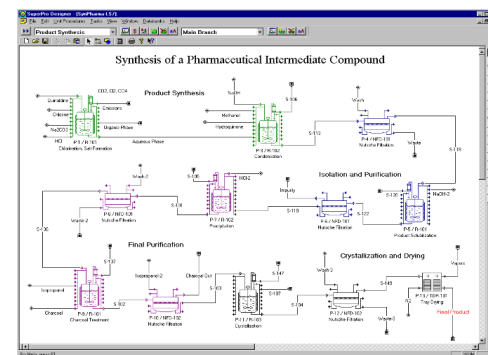
► **Intelligen, Inc.**

Who is Intelligen, Inc.?

Established in the early 90's - MIT spin off

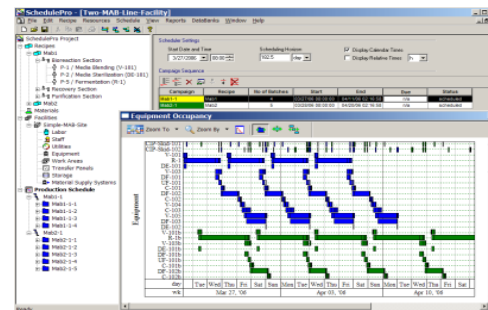
SuperPro Designer

- Detailed M&E Balances
- Equipment Sizing
- Cost of Goods Analysis
- Cycle Time Analysis
- Technology Transfer
- Environmental Impact



SchedulePro

- Production Planning
- Production Scheduling
- Capacity Analysis
- Facility Design
- Debottlenecking



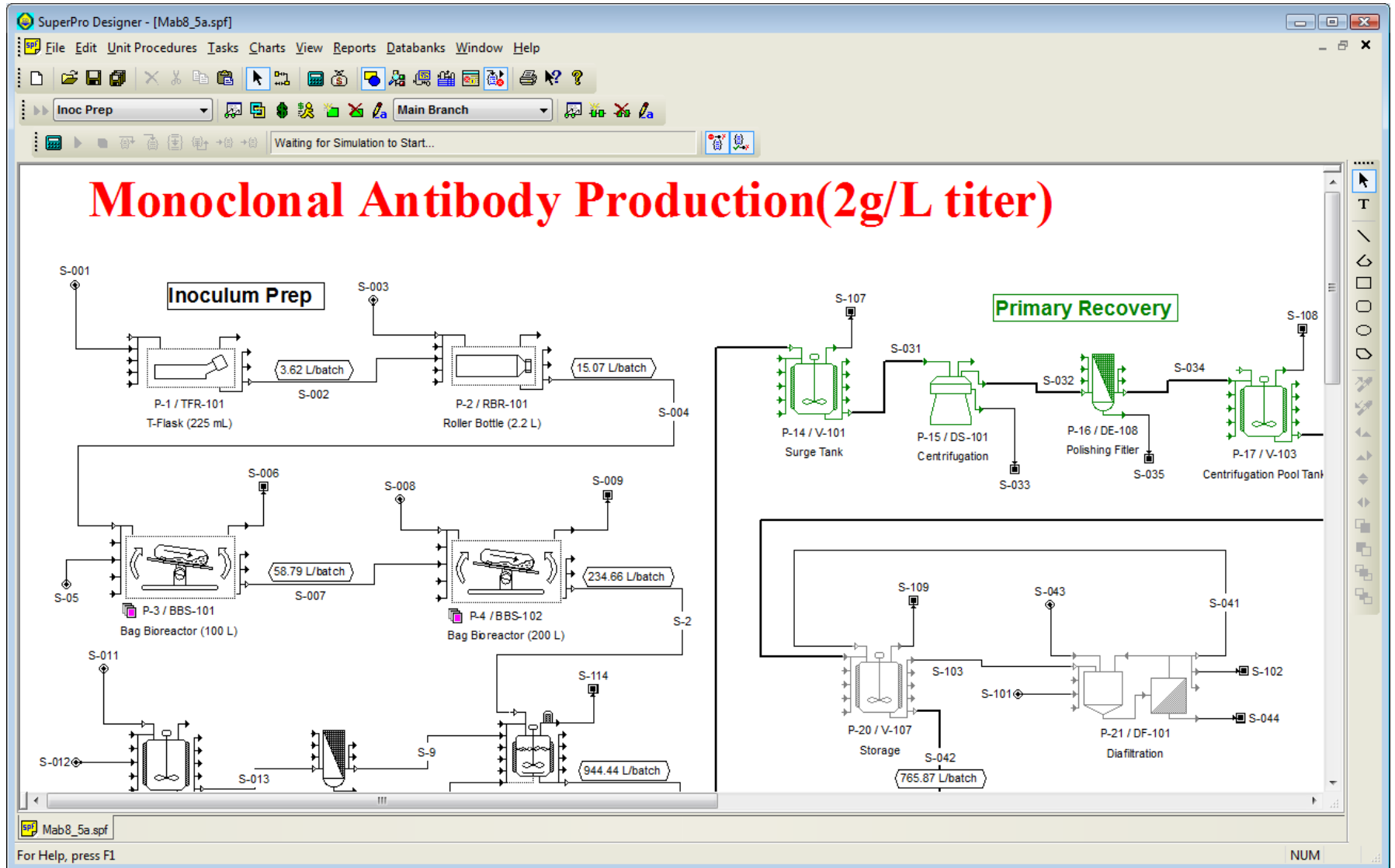
Intelligen, Inc.

The Realm of SuperPro Designer: Detailed Analysis and Evaluation of Single Processes

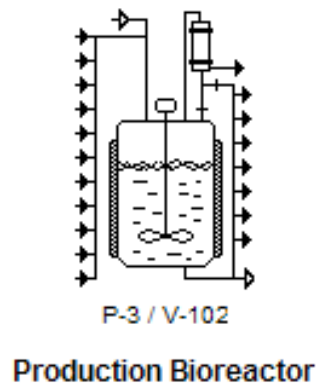
SuperPro Designer Functionality

- Process modeling capabilities, including:
 - Generation of material and energy balances
 - Environmental impact calculations
 - Resource tracking
 - Process scheduling
 - Equipment sizing and costing
 - Capital and operating cost estimation
- Cycle time analysis and debottlenecking
- Scale-up/scale-down
- Technology transfer

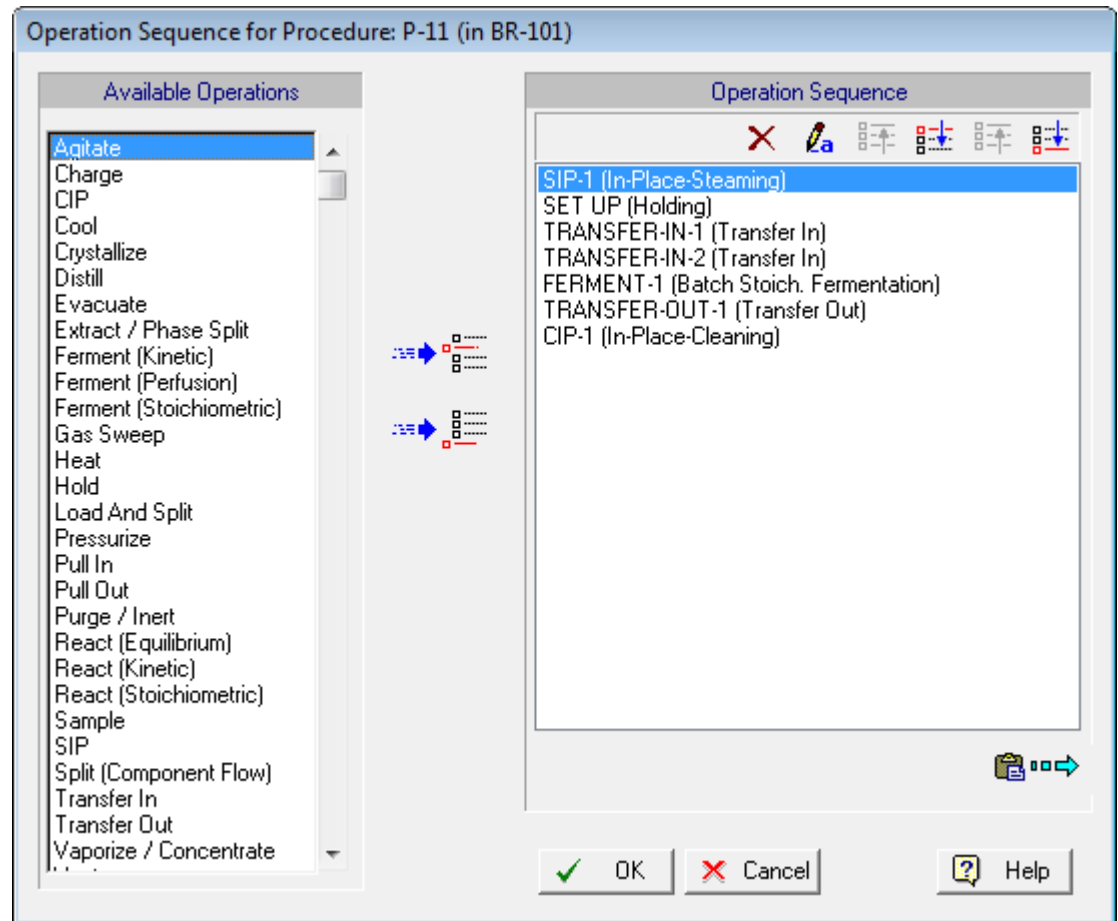
User Interface of SuperPro Designer



Detailed Modeling using Unit Procedures and Operations



Double-Click



Intelligen, Inc.

Flexible Operation Models (Charge Operation)

CHARGE-1 (Charge)

Oper.Cond's Volumes Vent/Emissions Labor, etc. Description Batch Sheet Scheduling

Charge Using In #1 : S-025

Amount Scaleable

☐ Use Amount on Stream

☒ Set by User

☐ Mass 9947.043 kg

☒ Volume 10000.000 L

Duration

Setup Time 0.00 min

Process Time

☒ Set by User 60.00 min

☐ Calculated Based on

☐ Max Flowrate 9947.043 kg/h

☐ Volumetric Flowrate 10000.000 L/h

☐ Set by Master-Slave Relationship Setup...

Match the duration of this operation to the duration of another operation or string of operations.

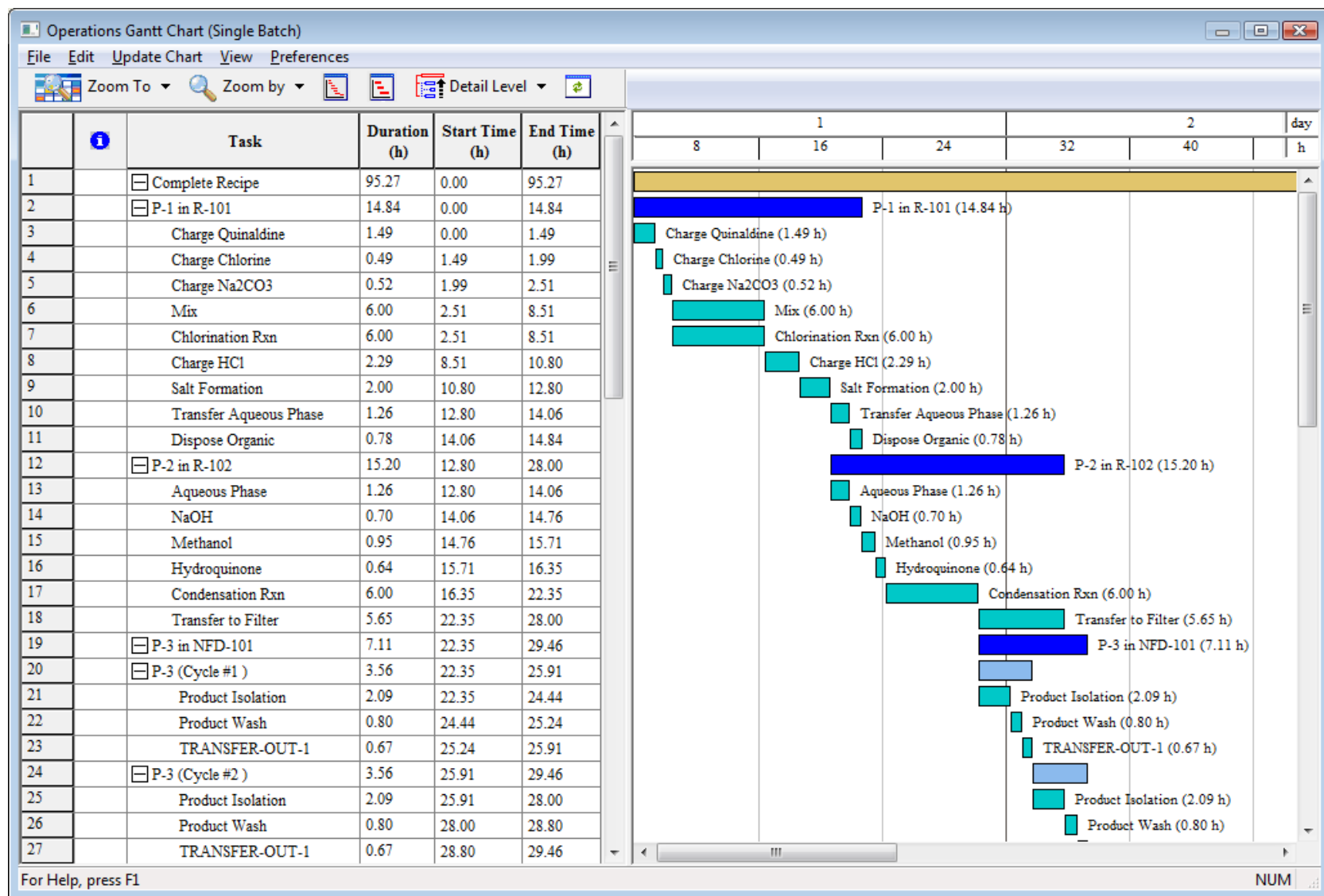
Ignore Labor

<< >> << >> << >> OK Cancel Help



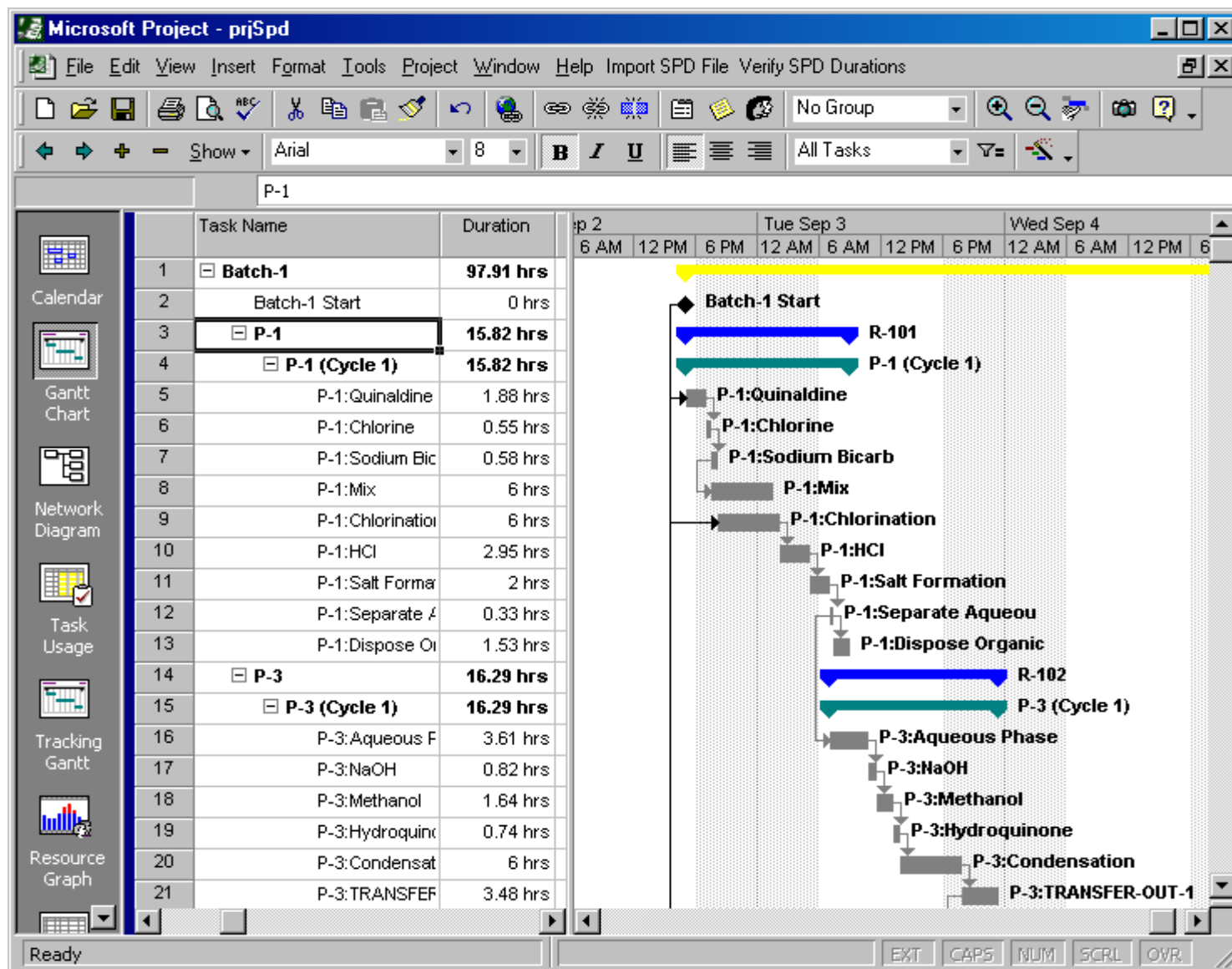
Selected Outputs of SuperPro Designer

Operations Gantt Chart



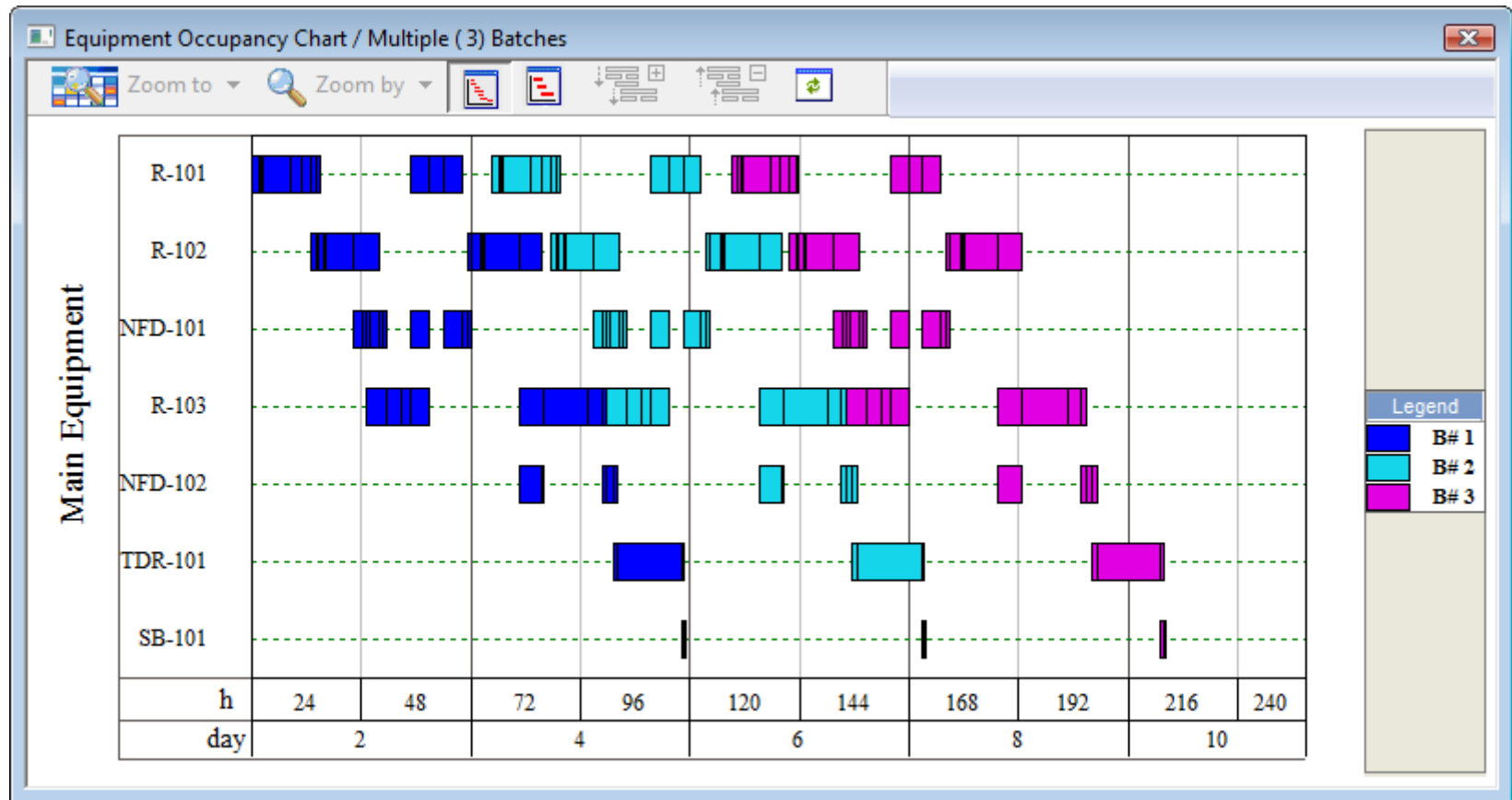
Intelligen, Inc.

Operations Gantt Chart – Exported to MS Project

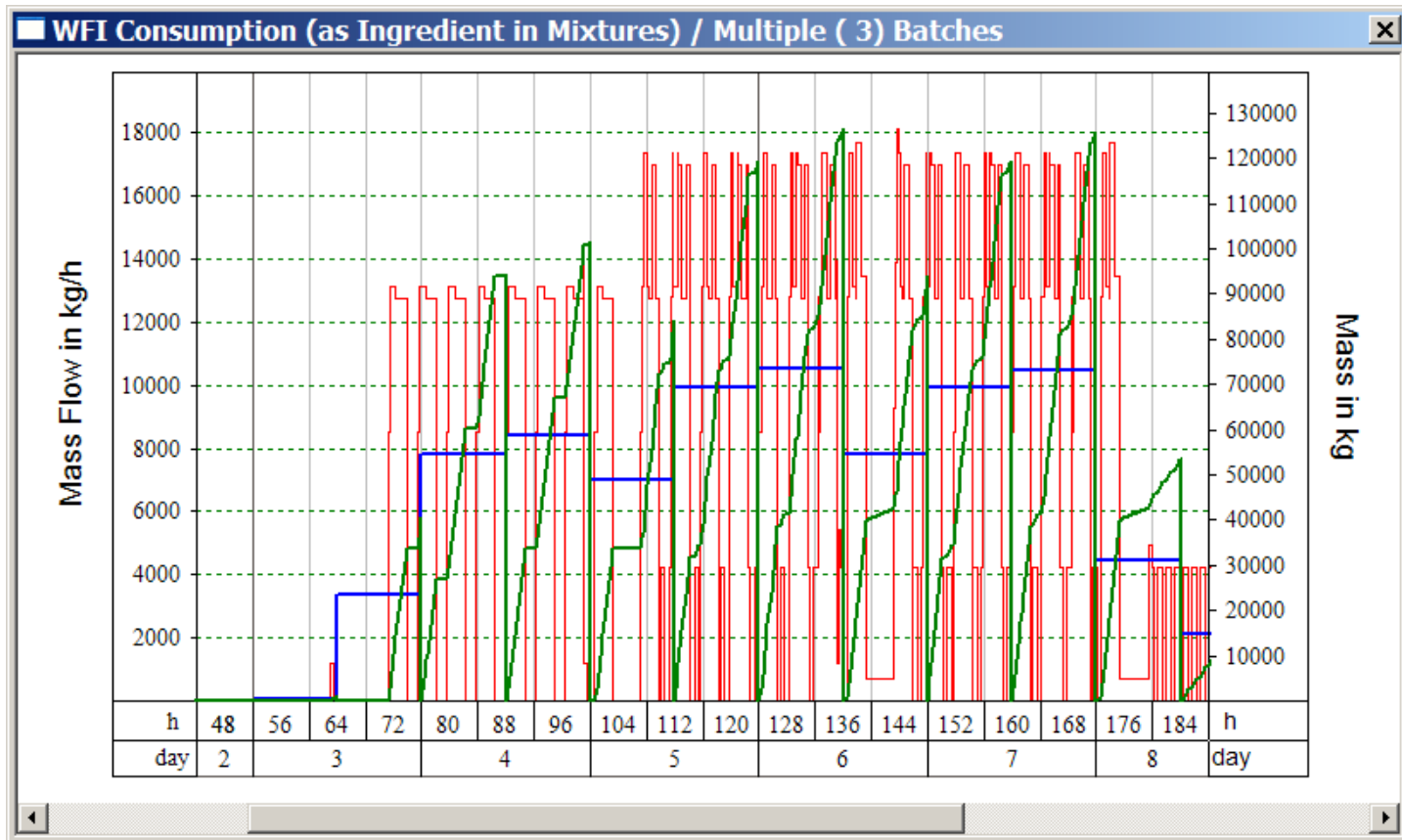


Intelligen, Inc.

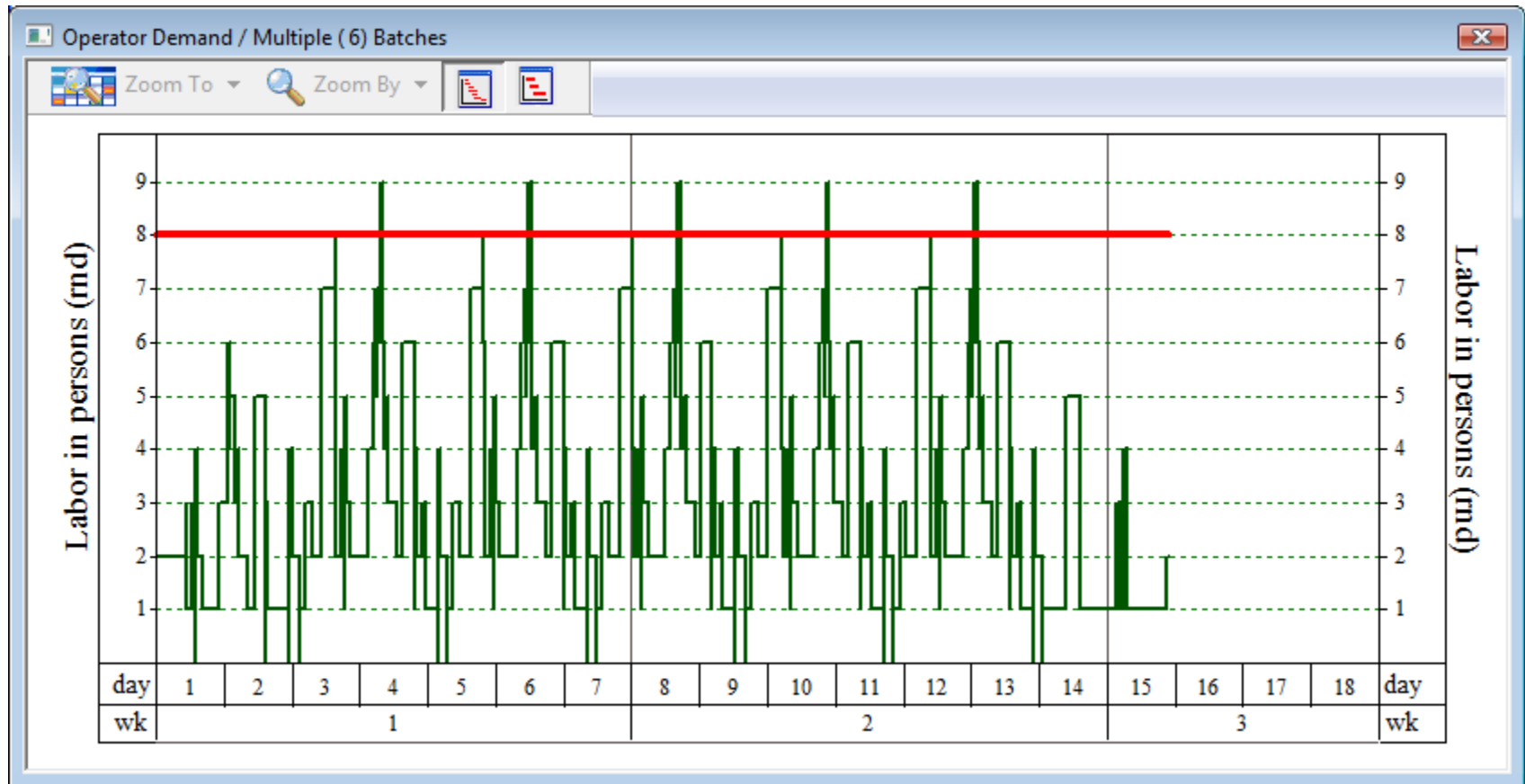
Equipment Occupancy Chart



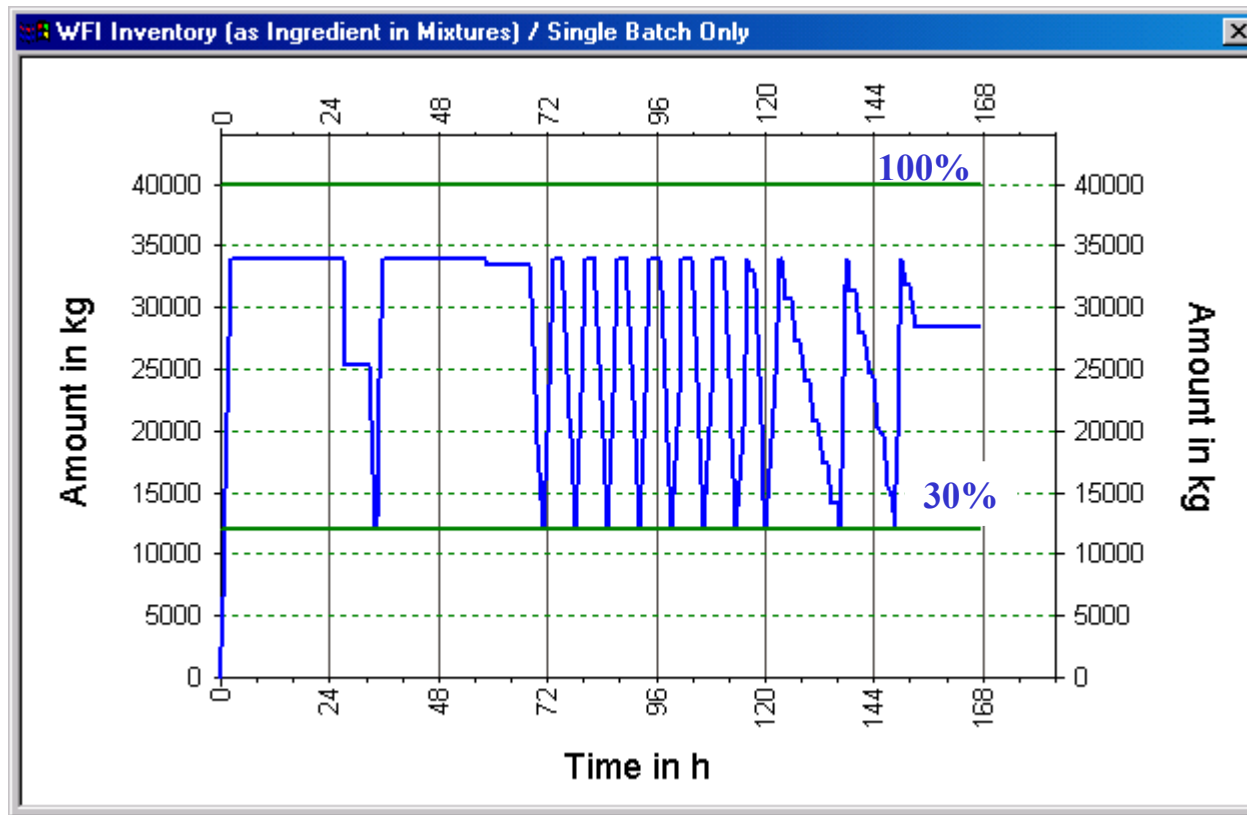
Resource Demand (Purified Water)



Labor Demand



Resource Inventory (WFI)



Material Balance Report

BGal8_5b_temp_SR.pdf - Adobe Acrobat Pro

File Edit View Window Help

Create [Icons]

3 / 23 112% [Icons]

Tools Comment Share

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Fermentation Section

Material	kg/yr
Process Water	14,759,199
Glucose	1,326,888
Salts	221,616
H3PO4 (5% w/w)	841,679
NaOH (0.5 M)	1,432,258
WFI	1,870,399
Air	12,263,638
Ammonia	85,320
TOTAL	32,800,997

Primary Recovery Section

Material	kg/yr
H3PO4 (5% w/w)	985,315
NaOH (0.5 M)	1,676,677
Process Water	1,094,794
WFI	2,189,589
TOTAL	5,946,375

Purification Section

Material	kg/yr
NaCl (0.1 M)	29,774,876
WFI	44,042,508
NaCl (0.5 M)	2,524,995
Tris Buffer	35,299,940
NaOH (0.5 M)	19,166,968
H3PO4 (5% w/w)	782,494
Process Water	869,437
TOTAL	132,461,218

BGal8_5b_temp_SR.pdf - Adobe Acrobat Pro

File Edit View Window Help

Create [Icons]

10 / 23 112% [Icons]

Tools Comment Share

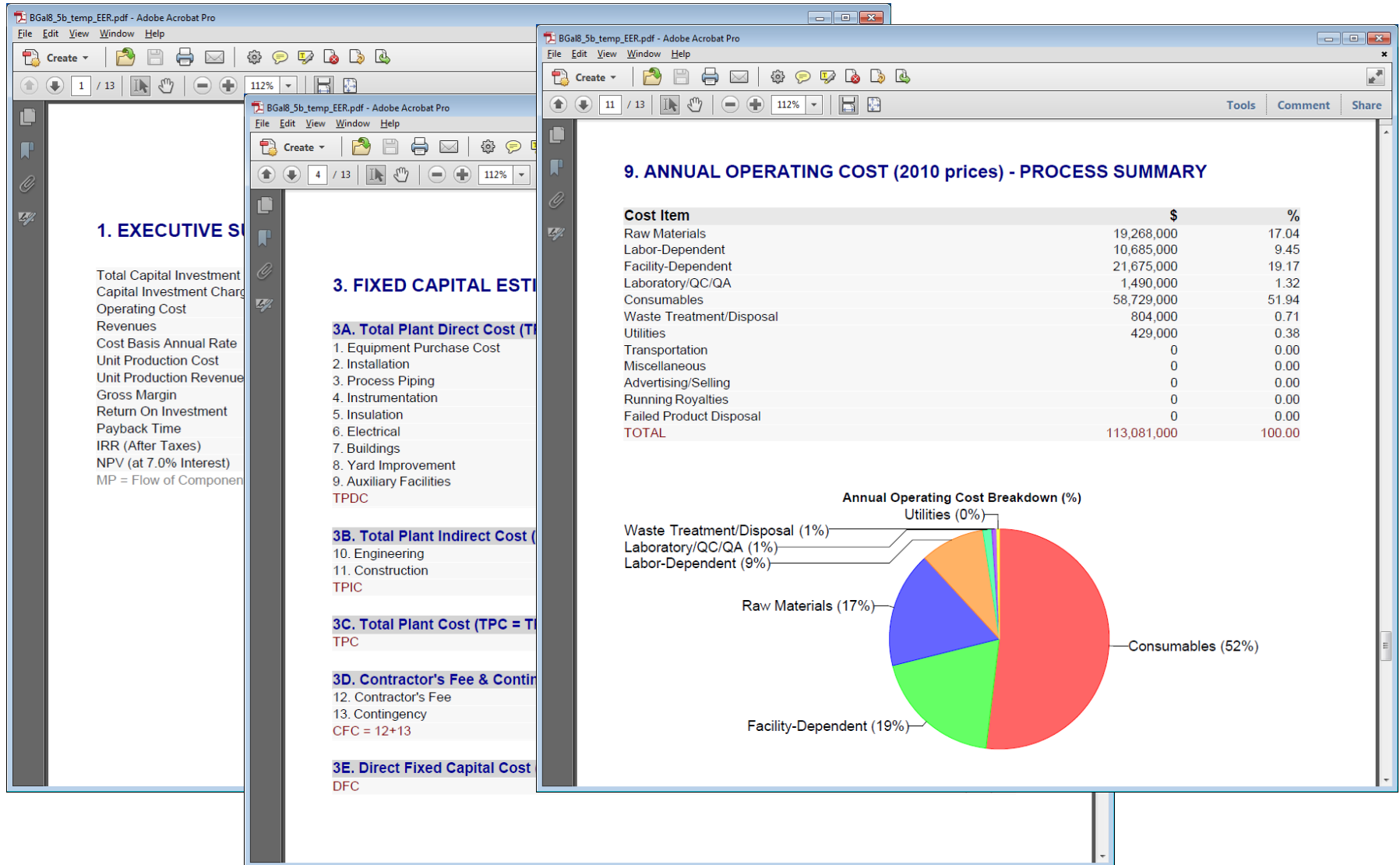
- Page 9 -

3. STREAM DETAILS

Stream Name	Water	Nutrients	S-103	S-104
Source	INPUT	INPUT	P-1	P-2
Destination	P-1	P-1	P-2	P-5
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	35.00
Pressure (bar)	1.01	1.01	7.34	7.34
Density (g/L)	1,000.00	1,445.72	1,032.05	1,032.05
Total Enthalpy (kW-h)	1,855.72	57.45	1,913.17	2,678.44
Specific Enthalpy (J/kg)	104,384.02	28,851.32	96,775.45	135,485.64
Heat Capacity (kcal/g-°C)	0.00	0.00	0.00	0.00
Component Flowrates (kg/batch)				
Glucose	0.000	6,143.000	6,143.000	6,143.000
Process Water	64,000.000	0.000	64,000.000	64,000.000
Salts	0.000	1,026.000	1,026.000	1,026.000
TOTAL (kg/batch)	64,000.000	7,169.000	71,169.000	71,169.000
TOTAL (m3/batch)	64.000	4.959	68.959	68.959



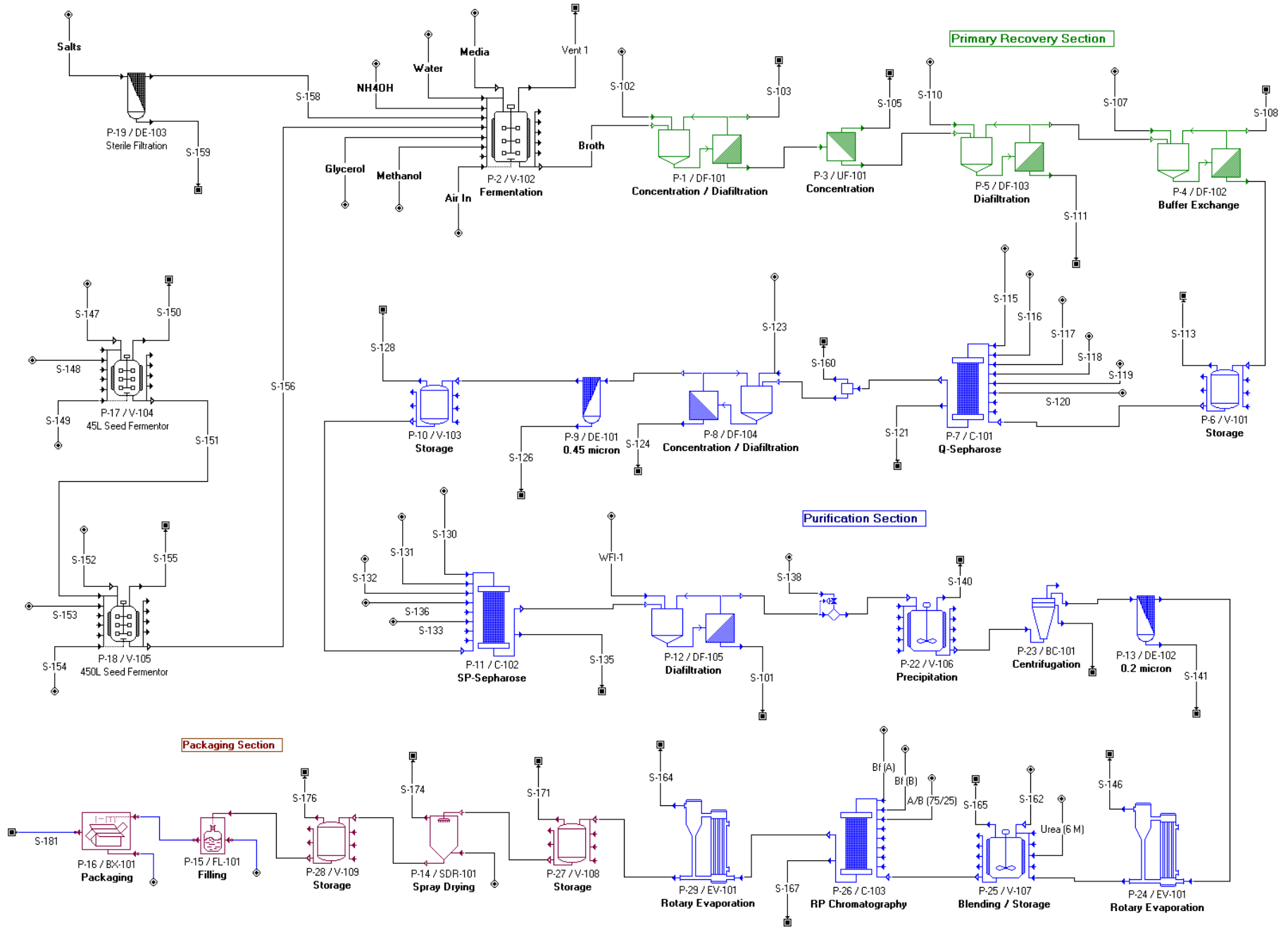
Financial Reports



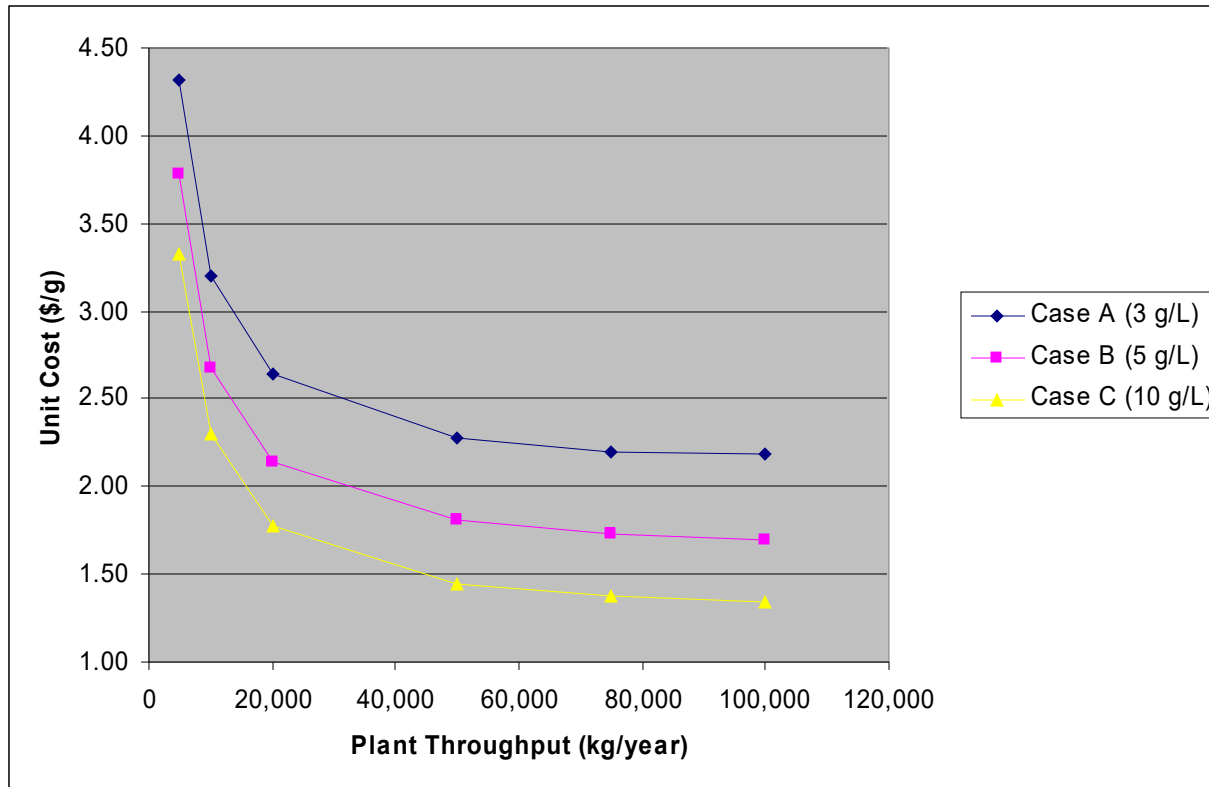
SuperPro Examples

Process Modeling for R&D Planning

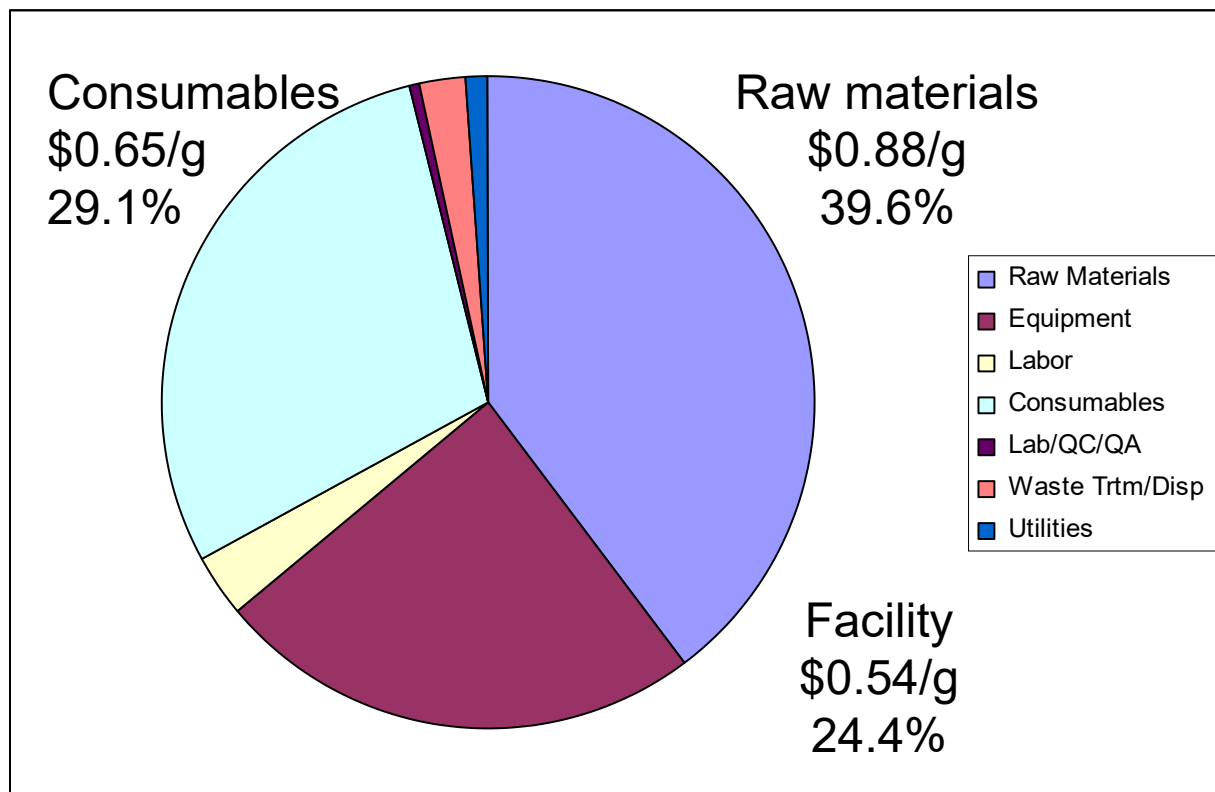
High Value Recombinant Product



COGs as a Function of Product Titer and Plant Throughput

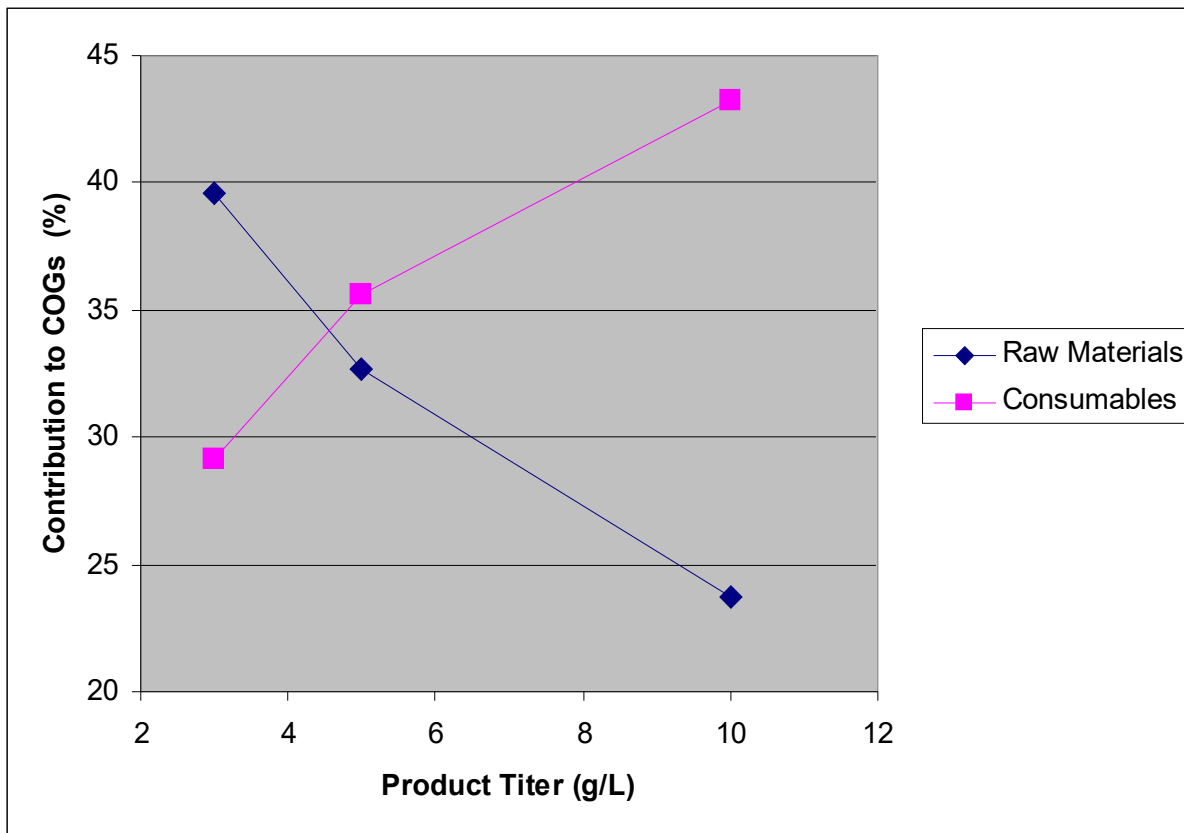


Breakdown of COGs (100 MT/year at 3 g/L)



Total COGs = \$2.22/g

Contribution of Raw Materials and Consumables to COGs (100 MT/year)

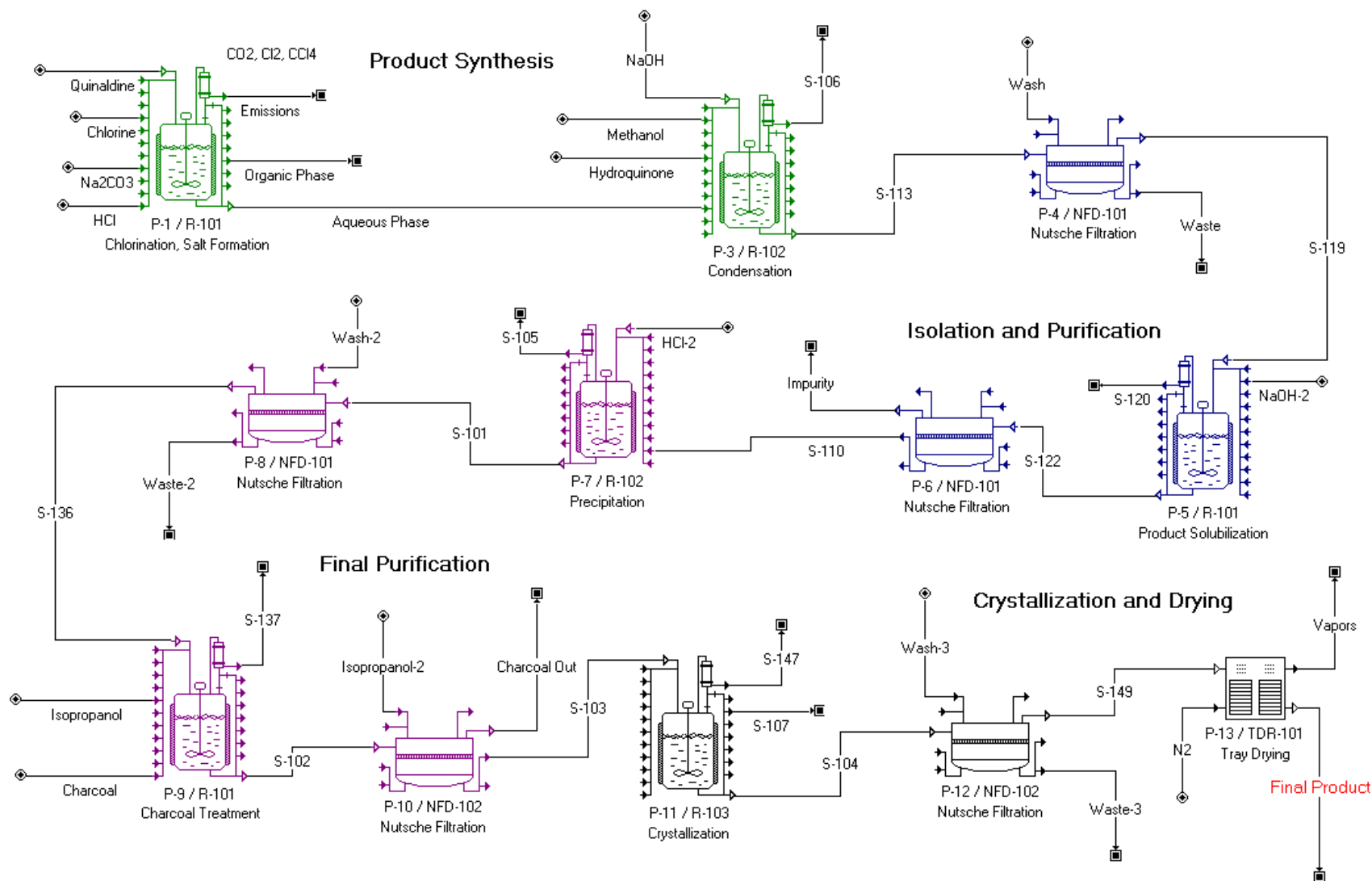


Small Molecule Pharmaceuticals

and

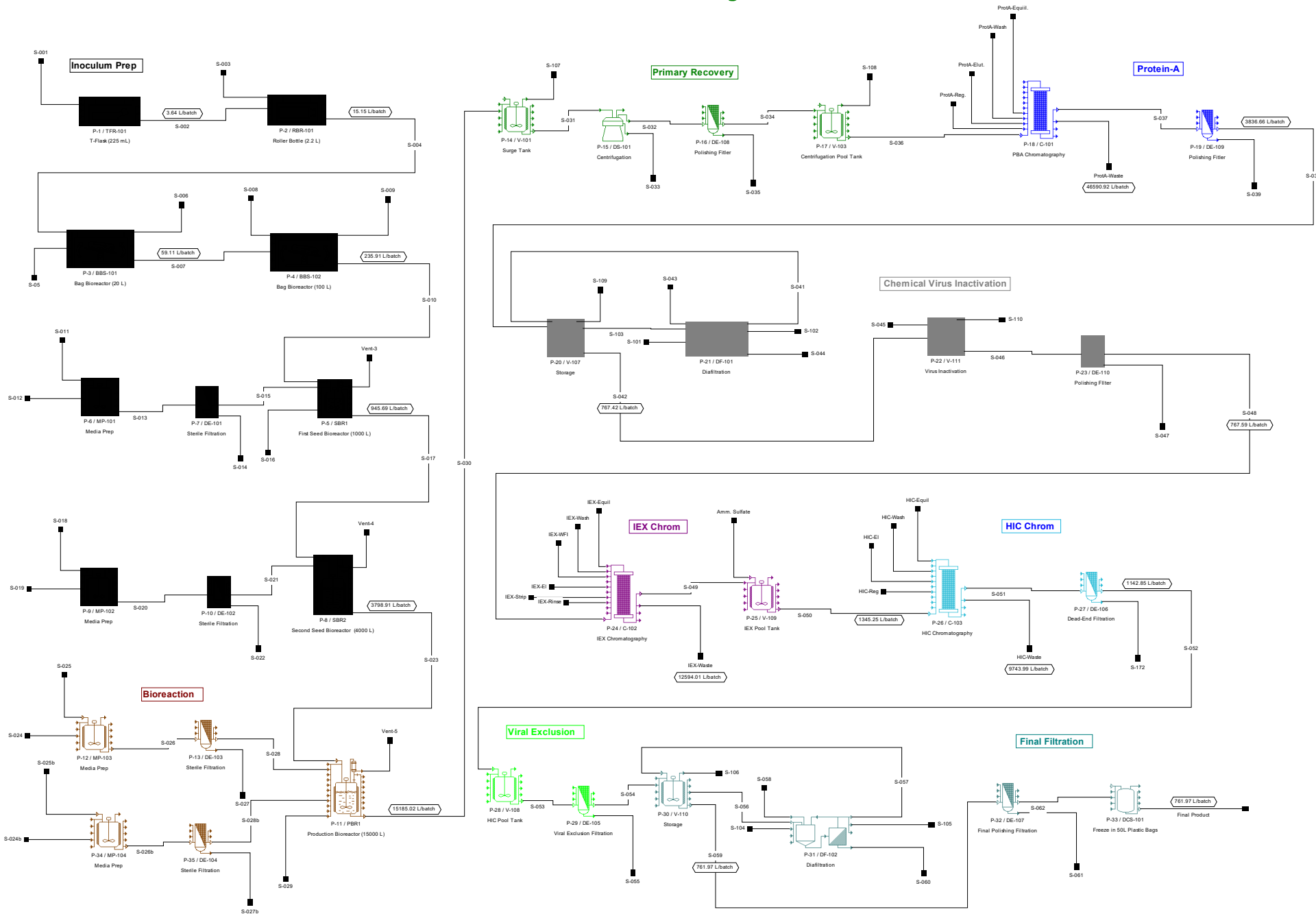
Fine Chemicals

Synthesis of a Pharmaceutical Intermediate Compound



Manufacturing of Biologics

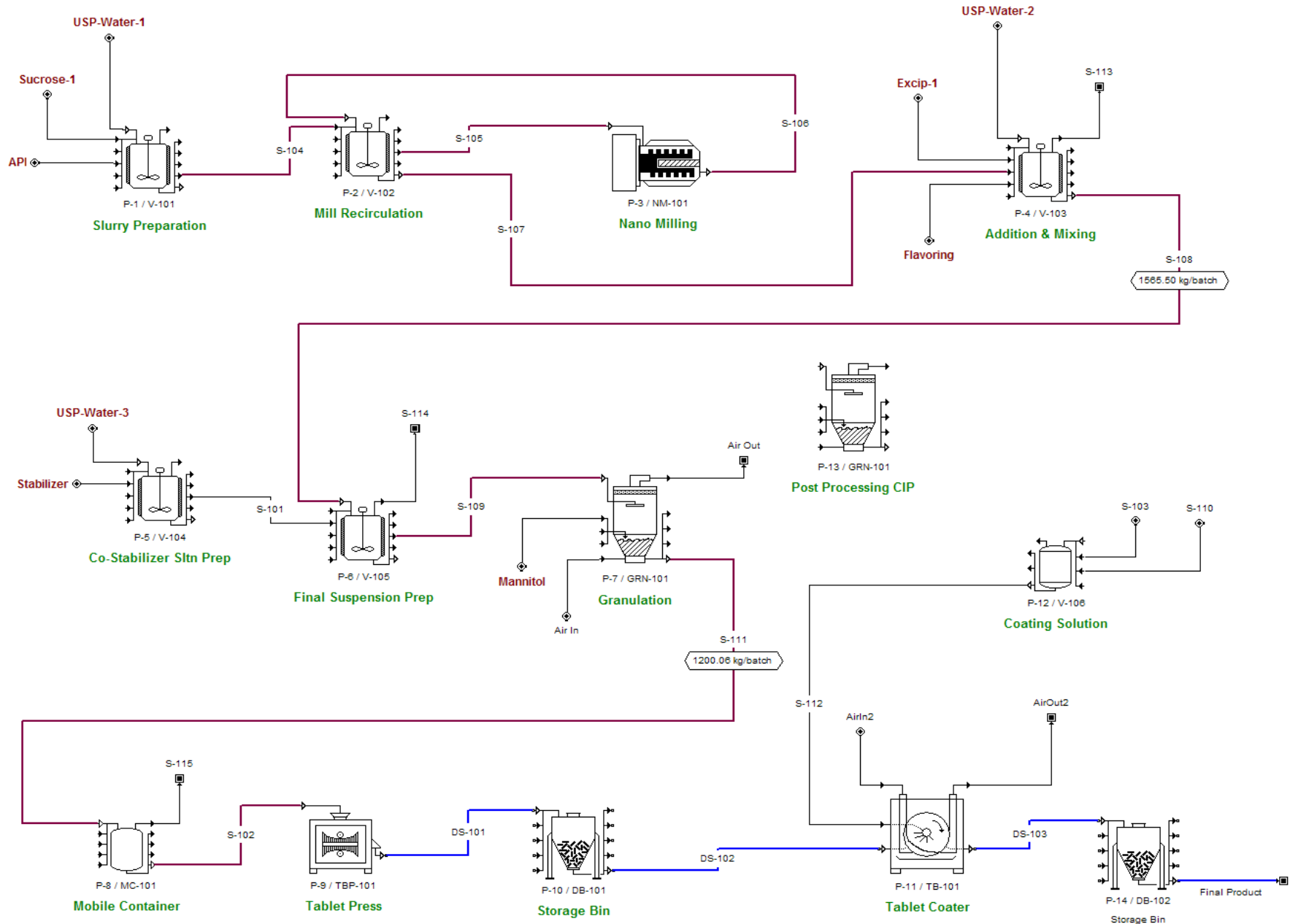
Monoclonal Antibody Production



Fine Pharmaceutical Processes

Tablet Manufacturing

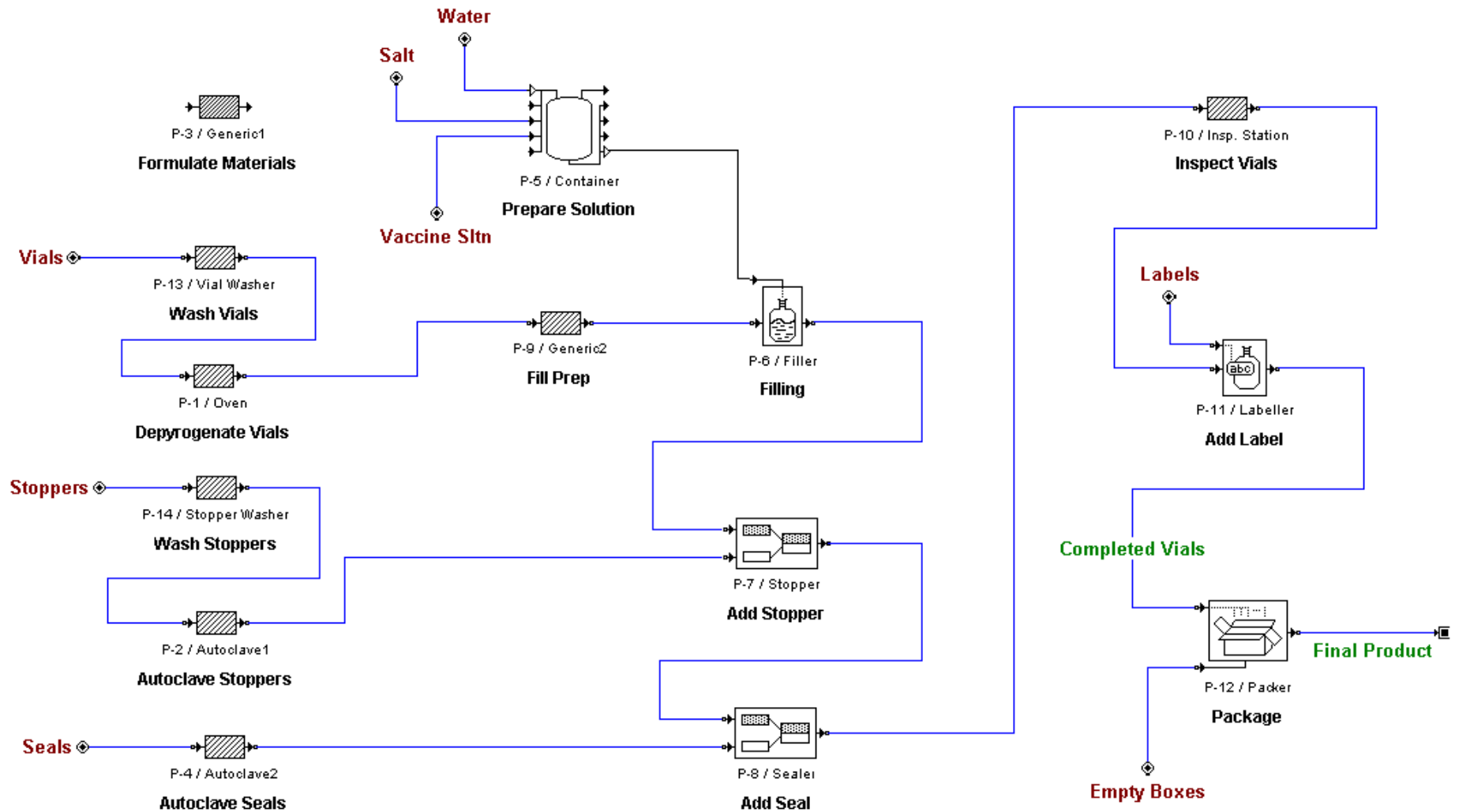
Pharmaceutical Tablet Manufacturing



Pharmaceutical Fill-Finish

Vial Manufacturing

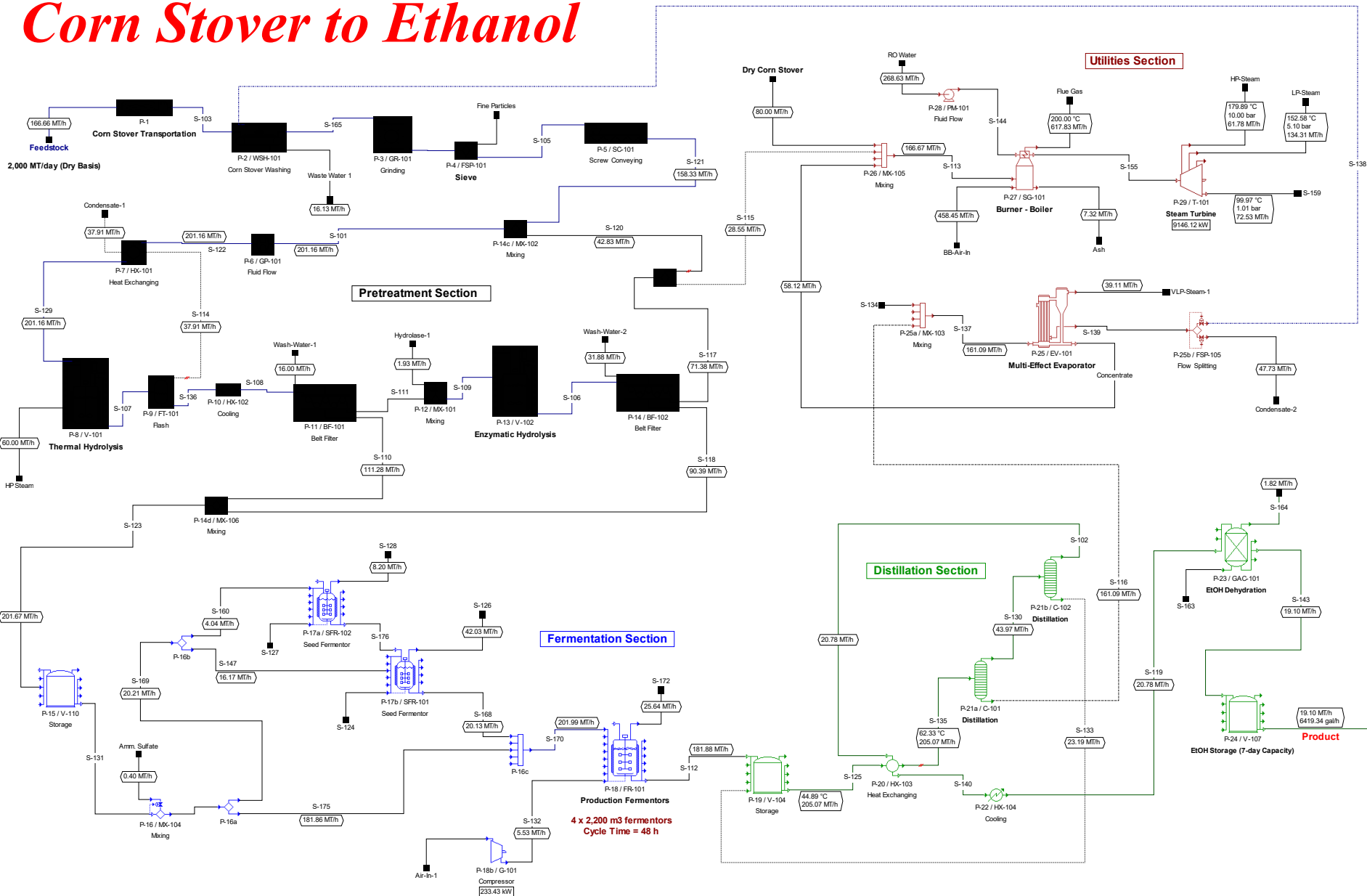
Pharmaceutical Vial Manufacturing



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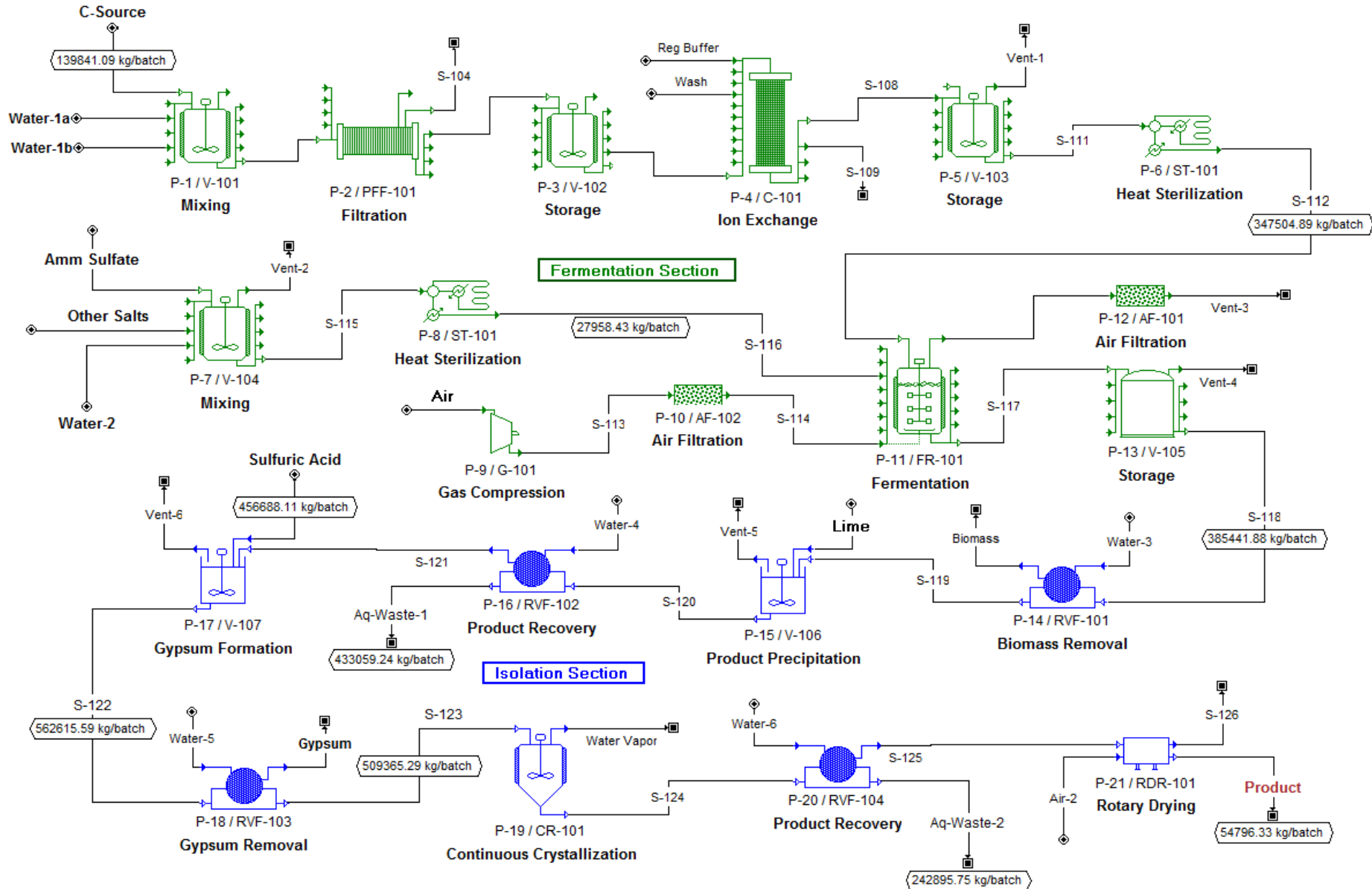
Production of Bio-Fuels and Biomaterials

Corn Stover to Ethanol

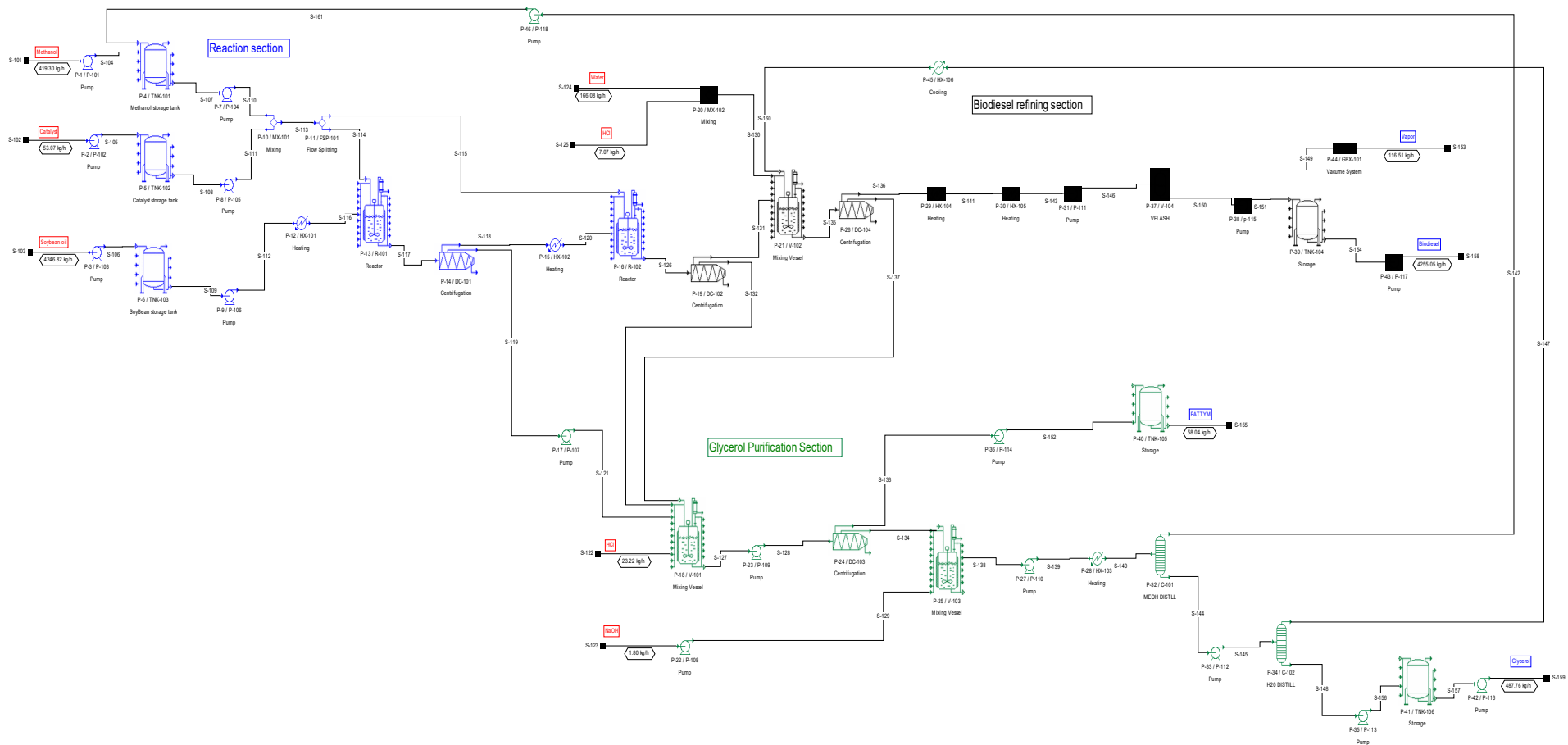


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Citric Acid Production

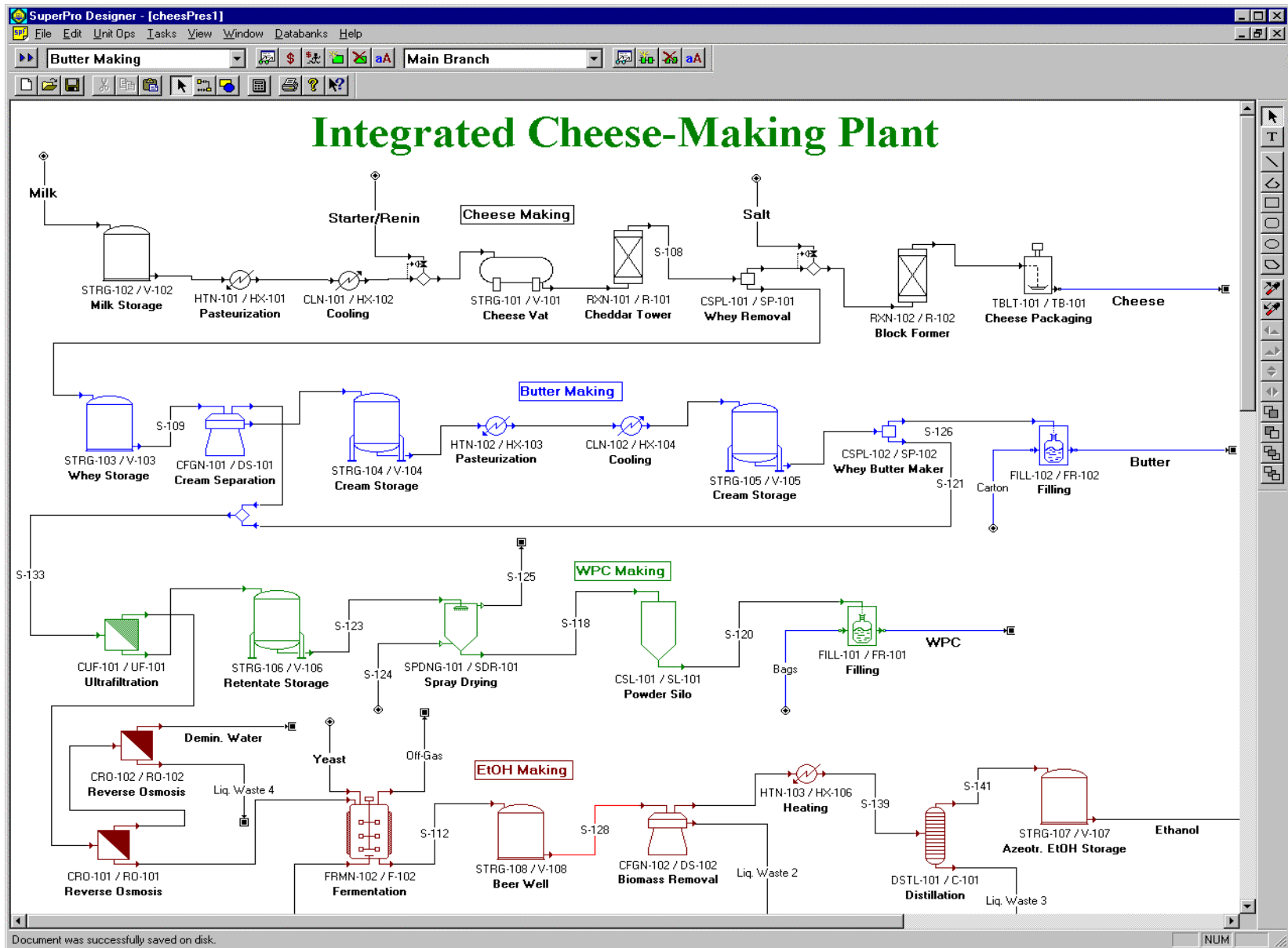


Soybean Oil to Biodiesel



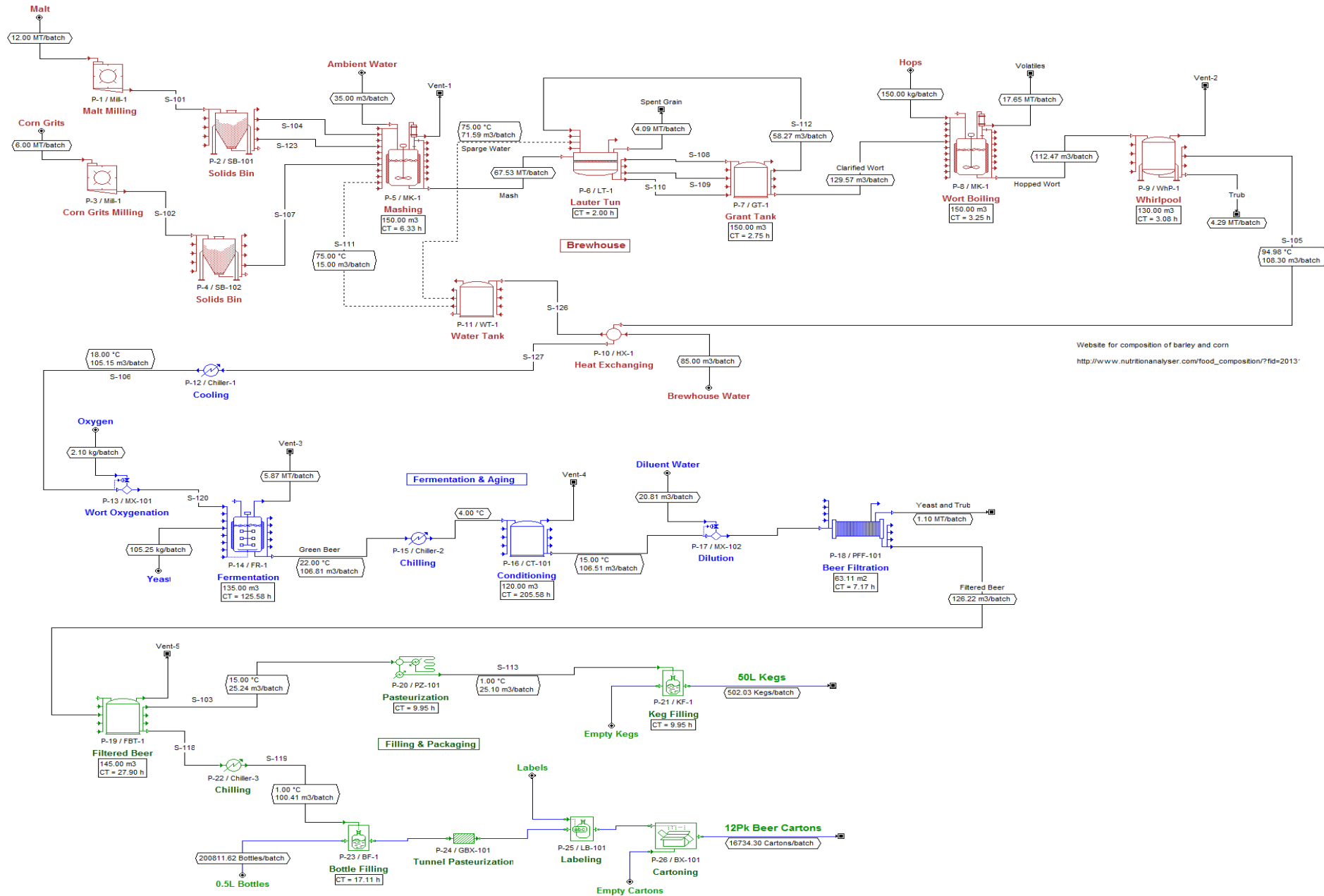
► **Intelligen, Inc.**

Food Processing

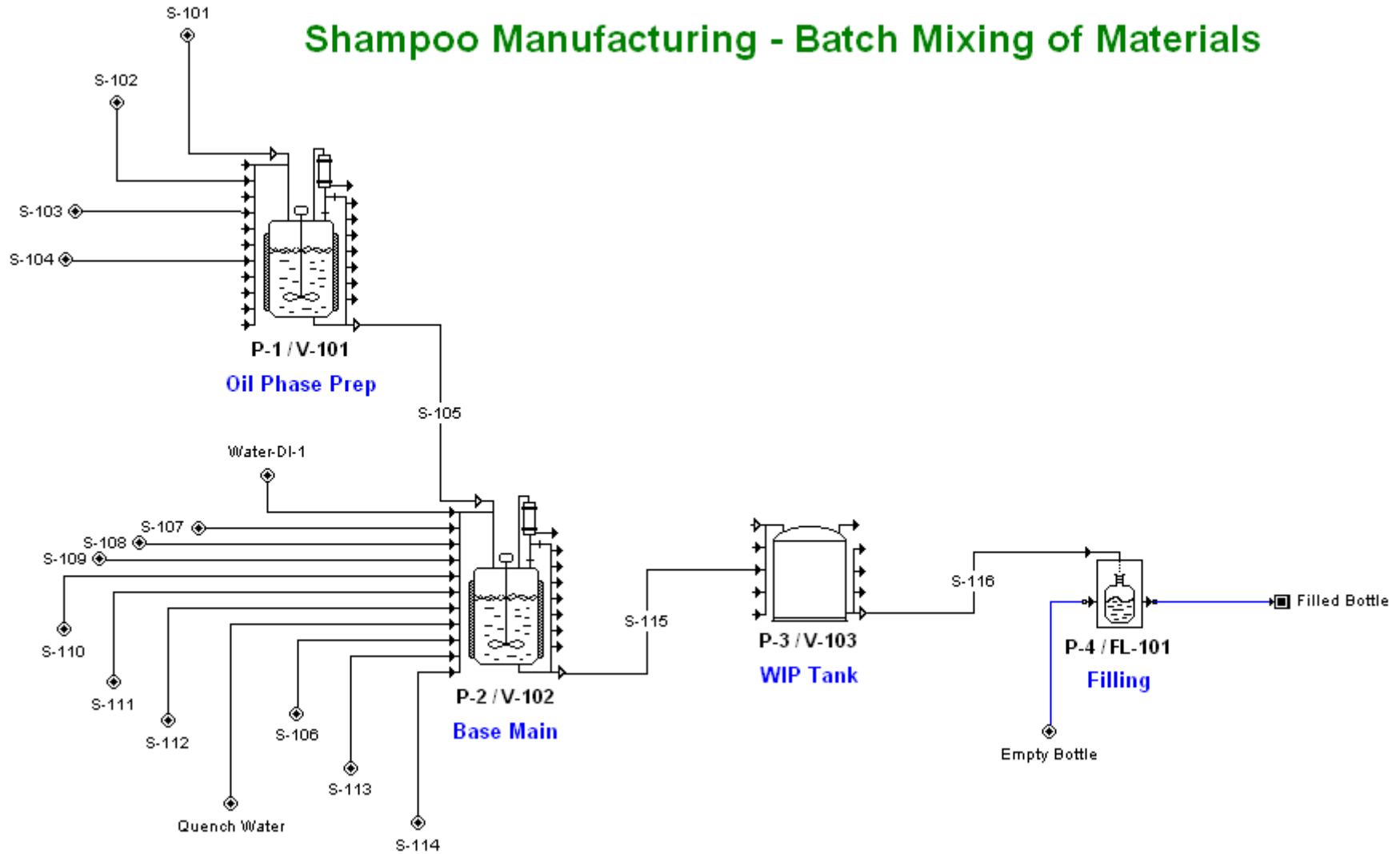


Consumer Products and Beverages

Beer Production



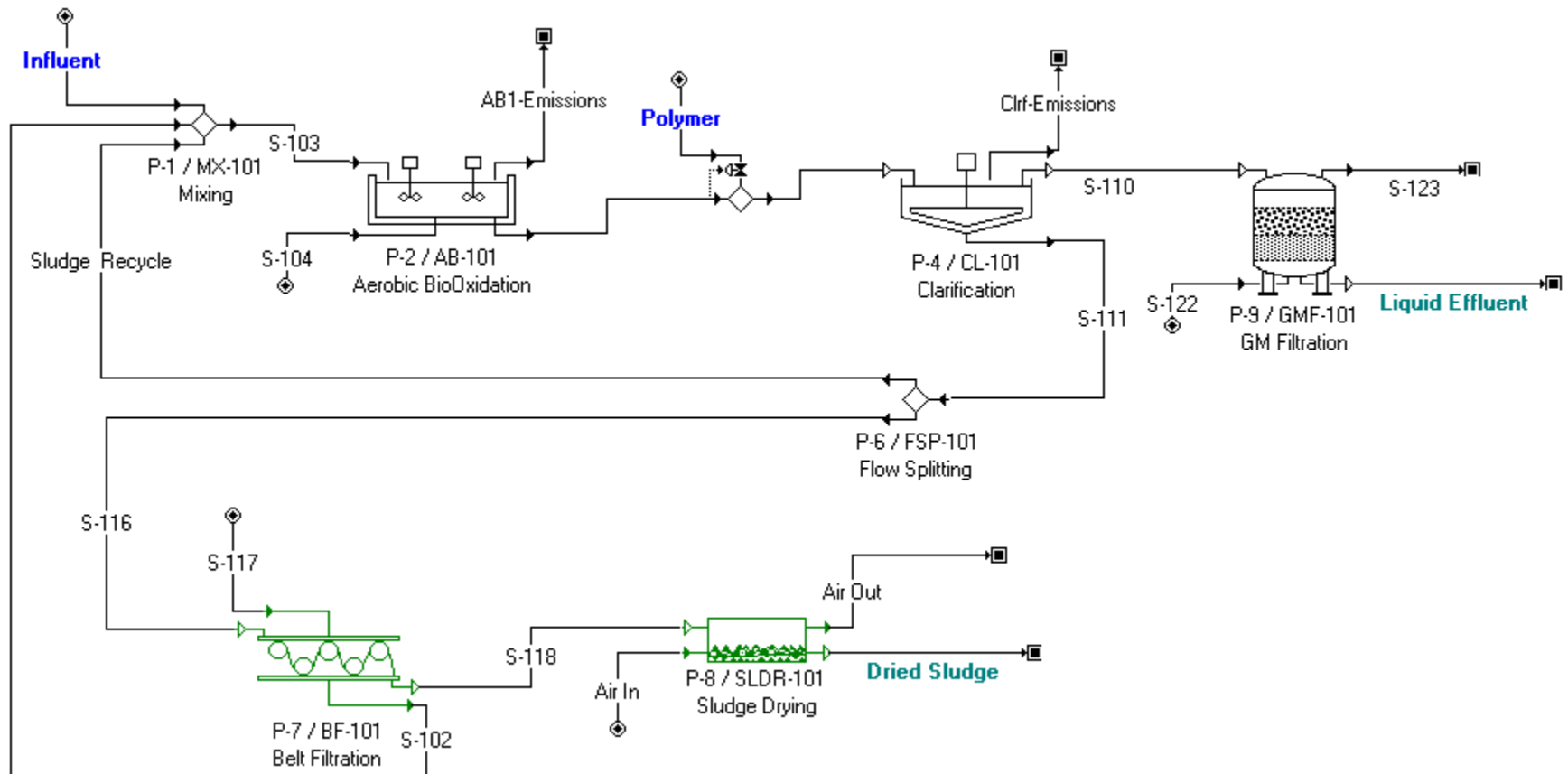
Shampoo Manufacturing - Batch Mixing of Materials



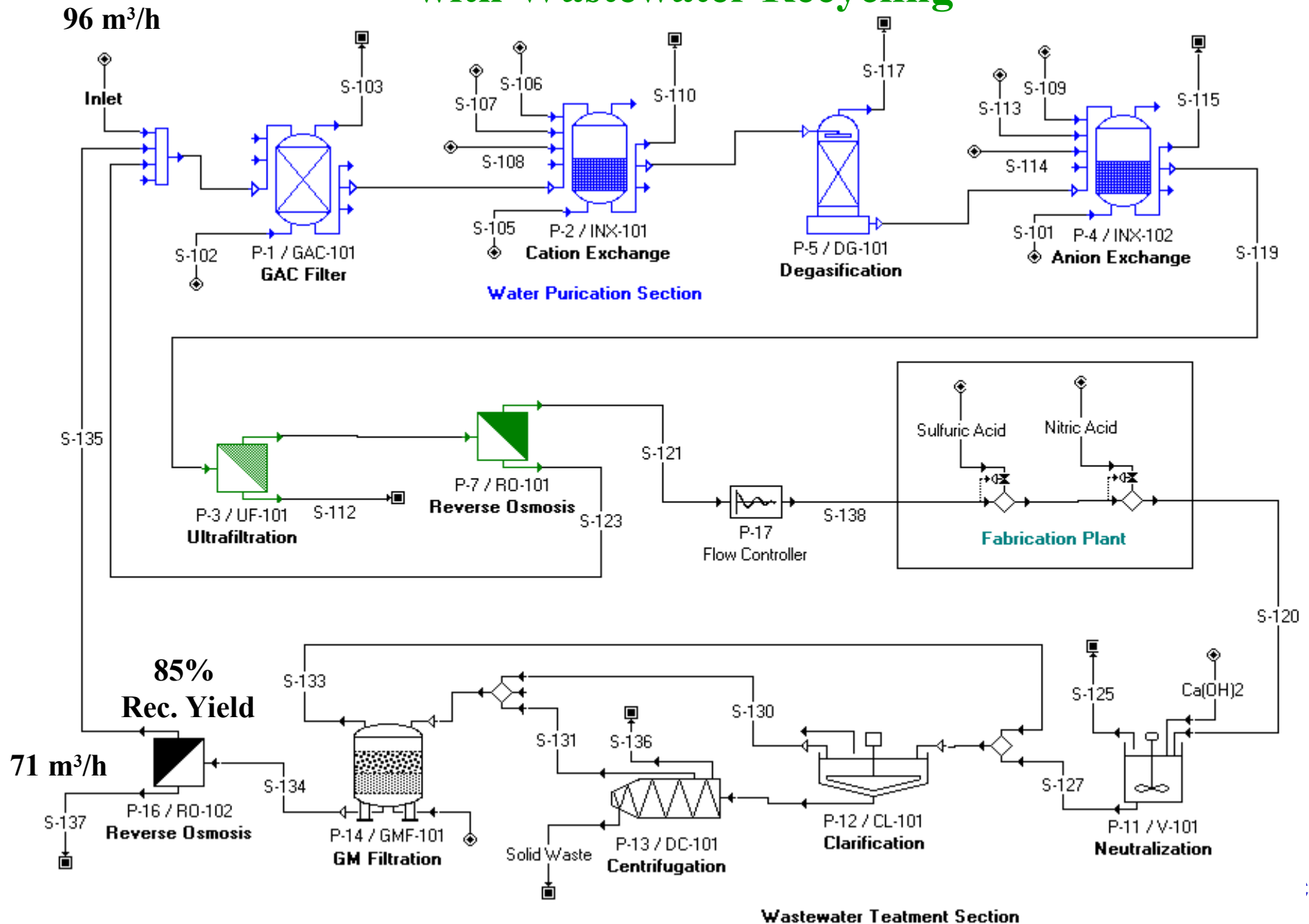
Intelligen, Inc.

Water / Environmental Perspective

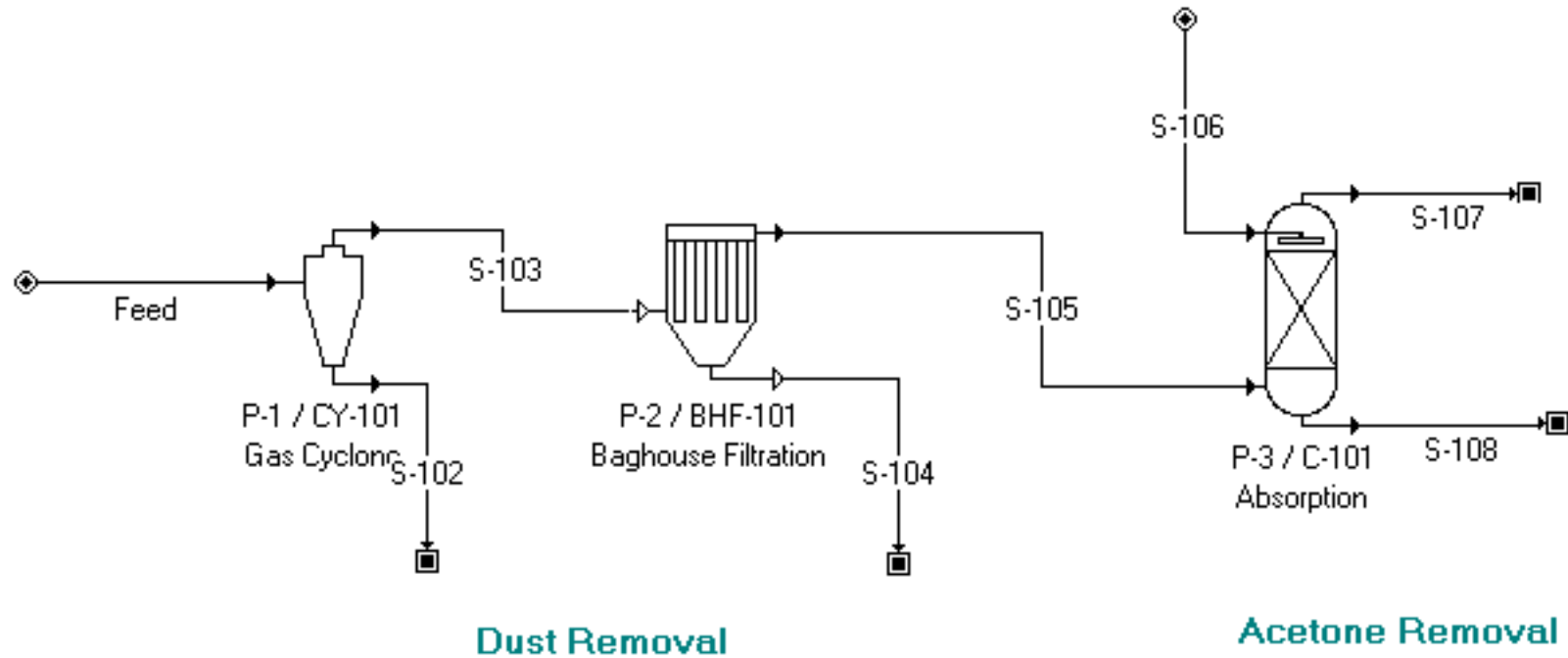
Industrial Wastewater Treatment



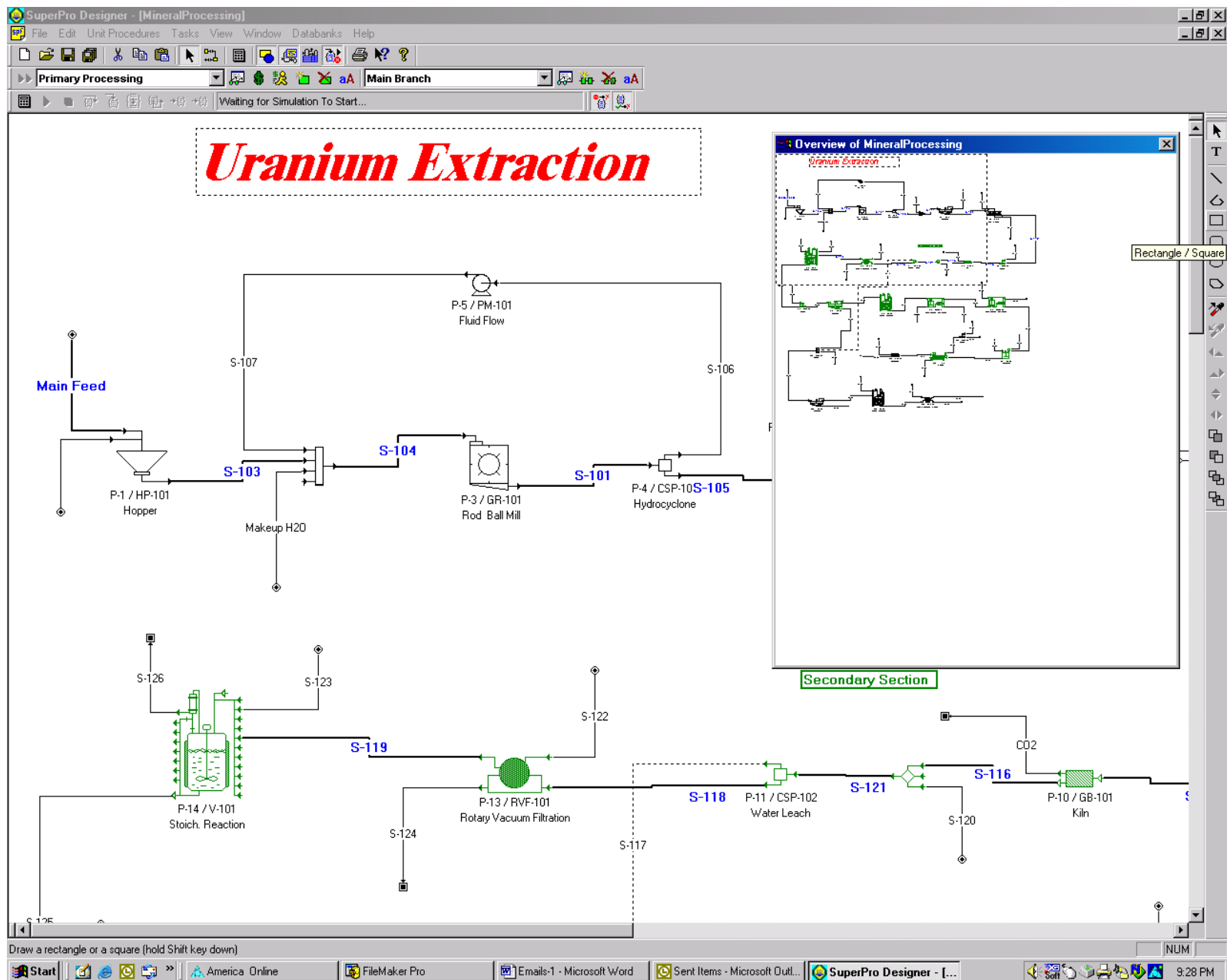
Water Purification and Wastewater Treatment with Wastewater Recycling



Air Pollution Control Process



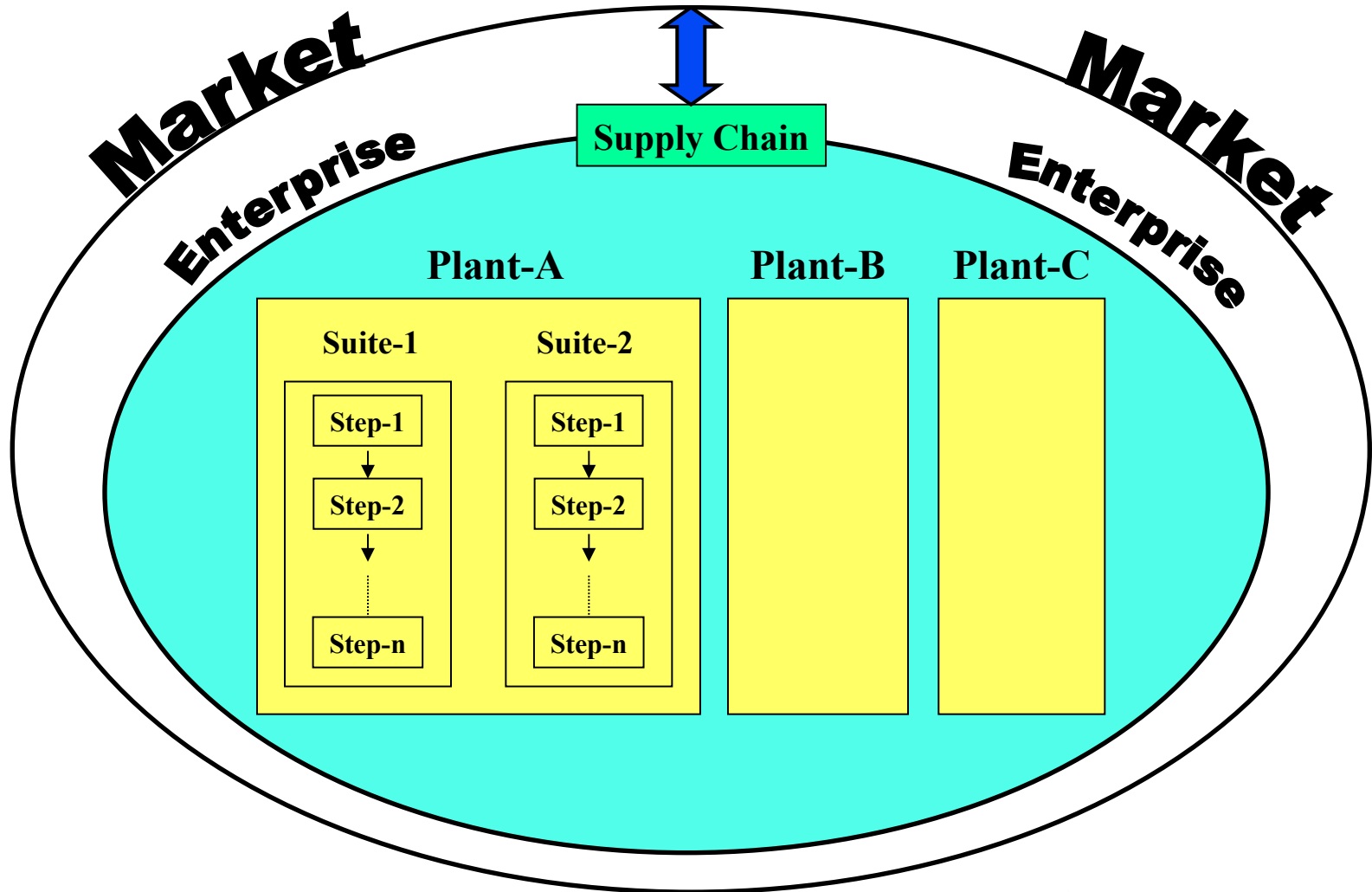
Mineral Processing



Modeling, Scheduling, and Debottlenecking of Multi-Product Facilities

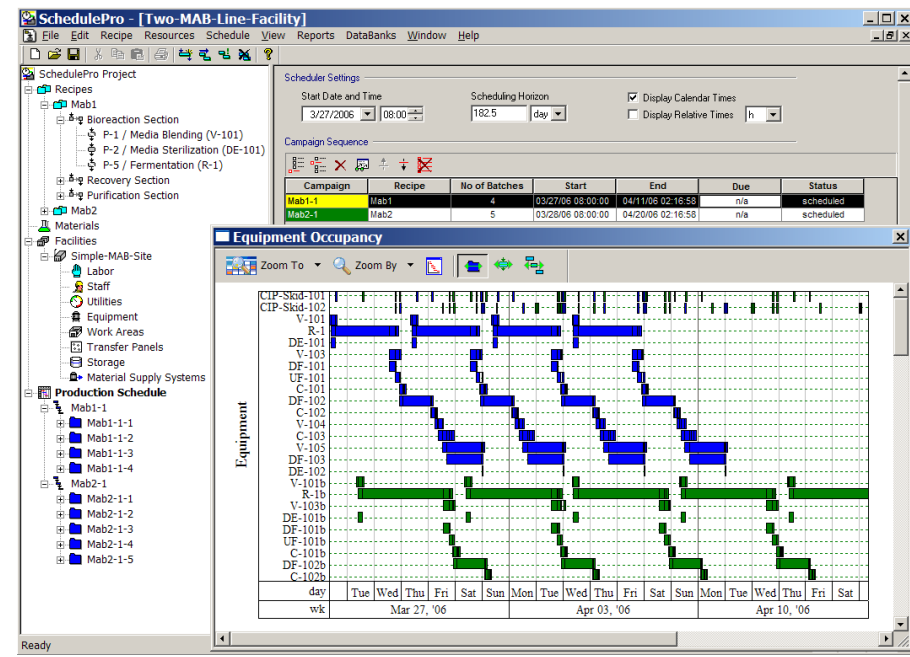
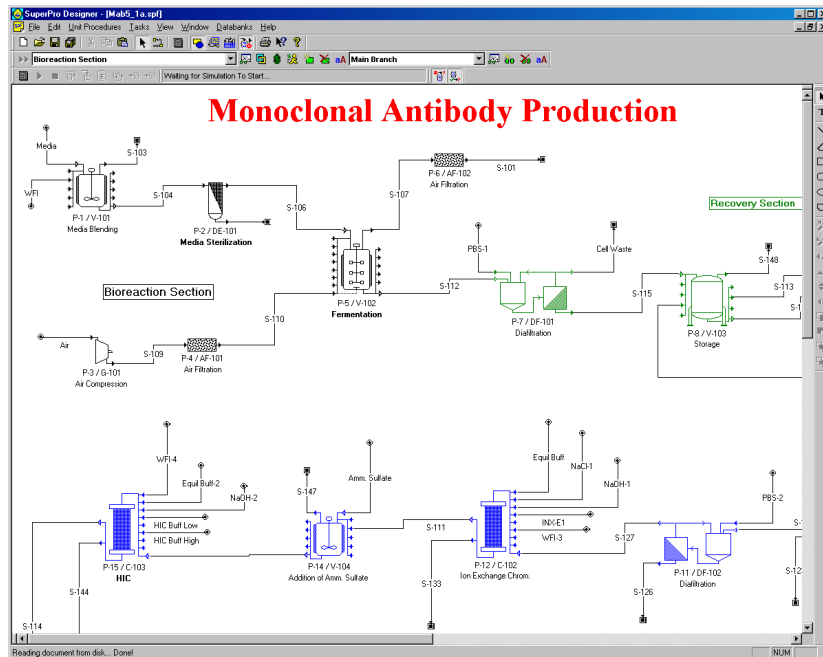
The Realm of SchedulePro

Process and Business Integration



Modeling and Scheduling of Multi-Product Facilities

< Intelligen Suite >



SuperPro Designer

Detailed Analysis
and Evaluation of
Single Processes

Recipe DB

SchedulePro

Modeling, Scheduling
and Debottlenecking of
Multi-Product Facilities



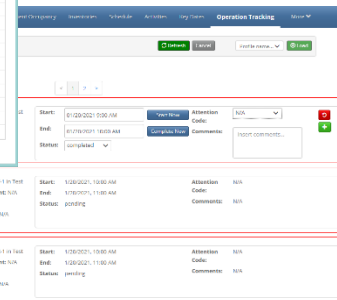
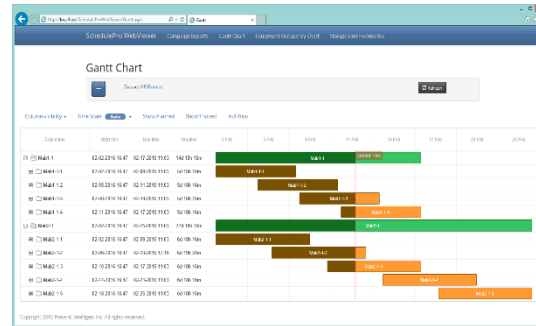
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SchedulePro Production Suite (Architecture)

WebTracker



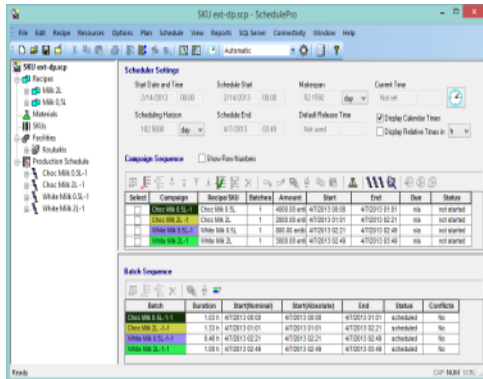
Management (view data)



Operators (Plant Floor)
Enter status updates

Local Files

SchedulePro



SQL/Application Server

User Access Control
and Auditing

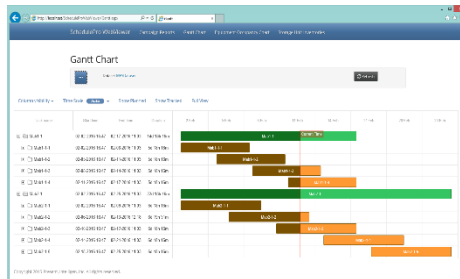
Production Planning & Scheduling



Intelligen, Inc.

Communication with Other Systems

Web Tracker



API



SQL Server

Your Application

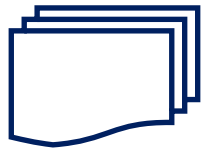
Custom Mapping



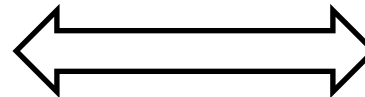
Your Analytics



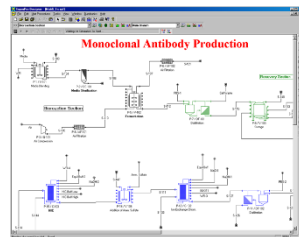
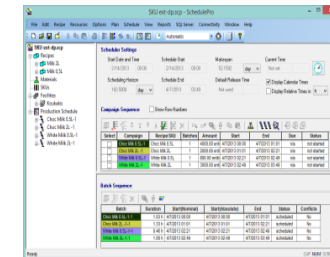
Configurable Text Files (ERP)



Recipes
Resources
Campaigns/workorders
Inventories



SchedulePro



SuperPro



Intelligen, Inc.

Recipes in SchedulePro

(According to ISA S-88 Guidelines)

The screenshot displays the SchedulePro software interface for a project named "Two-Protein-Line-Facility.scp". The interface is divided into several panes:

- Left Pane (Project Structure):** Shows a hierarchical tree of the project. It includes sections for "Protein1" (Bioreaction, Recovery, Purification), "Protein2", "Materials", "Facilities" (Labor, Staff, Utilities, Equipment, Work Areas, Transfer Panels, Storage, Material Supply Systems), and "Production Schedule" (Protein1-1, Protein2-1).
- Unit Procedure Pane:** Displays details for a selected unit procedure, "P-5 Fermentation". Fields include Name, Description, Equipment, Work Area, and Procedure Size (1).
- Operation Sequence Table:** A table listing operations and their cycle counts.
- Recipe Flow Chart:** A block diagram showing the sequence of unit procedures (P-1, P-2, P-5, P-7) and their associated materials and equipment.
- Gantt Chart:** A timeline view showing the duration of tasks and the overall project schedule.

Annotations highlight key features:

- A project may include any number of recipes** (pointing to the Project Structure pane).
- A recipe consists of unit procedures organized into sections** (pointing to the Unit Procedure pane).
- Recipes utilize resources of facilities** (pointing to the Facilities section in the Project Structure pane).
- A recipe is visualized with a block diagram and a Gantt chart** (pointing to the Recipe Flow Chart and Gantt Chart panes).

Operation	Cycle #	Aux. Equi	Duration
Transfer in aq. Media	1		
Ferment	1		
Transfer to Diafilter	1		
CIP-1	1		
SIP-1	1		

Task	Duration (h)	Start Time (h)	End Time (h)
Protein1	138.28	0.00	138.28
P-1 (BT-1 [L1])	6.62	0.00	6.62
P-2 (DE-1 [L1])	4.00	1.37	5.37
P-5 (R-1 [L1])	60.35	1.37	61.72
Transfer in aq. Media	4.00	1.37	5.37
Ferment	48.00	5.37	53.37
Transfer to Diafilter	5.10	53.37	58.47
CIP-1	1.25	58.47	59.72
SIP-1	2.00	59.72	61.72
P-7 (DF-1 [L1])	6.35	53.37	59.72
P-8 (ST-1 [L1])	10.23	53.37	63.60
P-9 (UF-1 [L1])	4.82	58.47	63.28
P-10 (C-1 [L1])	6.07	62.03	68.10
P-11 (DF-2 [L1])	29.97	62.35	92.32
P-12 (C-2 [L1])	6.00	90.32	96.32
P-14 (BT-2 [L1])	8.06	93.57	101.63
P-15 (C-3 [L1])	13.81	97.07	110.88

Unit Procedures in SchedulePro

The screenshot displays the SchedulePro software interface for a project named 'Two-Protein-Line-Facility.scp'. The left sidebar shows a hierarchical tree of the project structure, including Recipes (Protein1, Protein2), Bioreaction Section (P-1, P-2, P-5), Recovery Section, Purification Section (P-11 to P-19), Materials, Facilities (Biotech Facility, Labor, Staff, Utilities, Equipment, Work Areas, Transfer Panels, Storage, Material Supply Systems), Production Schedule, and Protein1-1. The 'Unit Procedure' configuration for 'P-5' is shown in the center, with fields for Name, Description, Equipment, Work Area, Procedure Size, and No. of Cycles. A yellow callout points to the 'Equipment' field, stating: 'A unit procedure includes one or multiple operations.' The 'Procedure Details for P-5' dialog box is open, showing the 'Main Equipment Pool' tab. It includes a 'Facility' dropdown set to 'Biotech Facility', a 'Match Type' checkbox, and a 'Fementor' dropdown. Below these are several checkboxes for equipment sharing and usage rules. A yellow callout points to the 'Equipment in Pool' section, stating: 'A unit procedure is assigned a pool of one or multiple equipment units'. The 'Equipment in Pool' section lists 'R-1 [L2] (in Biotech Facility)' and 'R-2 [L2] (in Biotech Facility)'. The 'Available Equipment' section lists 'R-1 [L1]'. The bottom of the dialog box has 'OK', 'Cancel', and 'Help' buttons.

Unit Procedure

Name: P-5
in Recipe: Protein2

Description:
Equipment:
Work Area:
Procedure Size:
No. of Cycles:

Operation Sequence

Operation
Transfer in aq. Media
Ferment
Transfer to Diafilter
CIP-1
SIP-1

Procedure Details for P-5

Properties | Main Equipment Pool | Work Area Pool | Scaling

Facility: Biotech Facility
Match Type: ☒
Fementor: P-1

☐ Shares Equipment Pool with Procedure
☐ Must Use the Same Equipment as Procedure
☐ Do not Share Equipment with Other Procedures
☐ Require Staggered Use of All Equipment
☐ Require Same Equipment for Entire Campaign

Equipment in Pool

R-1 [L2] (in Biotech Facility)
R-2 [L2] (in Biotech Facility)

Available Equipment

R-1 [L1]

OK Cancel Help

Operations in SchedulePro

Operation: CIP-1 in P-5

Heating/Cooling	Power	Material Inputs	Material Outputs
General	Duration	Scheduling	Auxiliary Equipment

☒ Duration Calculated (= Constant)

☒ Constant 75.0000 min ☐ Scales with Batch Size

☐ Rate-based Term

Total Nominal Duration 75.00 min

Operation durations may be fixed, rate dependent or linked to other operations

Operation: CIP-1 in P-5

Heating/Cooling	Power	Material Inputs	Material Outputs
General	Duration	Scheduling	Auxiliary Equipment

Auxiliary Equipment for CIP-1 in P-5

☒ Any Equipment

☐ Specify Type Air Filter

Available

Biotech Facility

- AF-1 [L1]
- AF-1 [L2]
- AF-2 [L1]
- AF-2 [L2]
- BT-1 [L1]
- BT-1 [L2]
- BT-2 [L1]
- BT-2 [L2]
- BT-3 [L1]
- BT-3 [L2]
- C-1 [L1]
- C-1 [L2]
- C-2 [L1]
- C-2 [L2]
- C-3 [L1]

Included

- CIP-Sk-2 (in Biotech Facility)
- CIP-Sk-1 (in Biotech Facility)

Use All Compatible ☐

Auxiliary equipment is associated with operations

Operation: CIP-1 in P-5

Heating/Cooling	Power	Material Inputs	Material Outputs
General	Duration	Scheduling	Auxiliary Equipment

Operation Scheduling

☐ Starts with Batch Start

☒ With Respect to Another Operation in this Procedure

Reference Operation Transfer to Diafilter

Link Relation (FS) Starts with end of reference operation

☐ With Respect to an Operation in Another Procedure

Reference Operation Transfer to Diafilter in procedure P-5

Link Relation

Time Shift (+ = delay, - = lead)

Fixed Time Shift 0.00 h

☒ Use Flexible Shift 12.00 h Maximum delay/lead

☐ Is Interruptible 0.00 h Maximum total break time

☐ Limit Number of Break Instances to 1 times

☐ Set Minimum Time Between Breaks to 1.00 h

Operation Can Shift or Break for:

☐ Facility Closure ☐ Utilities Availability ☒ Material Availability (Rate-based or Inventory)

☒ Equipment Availability ☐ Labor/Staff Availability

Outages

☐ Operation Can Be Scheduled within Periods of Facility/Equipment Outages

☐ Ignore Outages Only If Operation Is Started During Normal Operating Hours

Scheduling precedence relations

Planning Campaigns

The screenshot displays the 'Two-Protein-Line-Facility.scp - SchedulePro' application window. The main interface includes a menu bar (File, Edit, Recipe, Resources, Schedule, View, Reports, Connectivity, Window, Help), a toolbar, and a project tree on the left. The project tree shows a hierarchy: SchedulePro Project > Recipes > Protein1 > Protein1-1 through Protein1-6, and Protein2-1 through Protein2-5. The main workspace is divided into two panes: 'Campaign Sequence' and 'Batch Sequence'.

The 'Campaign Sequence' pane shows a table with columns: Select, Campaign, Recipe, No of Batches, and Amount. It lists two campaigns: Protein1-1 (6 batches, 13200.00) and Protein2-1 (5 batches, 12500.00).

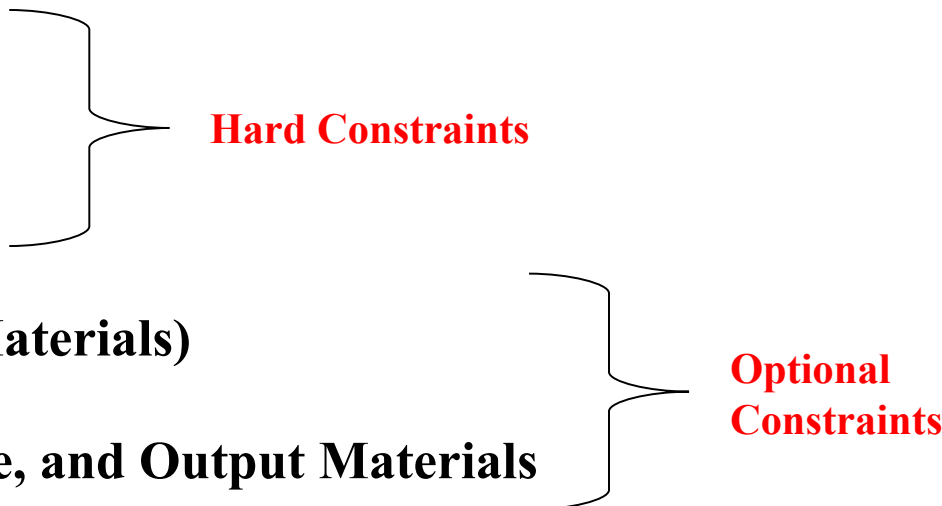
The 'Batch Sequence' pane shows a table with columns: Batch, Duration, and Start(N). It lists 11 batches, alternating between Protein1 and Protein2 campaigns.

The 'Campaign Setup' dialog box is open, showing the 'ID/Amount' tab. It contains the following fields and controls:

- Recipe and ID:**
 - ID: Camp-3 (with 'Set from Recipe' button)
 - Recipe: Protein1 (dropdown)
 - Nominal Batch Size: 2200.0000 L of Fermentor Broth
- Display Color:** A green color bar (with 'Set from Recipe' button and a color picker icon).
- Batch Name Base:** Protein1-2
- Batch Starting Sequence No.:** 1
- ☐ Use Names from File
- Amount:**
 - ☒ Set Number of Batches: 1
 - ☐ Set Order Amount: 2200.0000 L
- Batch Size:**
 - ☒ Specify Batch Size for Campaign: Maximum based on equipment (n/a)
 - ☐ Set Batch Size: 2200.0000 L (with 'Set to Maximum' button)
 - ☒ Set Scale Factor: 1.0000
- Buttons:** Recalculate (with calculator icon), OK, Cancel, and Help.

Scheduling Campaigns and Batches

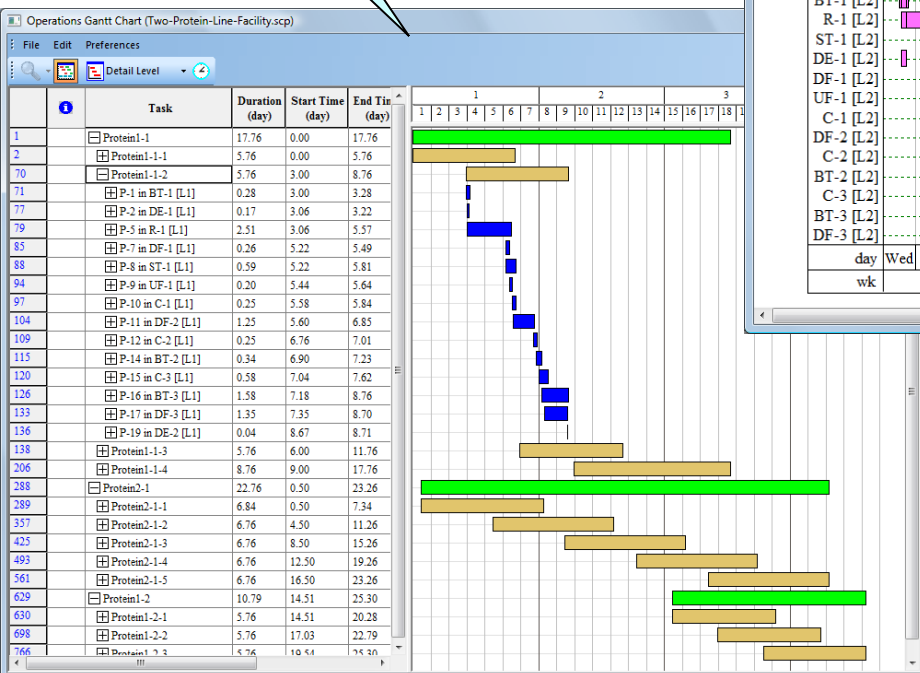
Constraints Considered by SchedulePro

- Facilities & Work Areas
 - Equipment (Main and Auxiliary)
 - Resources (Labor, Utilities, Raw Materials)
 - Inventories of Supply, Intermediate, and Output Materials
- Hard Constraints**
- Optional Constraints**
- 

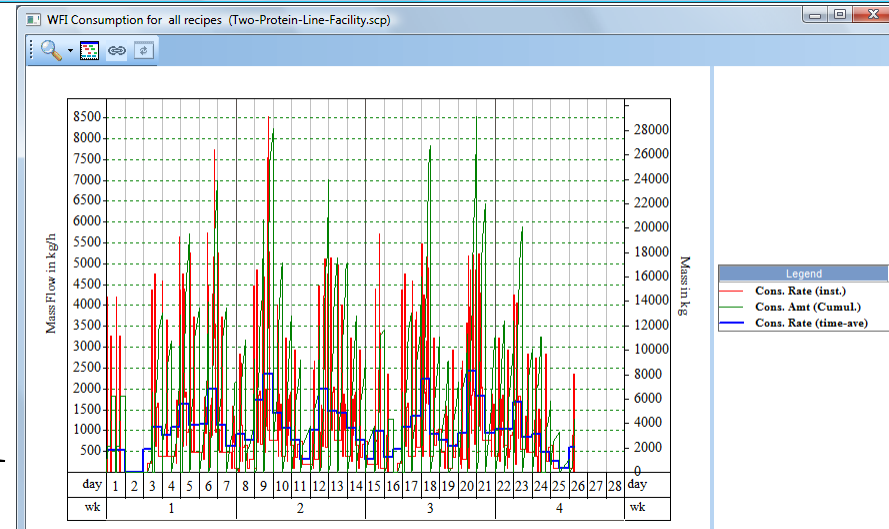
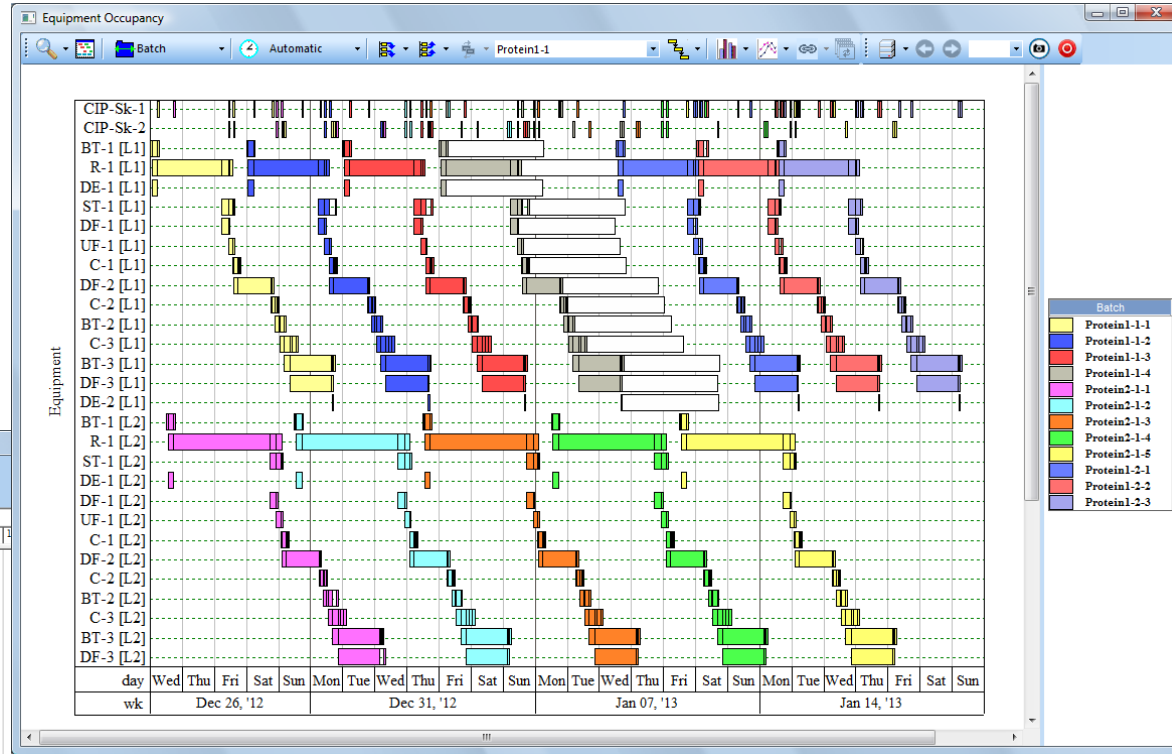
Visualizing the Results

Equipment
Occupancy
Chart

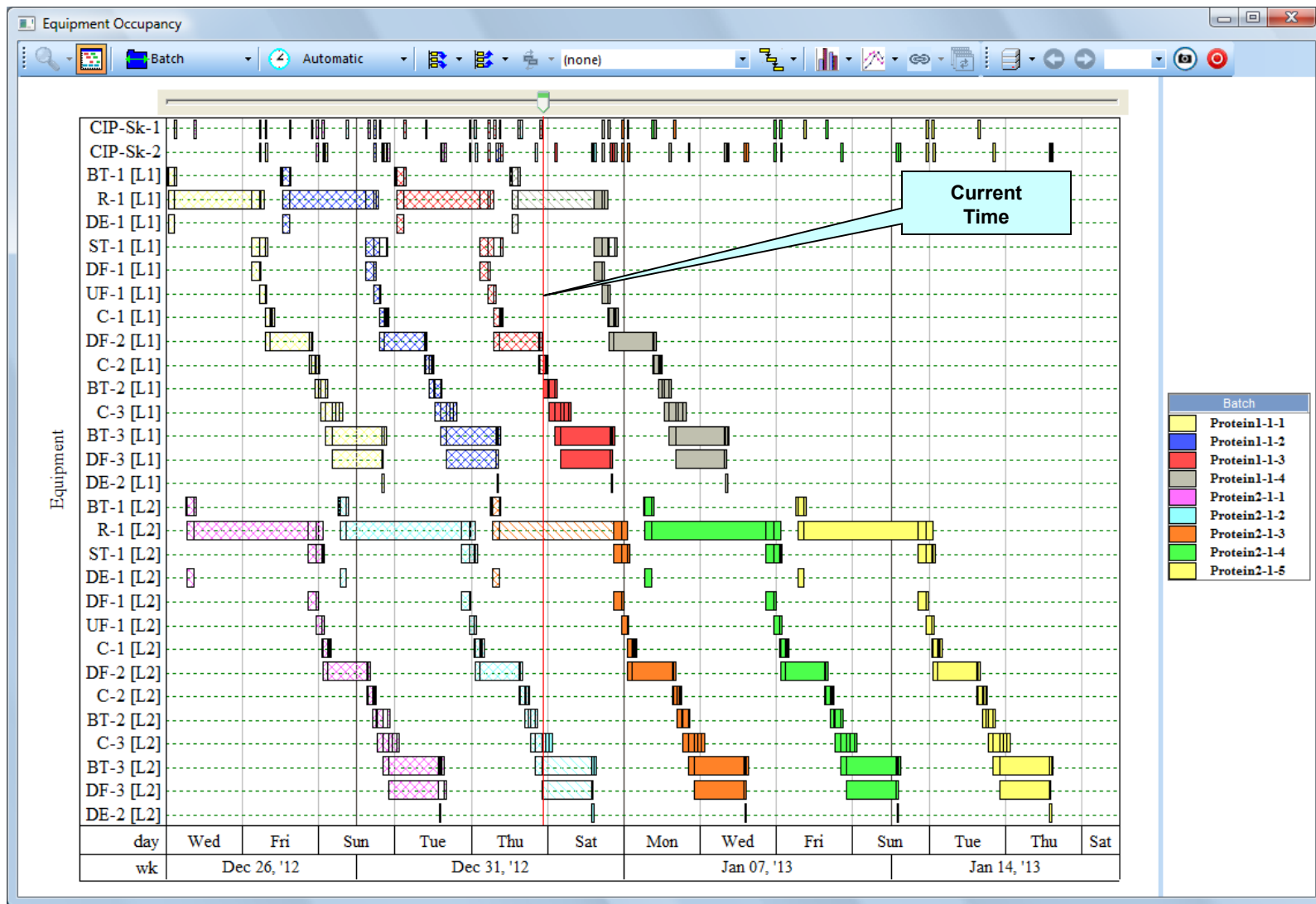
Gantt
Chart



Resource
Chart

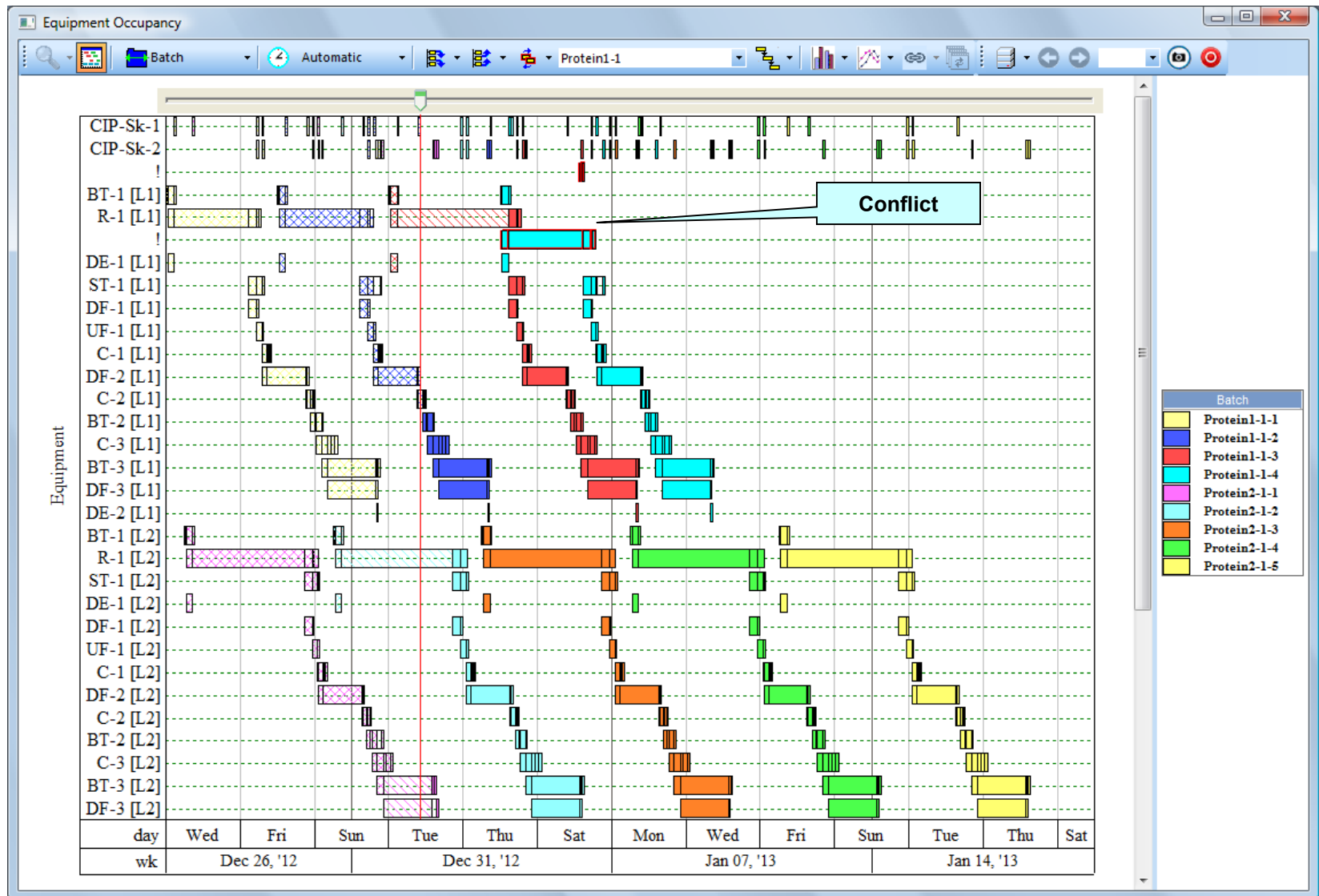


Tracking the Status of Production

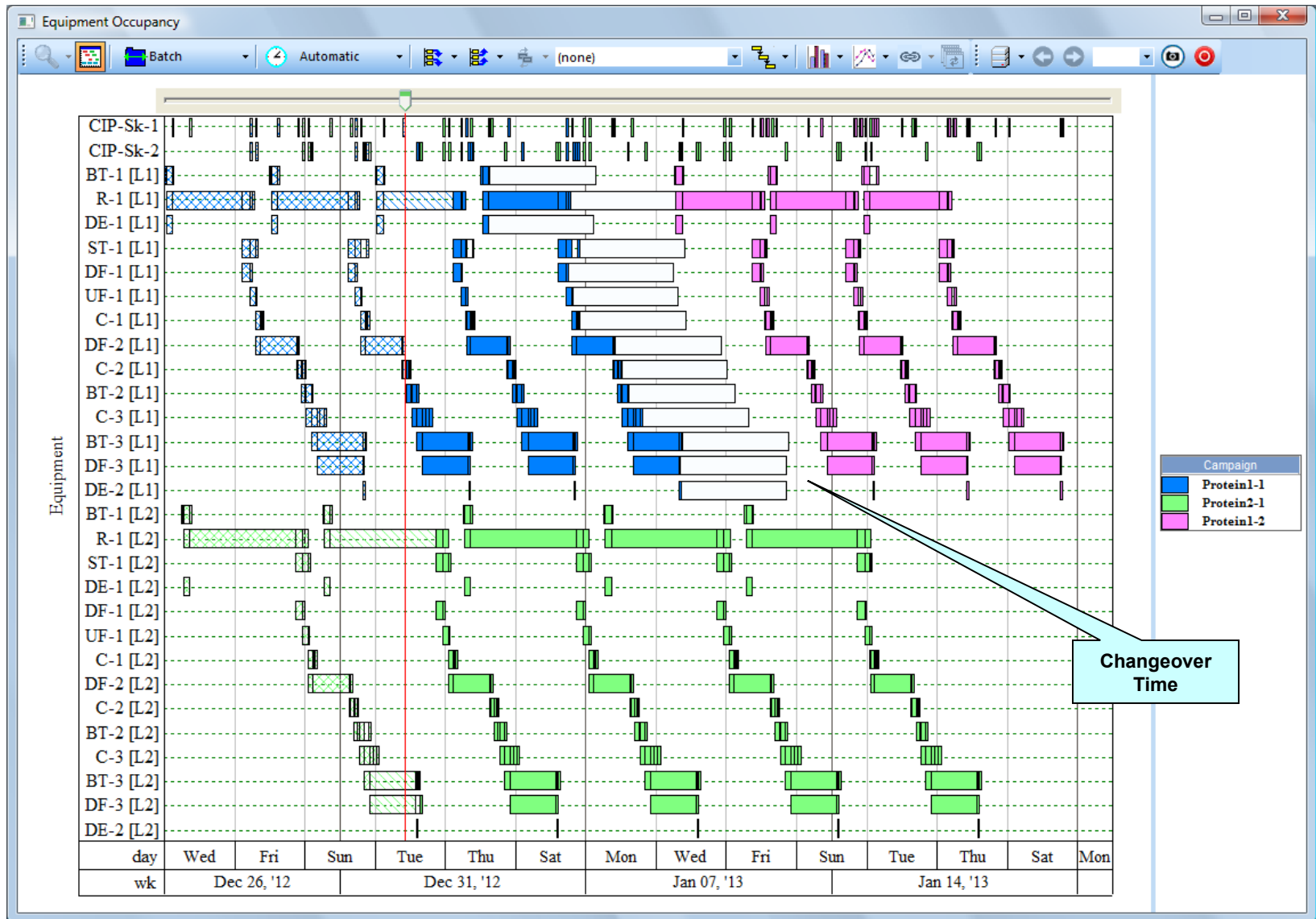


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Considering Delays and Visualizing Conflicts



Scheduling Additional Campaigns



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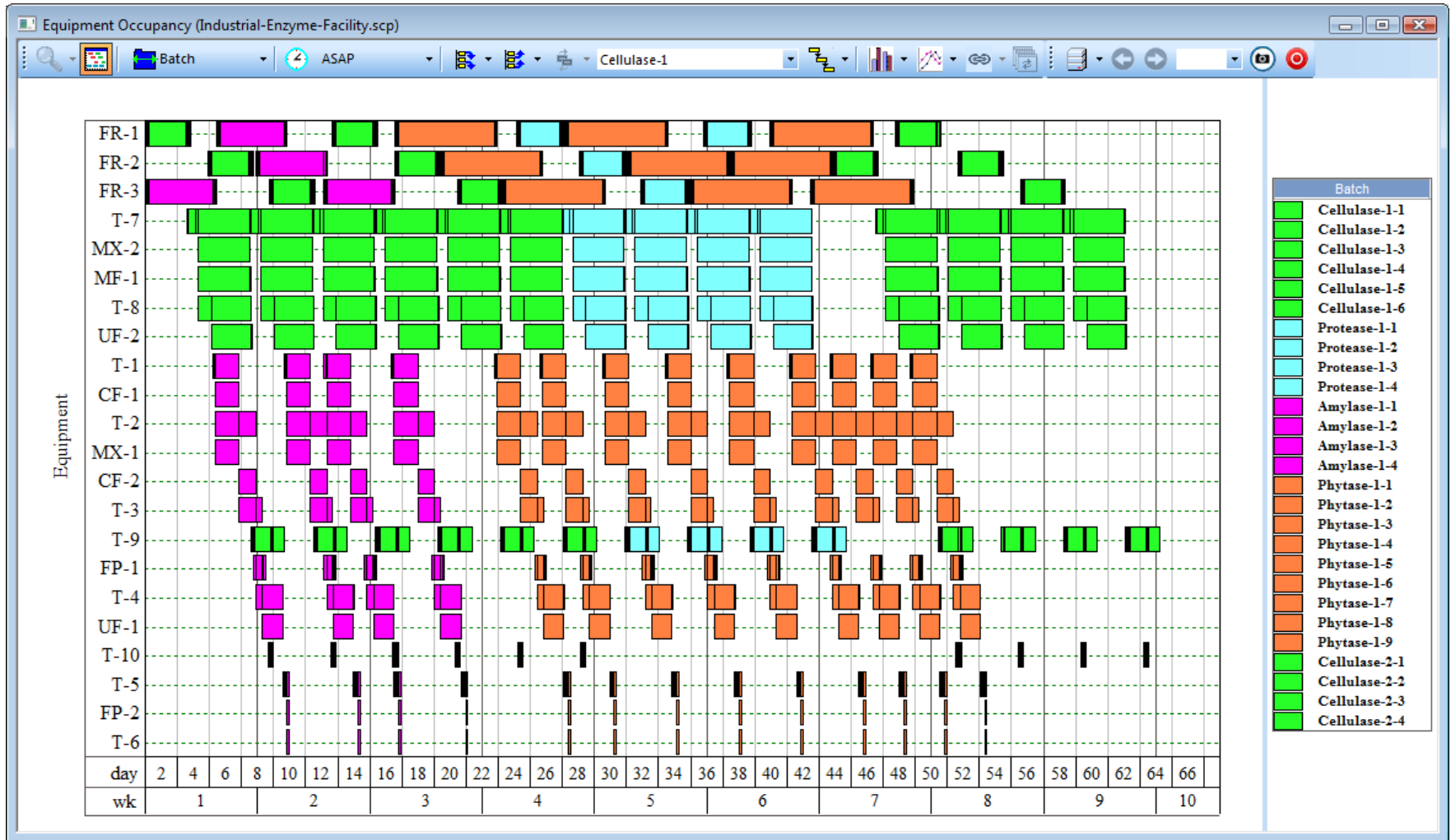
Viewing Multiple Linked Charts



SchedulePro Example

Production of Industrial Enzymes

Industrial Enzyme Manufacturing Facility

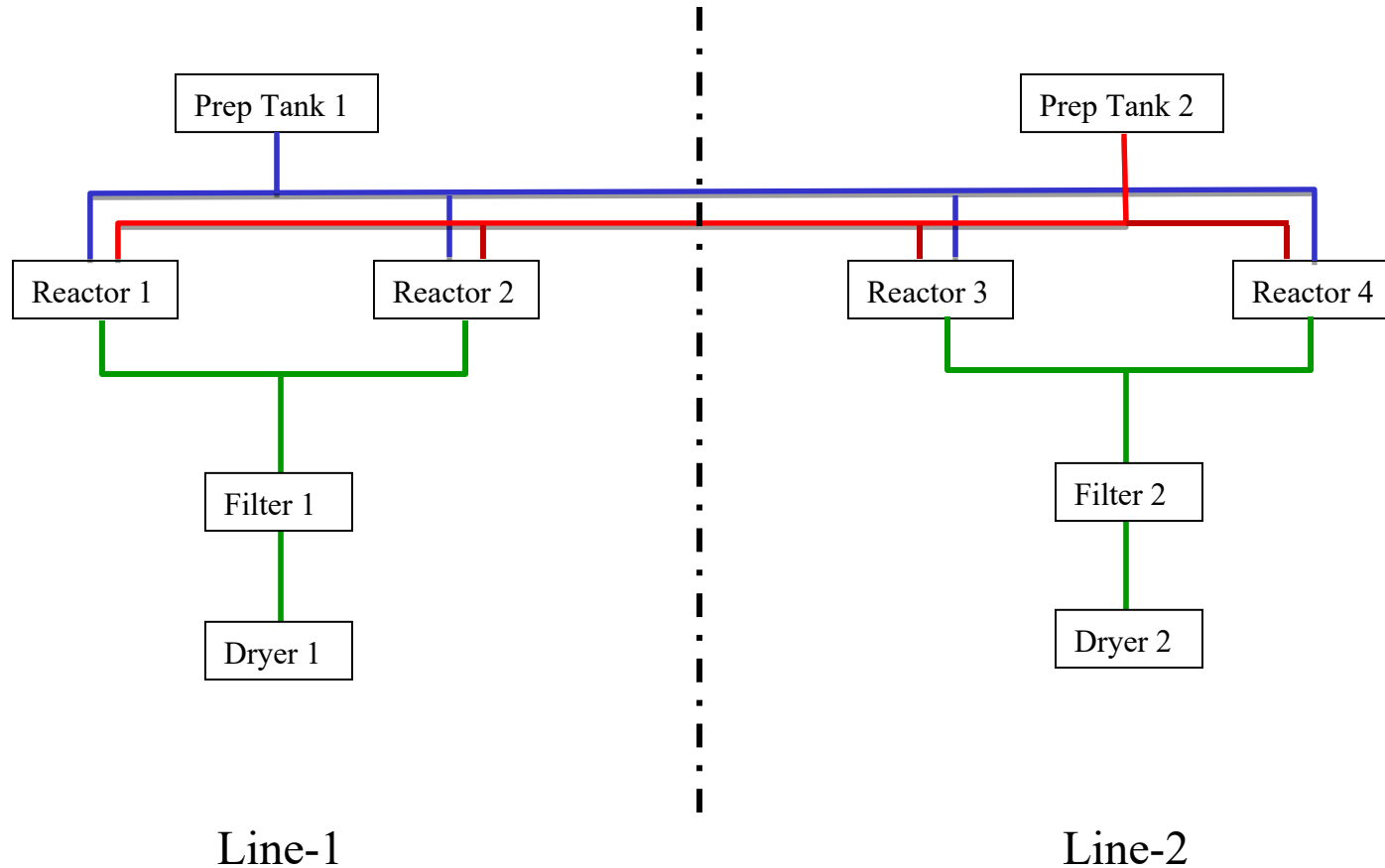


Intelligen, Inc.

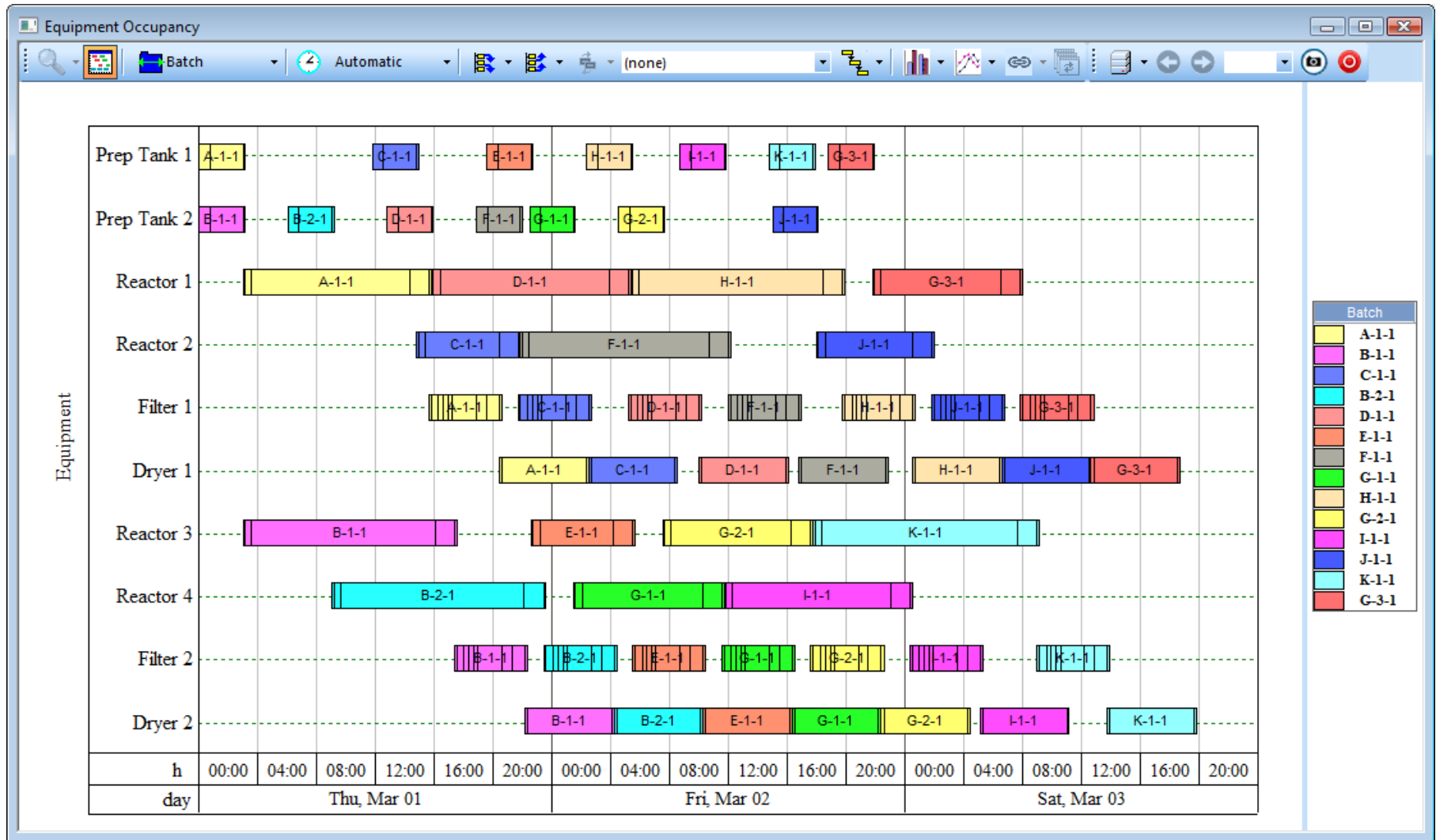
SchedulePro Example

Processing of Agricultural Materials

Processing of Agricultural Materials – Equipment Layout



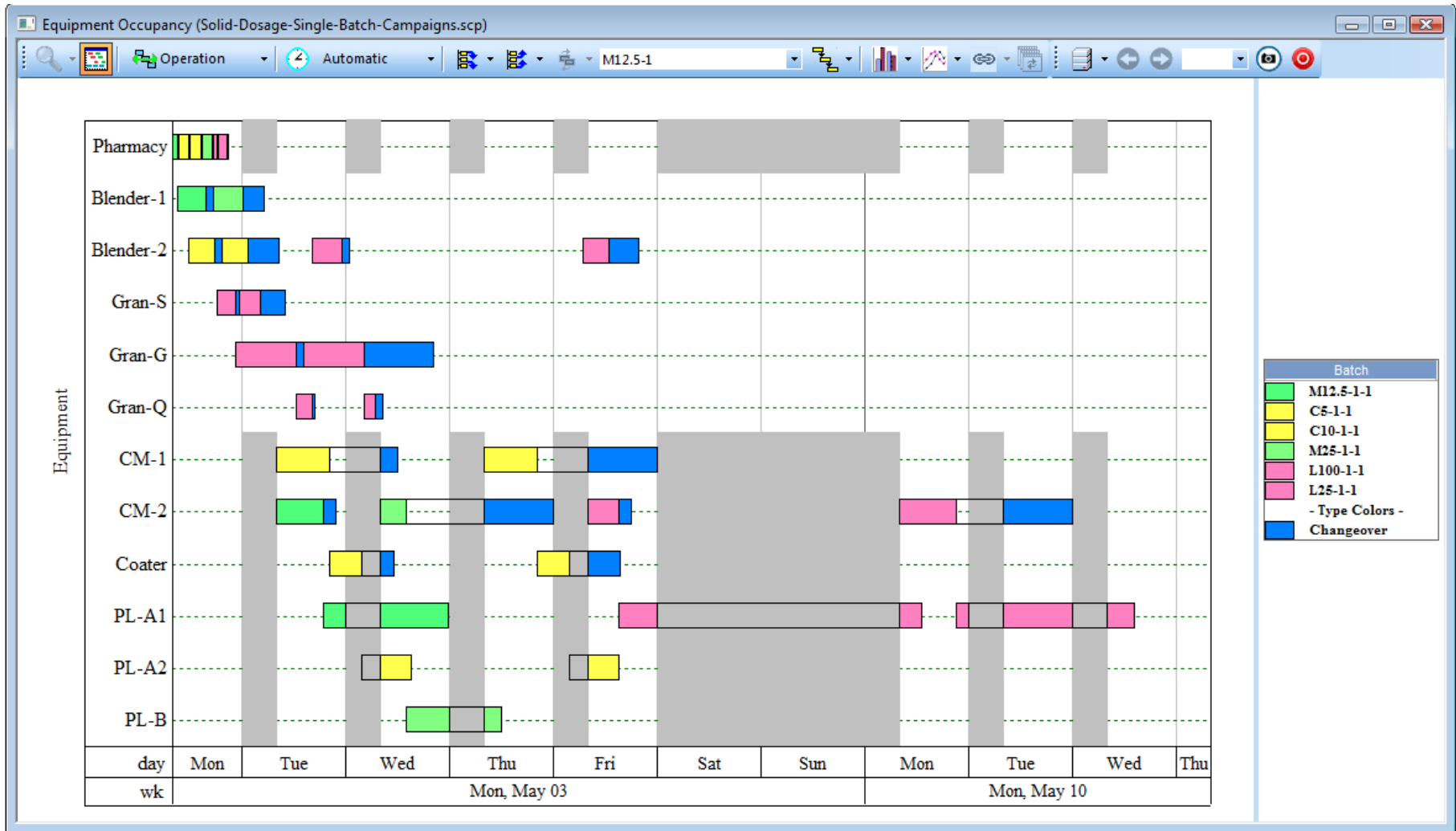
Processing of Agricultural Materials



SchedulePro Example

Production of Pharmaceutical Tablets - Solid Dosage Manufacturing -

Pharma Tablets – Single Batch Campaigns



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Pharma Tablets – Changeover Matrix

Changeover Matrix

Name: B40 Changeover

States Based on: Product Type (Recipe Classification Category)

Nominal Duration: 0 min

Min Time for "Idle" State: 4 day

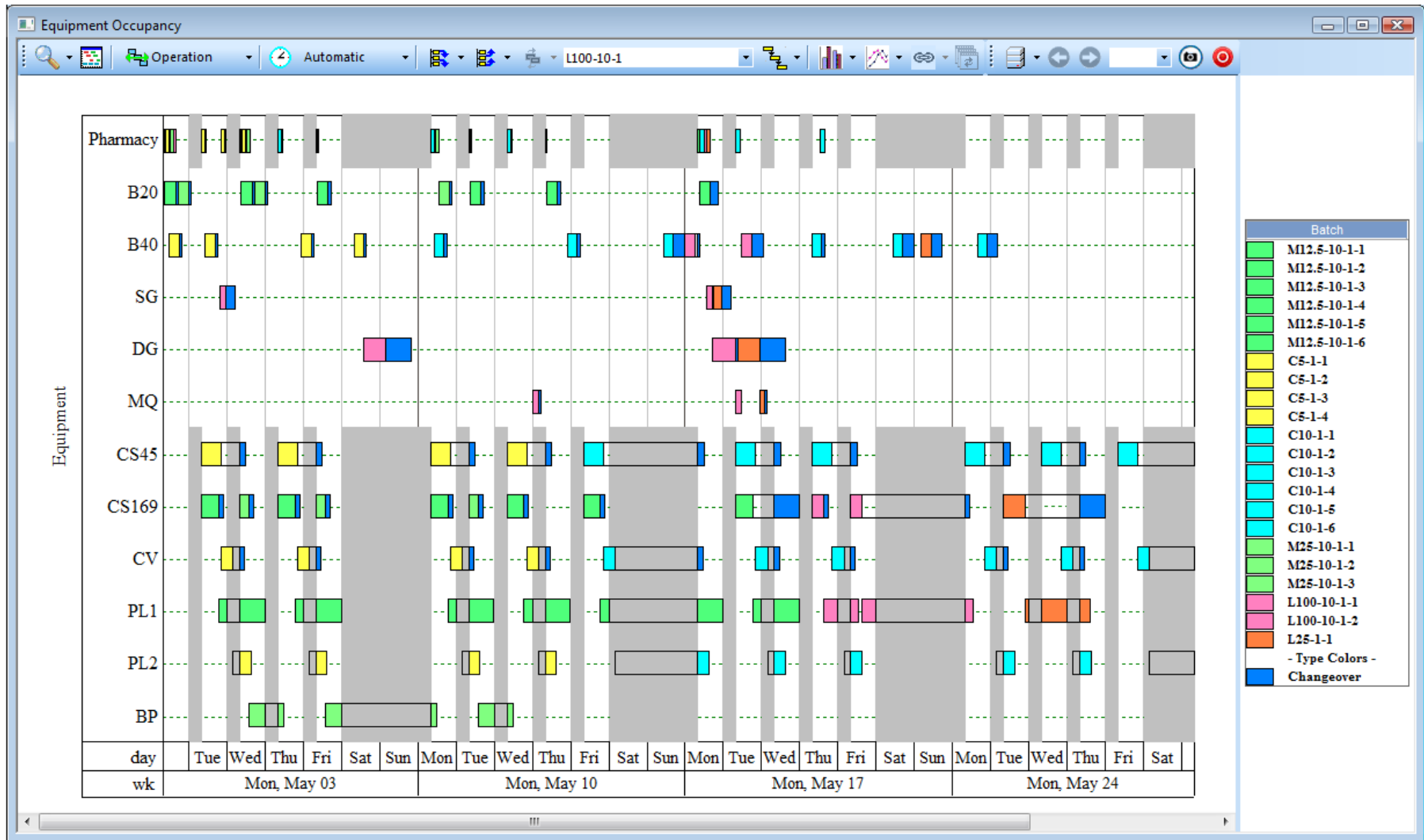
Matrix is Symmetrical ☒

Duration (min)	Idle	C	L	M
Idle	0.00	420.00	420.00	420.00
C	420.00	100.00	420.00	420.00
L	420.00	420.00	100.00	420.00
M	420.00	420.00	420.00	100.00

OK Cancel

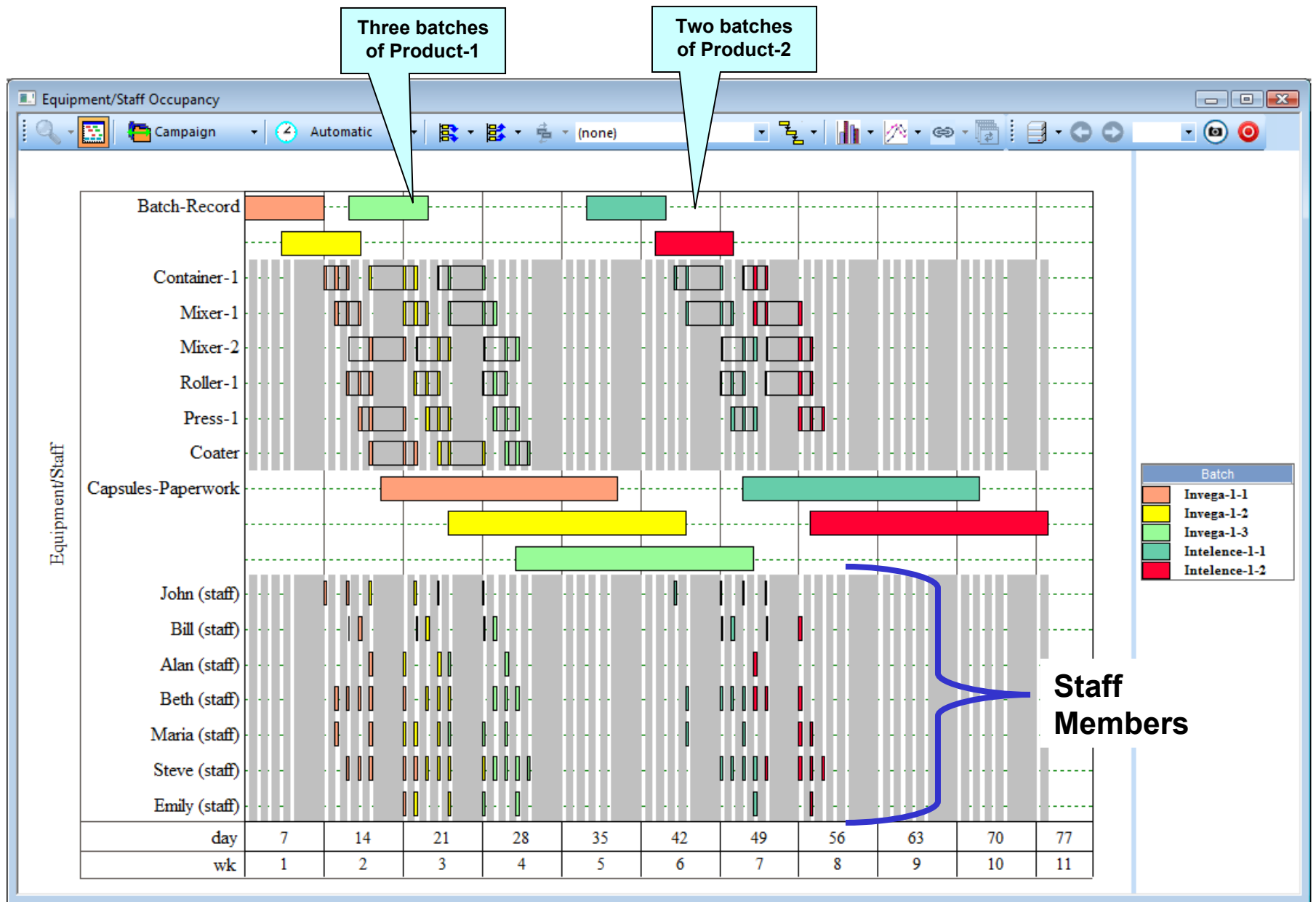


Pharma Tablets – Multi-Batch Campaigns



SchedulePro Example

Clinical Manufacturing of Pharma Tablets



Assigning Staff Members to an Operation

Operation: Compress in Compression

Heating/Cooling Power Material Inputs Material Outputs
General Duration Scheduling Auxiliary Equipment Transfer Panels Staff Labor

Staff Assignment for Compress in Compression

Available

Pilot Plant

Beth
Emily
John
Maria
Steve

Included

Bill (in Pilot Plant)
Alan (in Pilot Plant)

Use 1 persons Use All

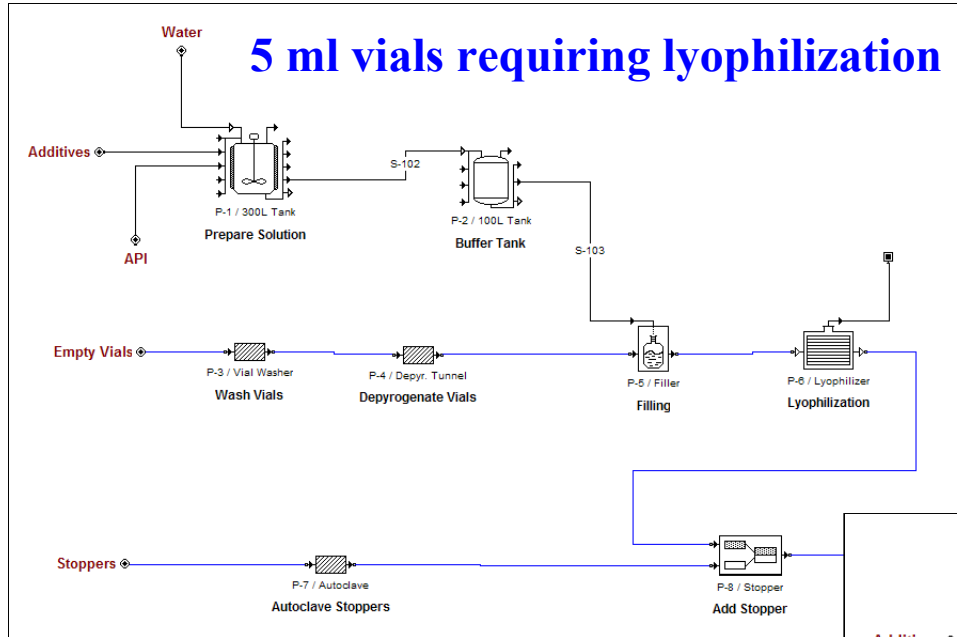
OK Cancel Help

SchedulePro Example

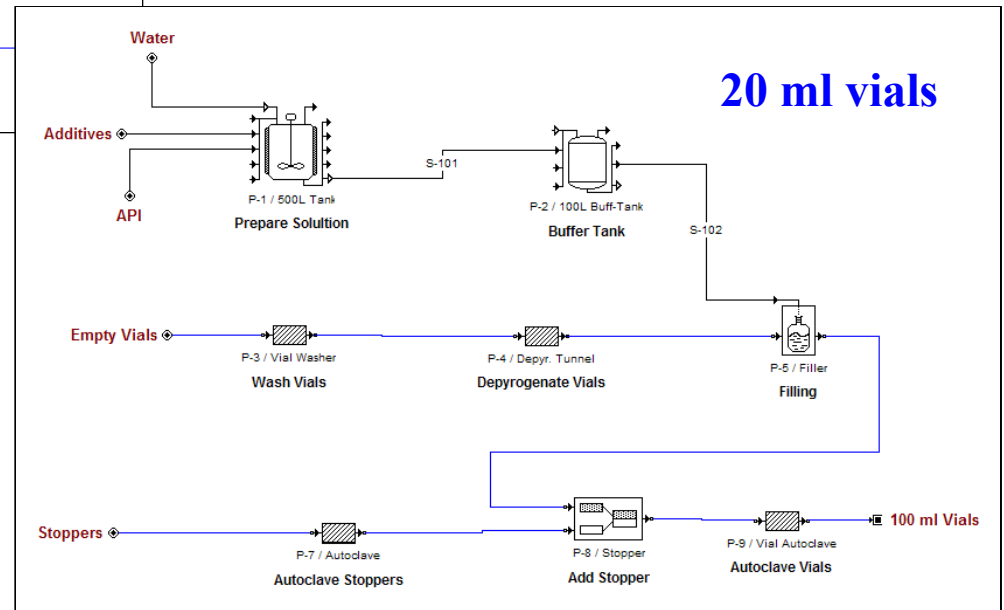
Manufacturing of Pharmaceutical Vials

Vial Manufacturing Recipes

5 ml vials requiring lyophilization

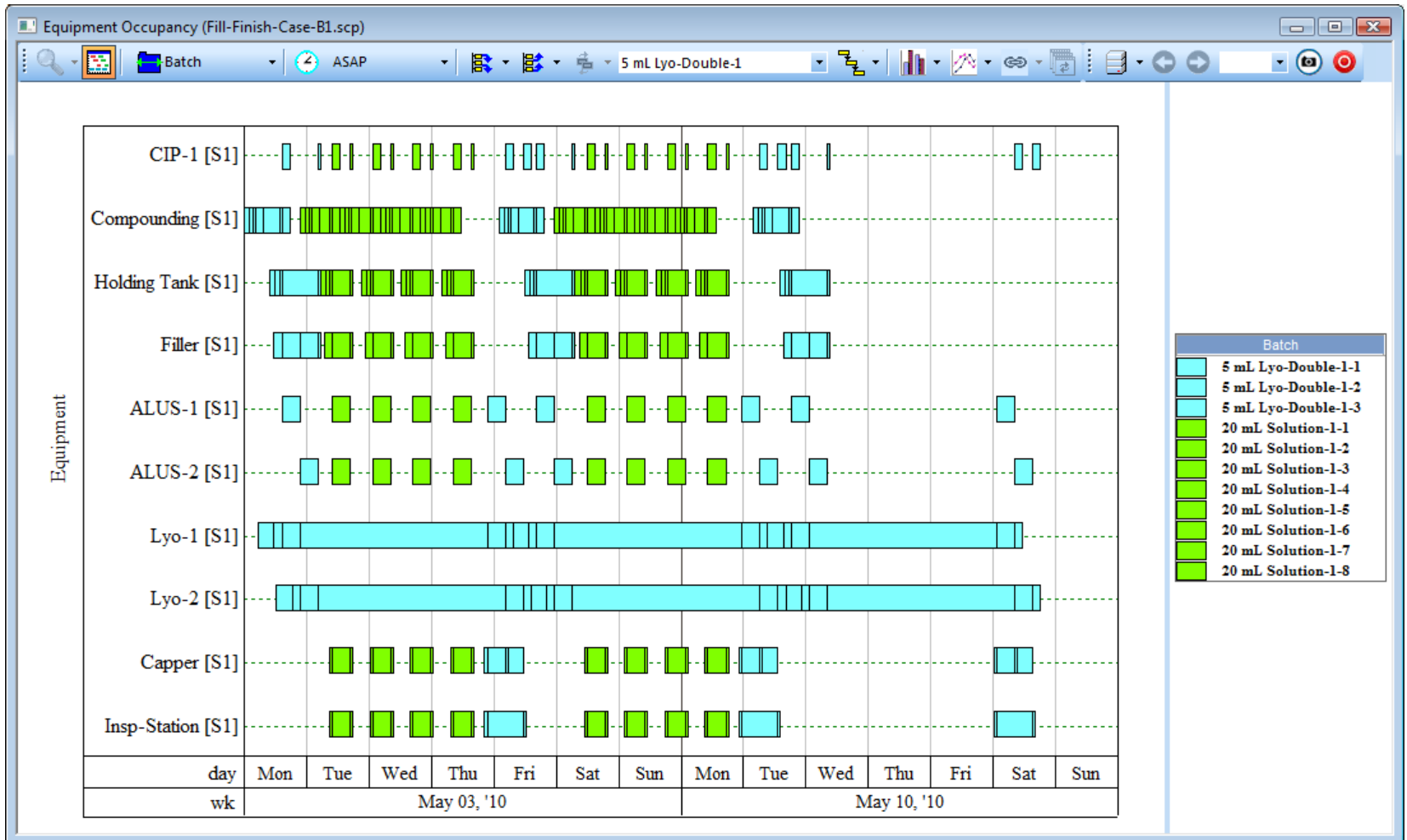


20 ml vials



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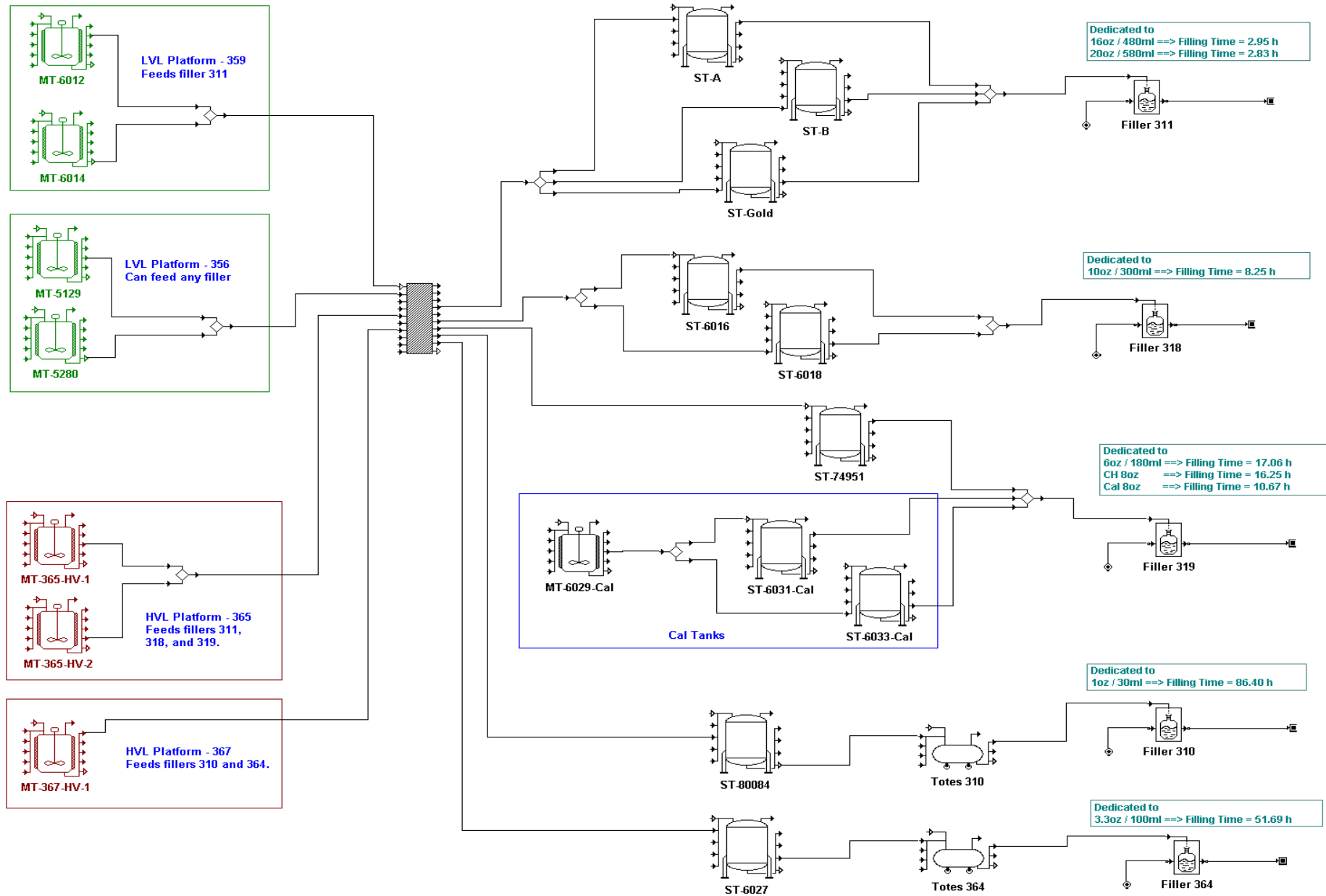
Campaign of 3 batches of 5-ml vials (blue color) combined with a campaign of 8 batches of 20-ml vials (green color). The two recipes share tanks and filler.



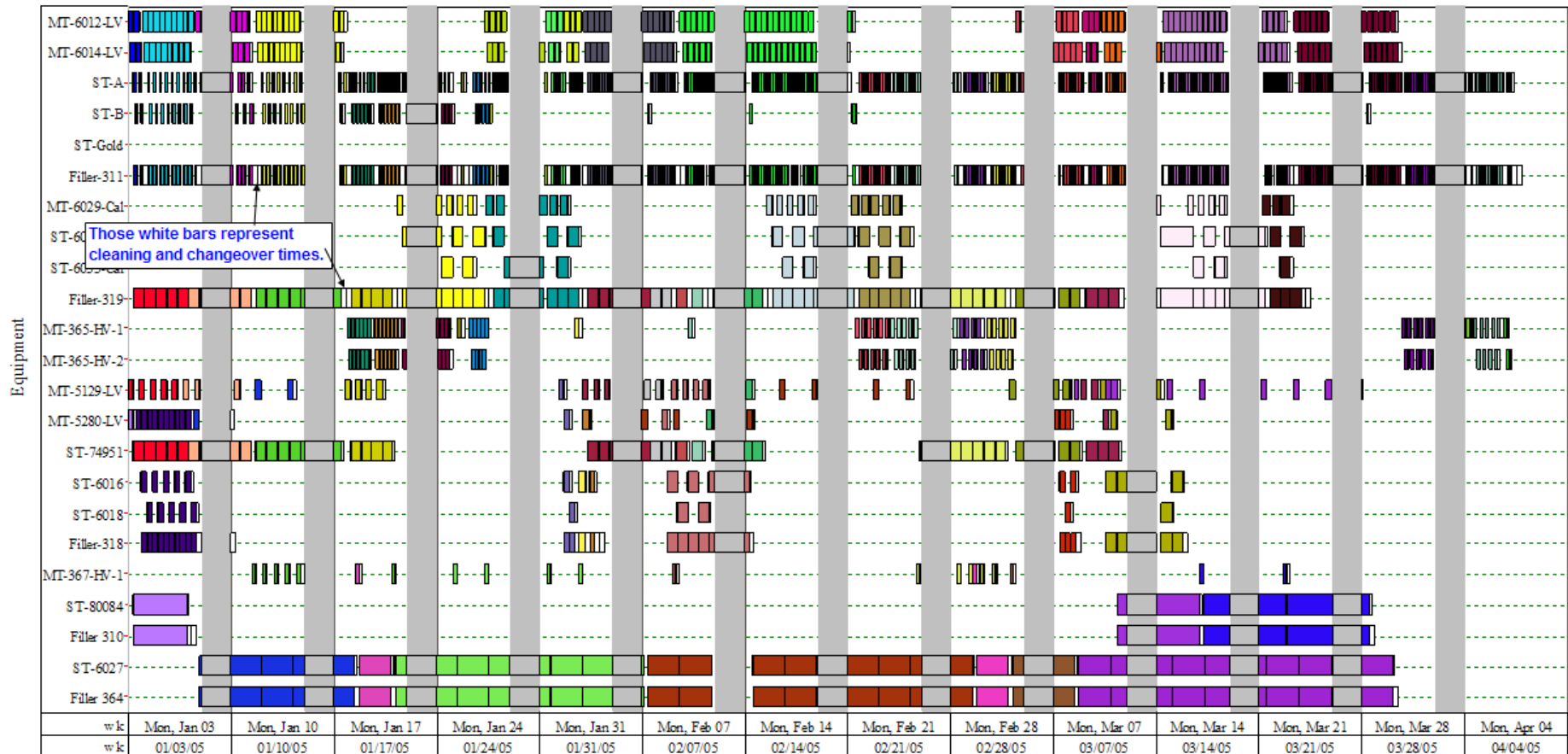
SchedulePro Example

Manufacturing of Consumer Healthcare Products (Skin Moisturizers)

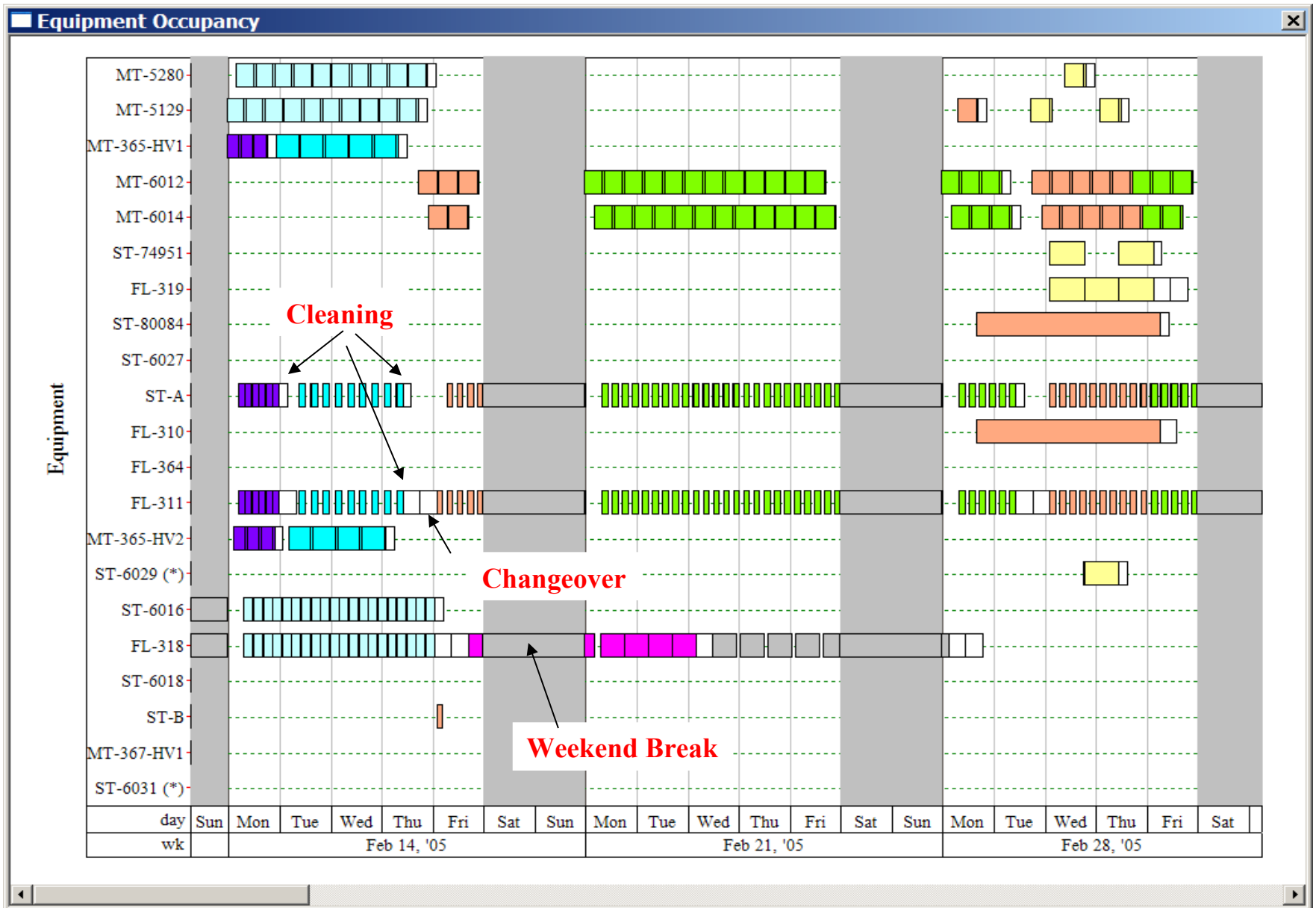
Manufacturing of Skin Care Products – Capacity Analysis



Production Schedule for a Three-Month Period



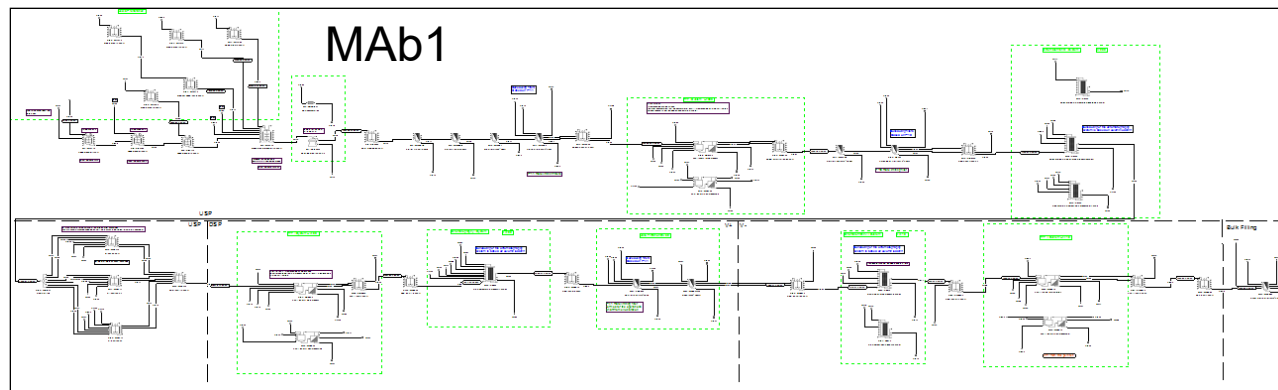
Closer View



SchedulePro Example

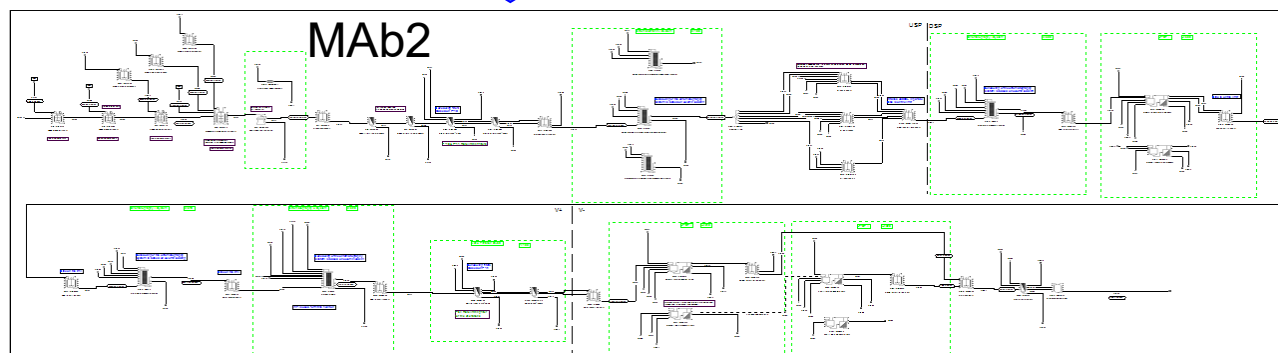
Designing a Two-Line Bio-Pharmaceutical Manufacturing Facility

Facility with Two MAb Product Lines



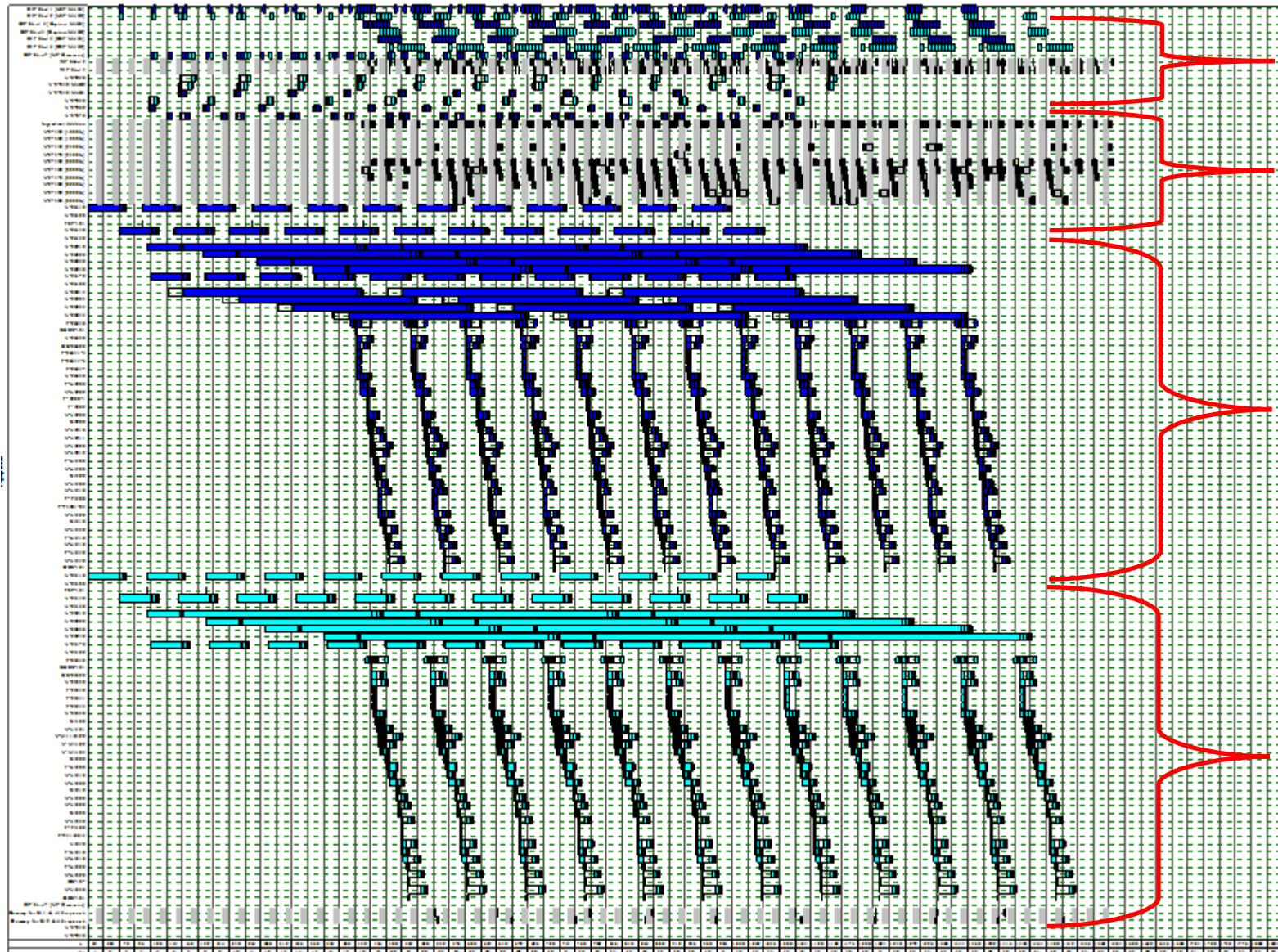
Four production bioreactors feeding a single purification line.

Common Media and Buffer Prep Areas and Utilities



Four production bioreactors feeding a single purification line.

Twelve Batches of Each Product Line



CIP Skids

Media &
Buffer Prep

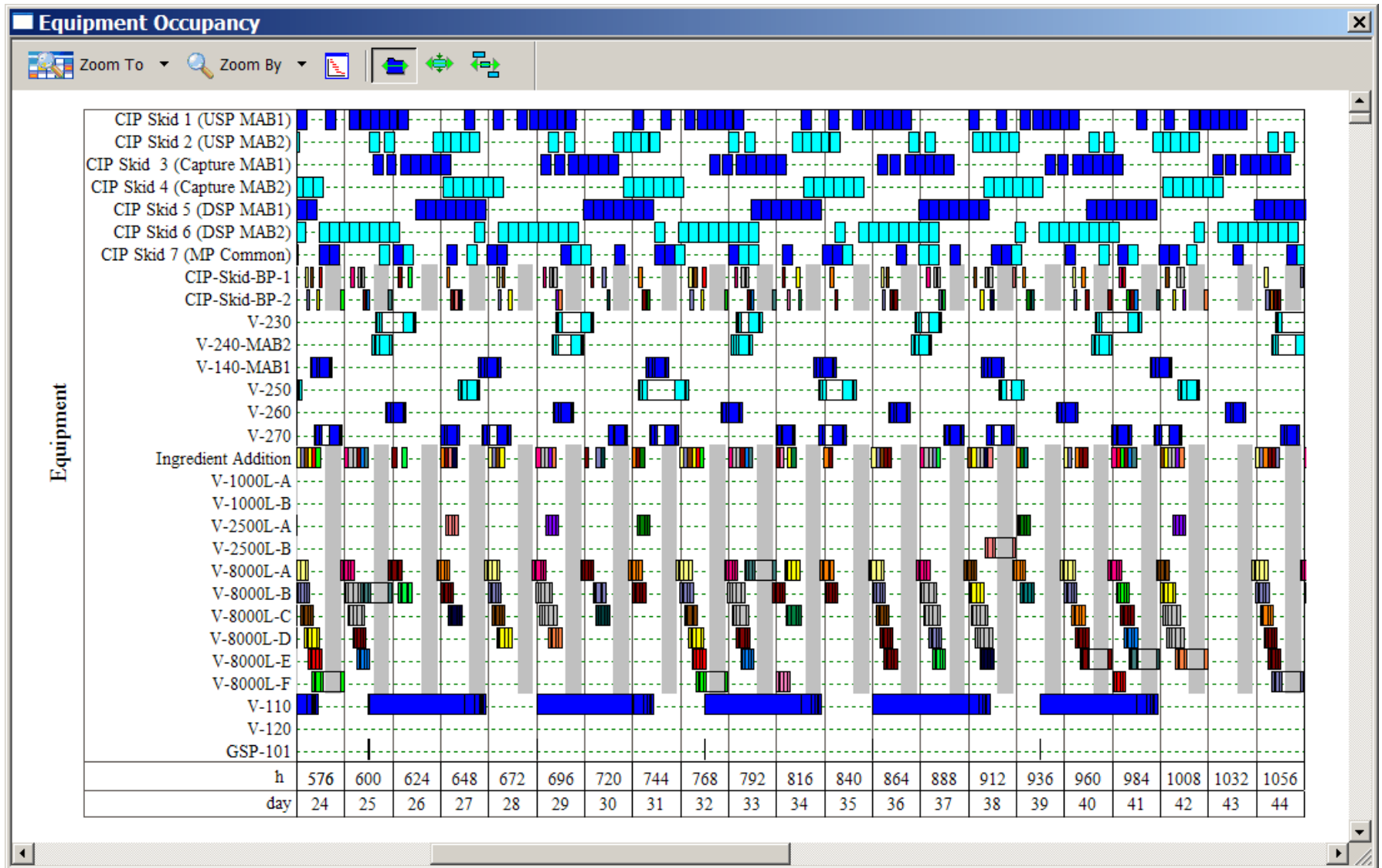
Mab 1

Mab 2

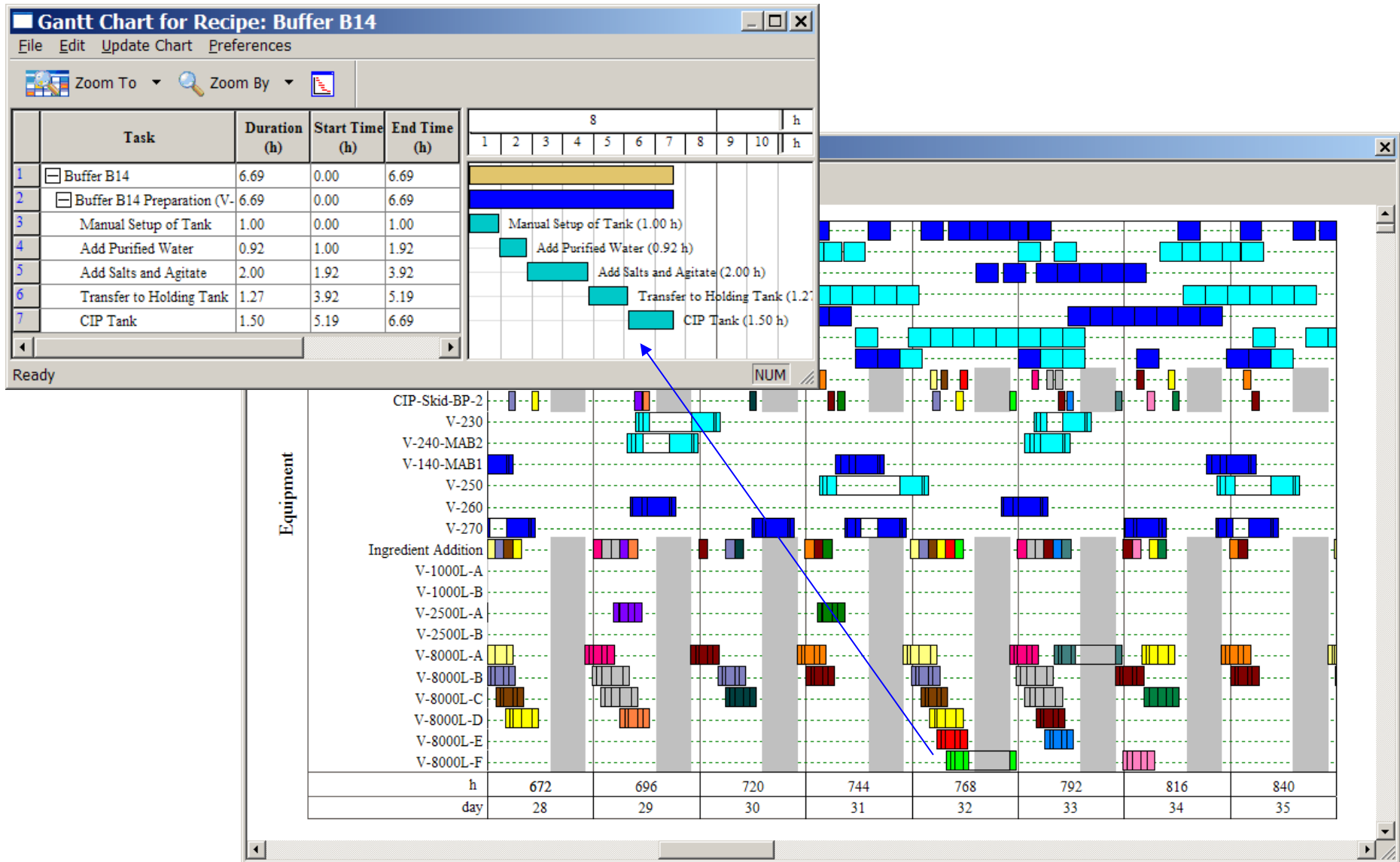


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Buffer Preparation

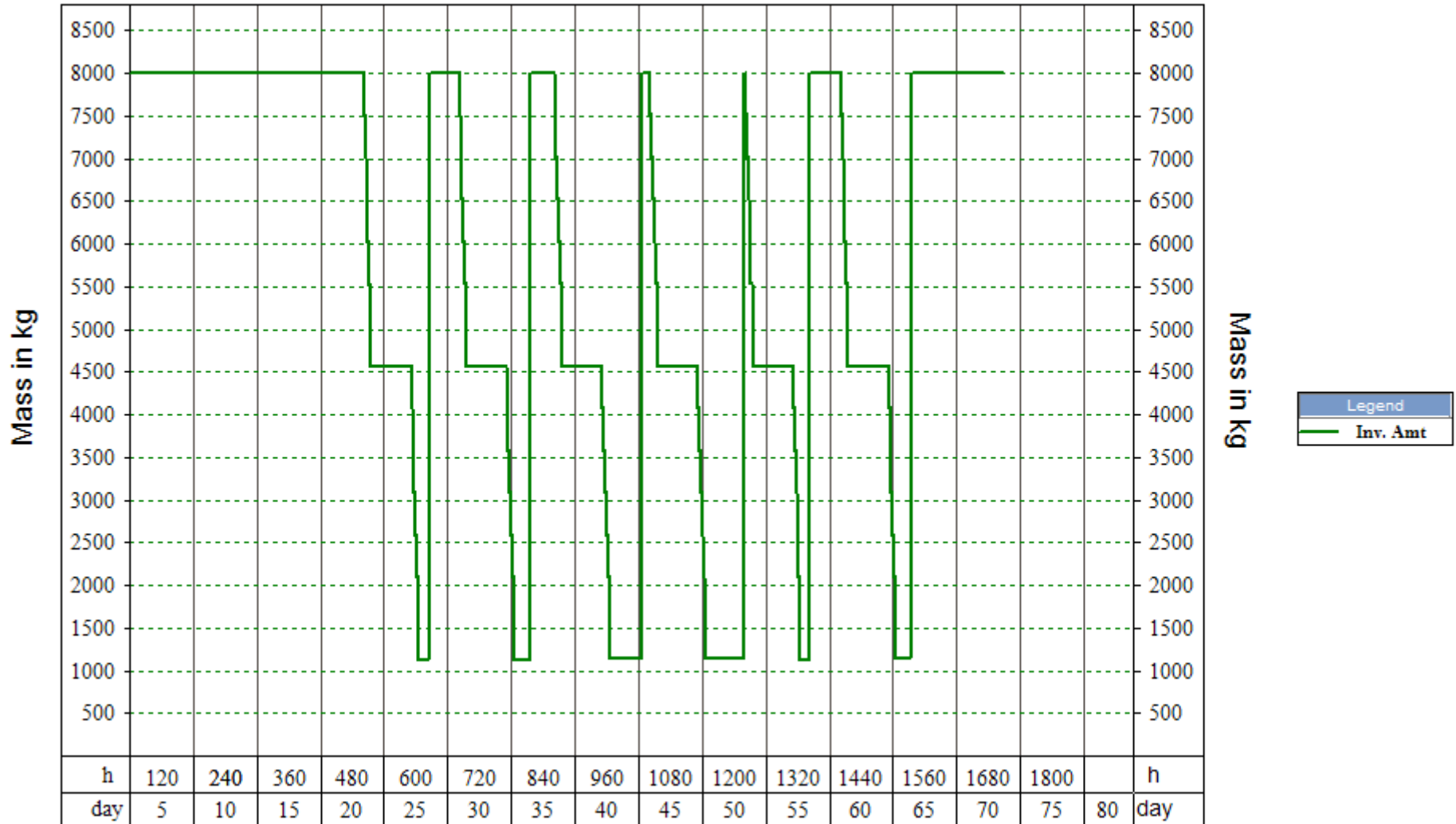


Buffer Preparation – Closer View



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Inventory of Buffer B14



Flexibility for Schedule Generation

Operation: RIP in Buffer Preparation

Heating/Cooling Power Material Inputs Material Outputs
General Duration Scheduling Auxiliary Equipment Transfer Panels Staff Labor

Operation Scheduling

☐ Starts with Batch Start

☒ With Respect to Another Operation in this Procedure

Reference Operation: Transfer out

Link Relation: (FS) Starts with end of reference operation

☐ With Respect to an Operation in Another Procedure

Reference Operation: Transfer out in procedure Buffer Preparation

Link Relation:

Additional Links (Advanced)...

Time Shift (+ = delay, - = lead)

Fixed Time Shift: 0.00 min

☒ Use Flexible Shift: 10.00 h Maximum delay/lead

☐ Is Interruptible: 0.00 h Maximum total break time

☐ Limit Number of Break Instances to: 1

☐ Set Minimum Time Between Breaks to: 1.00 h

Operation Can Shift or Break for:

☒ Facility Closure ☒ Utilities Availability ☒ Material Availability (Rate-based or Inventory)

☒ Equipment Availability ☒ Labor/Staff Availability

Outages

☐ Operation Can Be Scheduled within Periods of Facility/Equipment Outages

☐ Ignore Outages Only if Operation Is Started During Normal Operating Hours

OK Cancel Help

Procedure Details for Buffer Preparation

Properties Main Equipment Pool Work Area Pool Scaling

Facility: BP Match Type: Batch Generic Bo

☐ Shares Equipment Pool with Procedure

☐ Must Use the Same Equipment as Procedure

☐ Do not Share Equipment with Other Procedures

☐ Require Staggered Use of All Equipment

☐ Require Same Equipment for Entire Campaign

Equipment in Pool

Available Equipment

Adding Ingredients constraint
Dummy for E11 & A16 replenish
Dummy for E12 & A6 replenish
RIP Skid 2
RIP Skid 3
V-27430 (1000 L)
V-27440 (2500 L)
V-27560 (1000 L)
V-27570 (2500 L)

V-27450 (8000 L) (in BP)
V-27460 (8000 L) (in BP)
V-27470 (8000 L) (in BP)
V-27480 (8000 L) (in BP)
V-27490 (8000 L) (in BP)
V-27500 (8000 L) (in BP)

OK Cancel Help

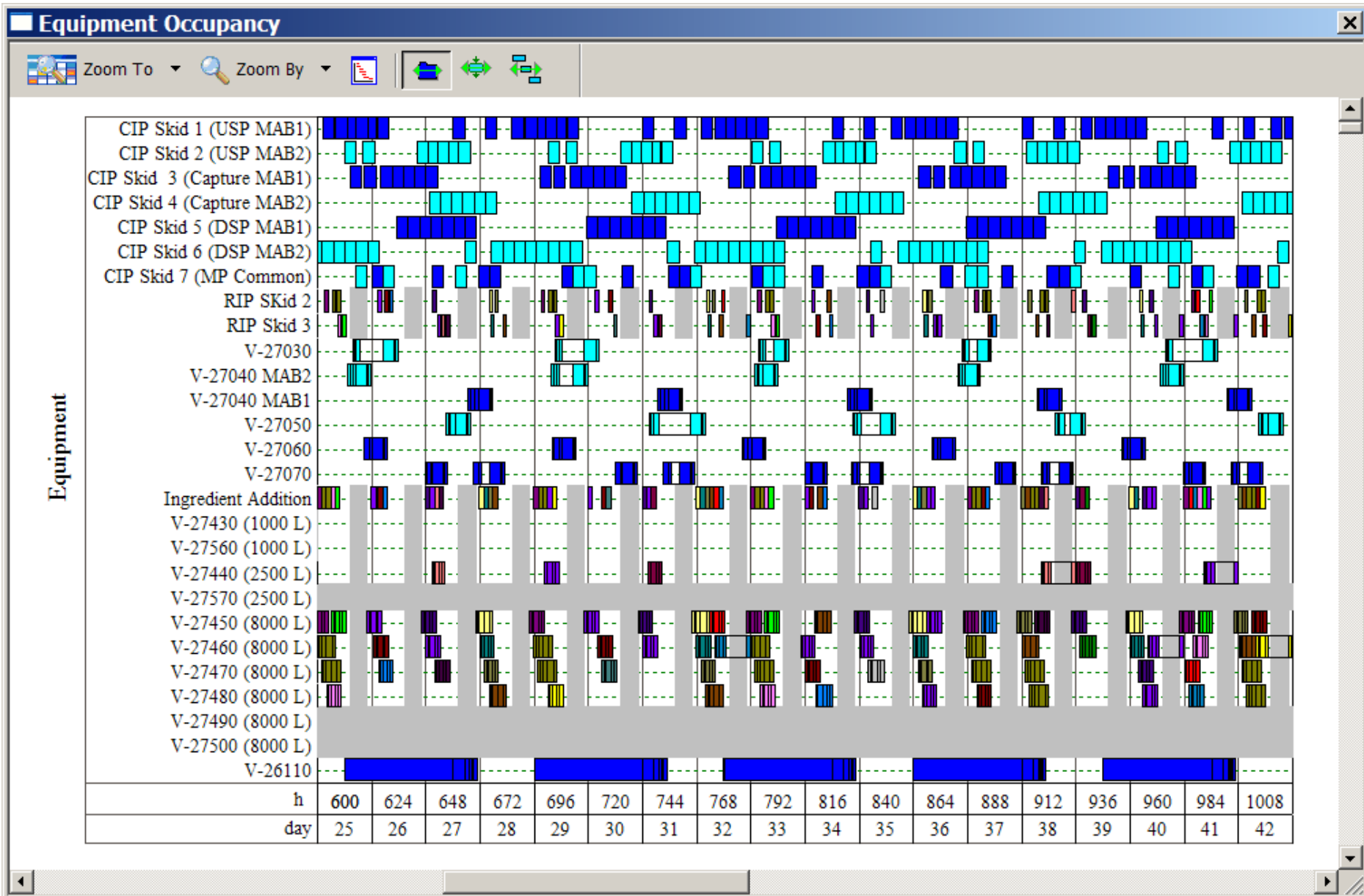
Equipment Pool

Flexible Start Time



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Operating with Fewer Buffer Prep Vessels



Sizing of Purified Water Systems

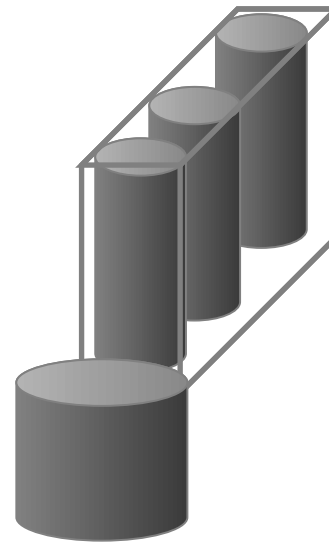
Sizing Shared Utilities (WFI)

Purified water is used for:

- Buffer preparation
- Cleaning
- Directly in the process

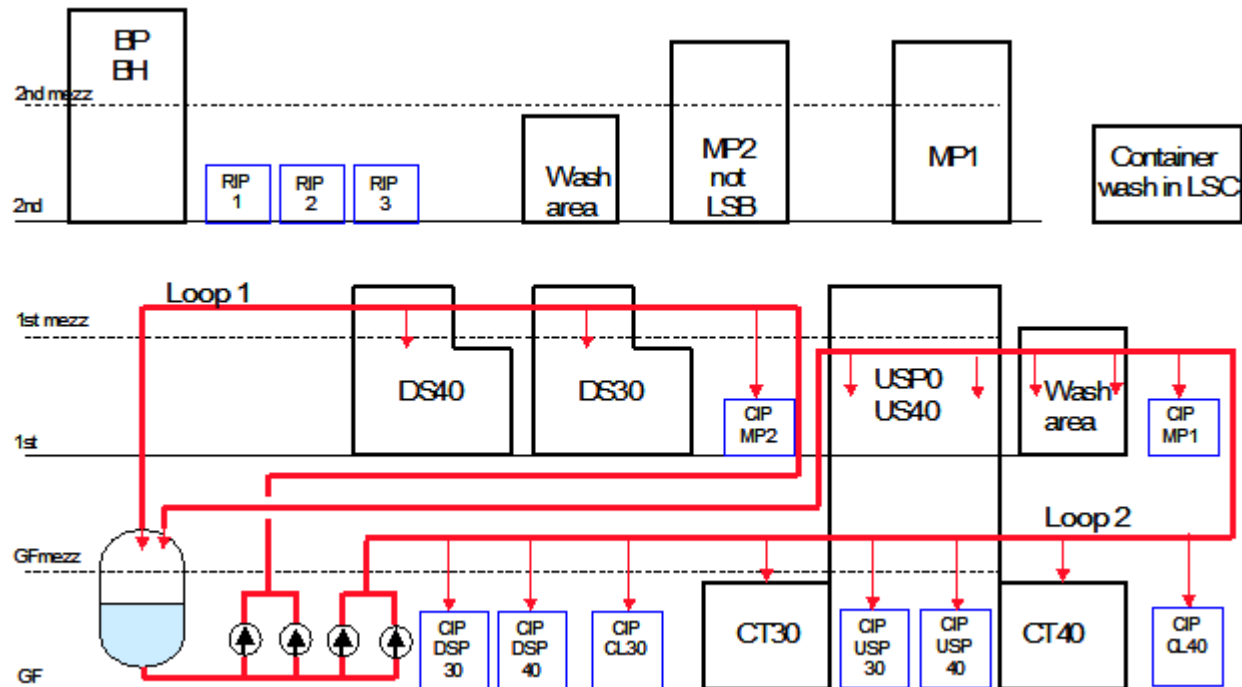
Systems Consist of

- Still
- Surge Tank
- Circulation system

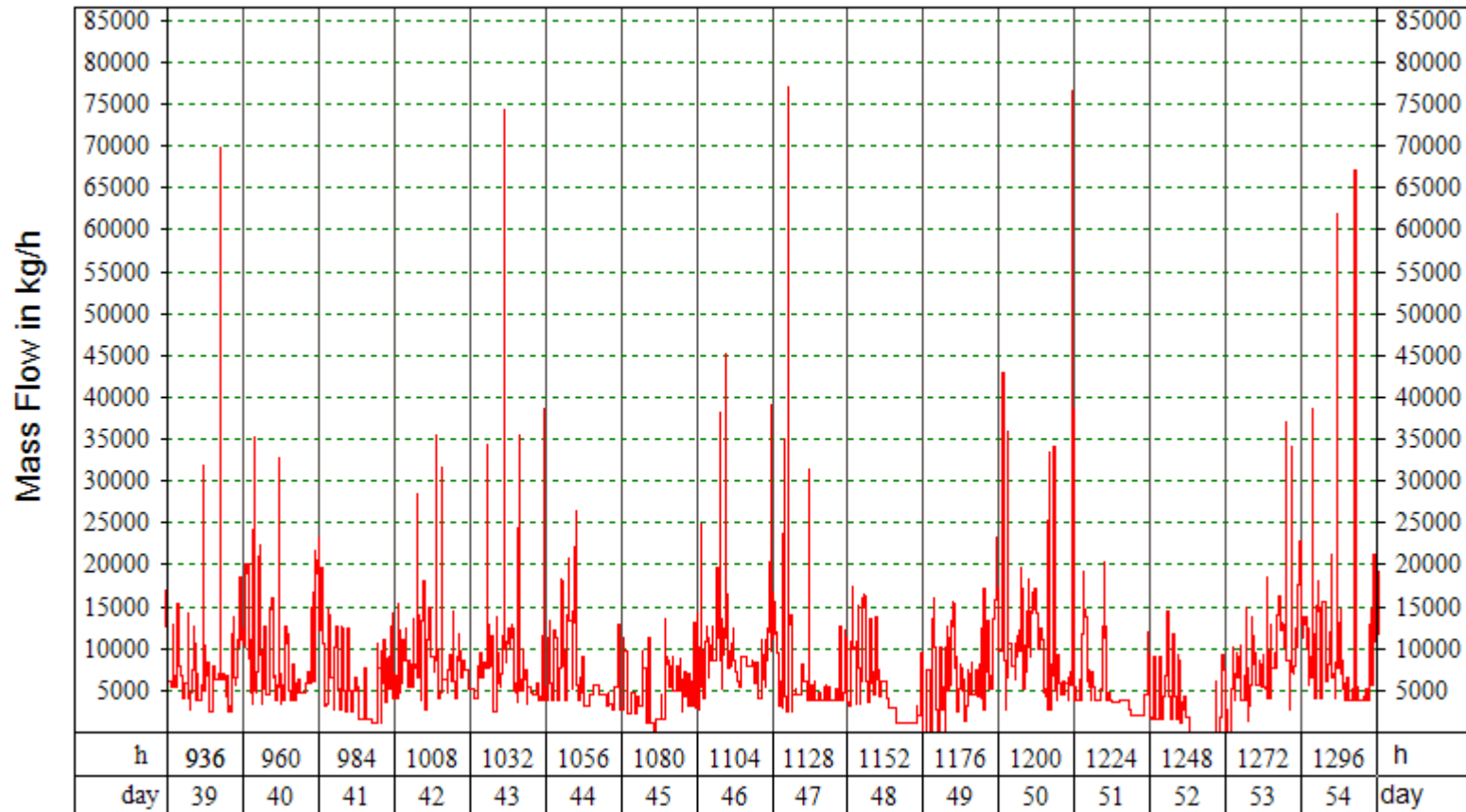


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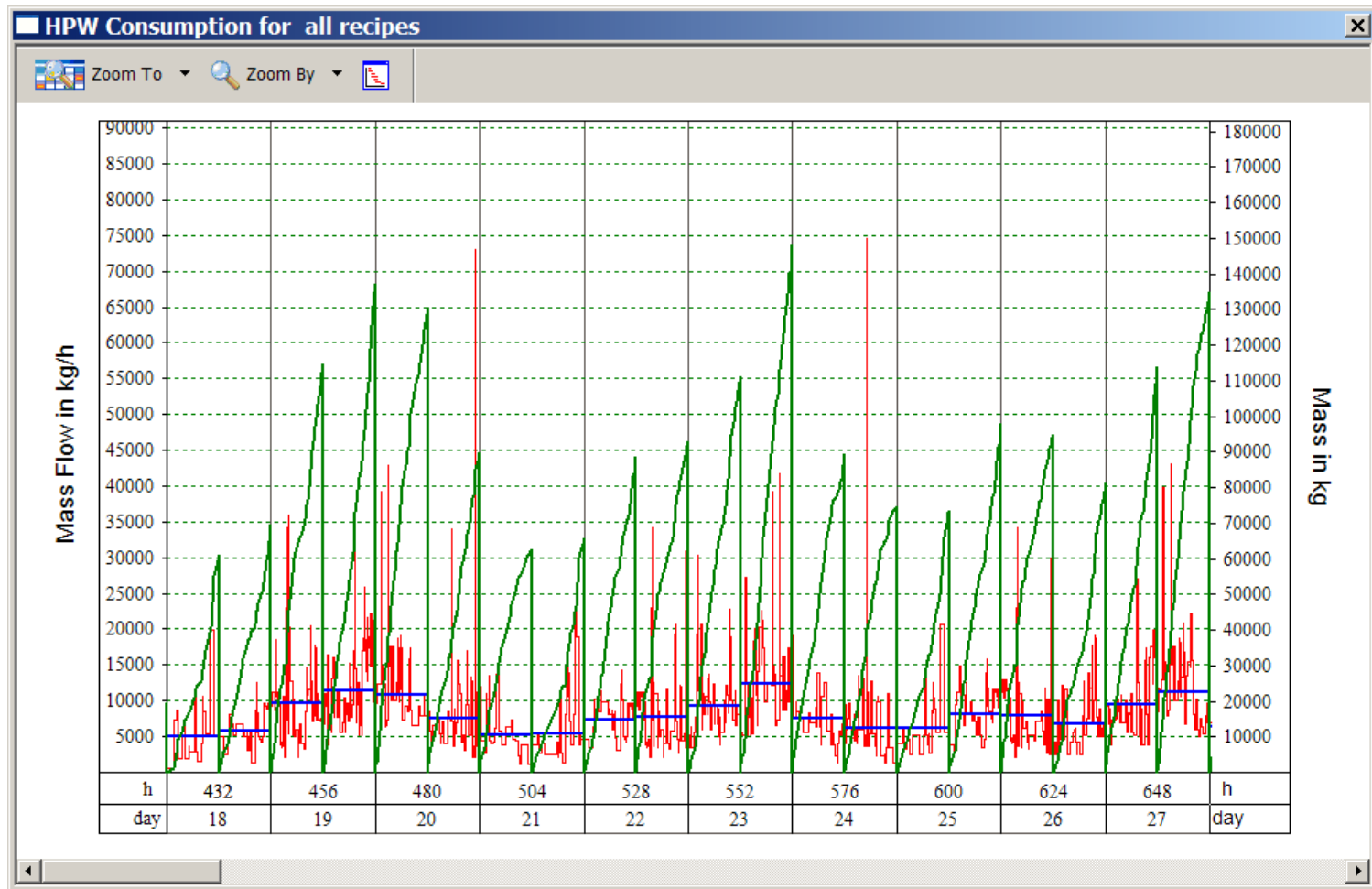
WFI Distribution System



WFI Demand as a Function of Time

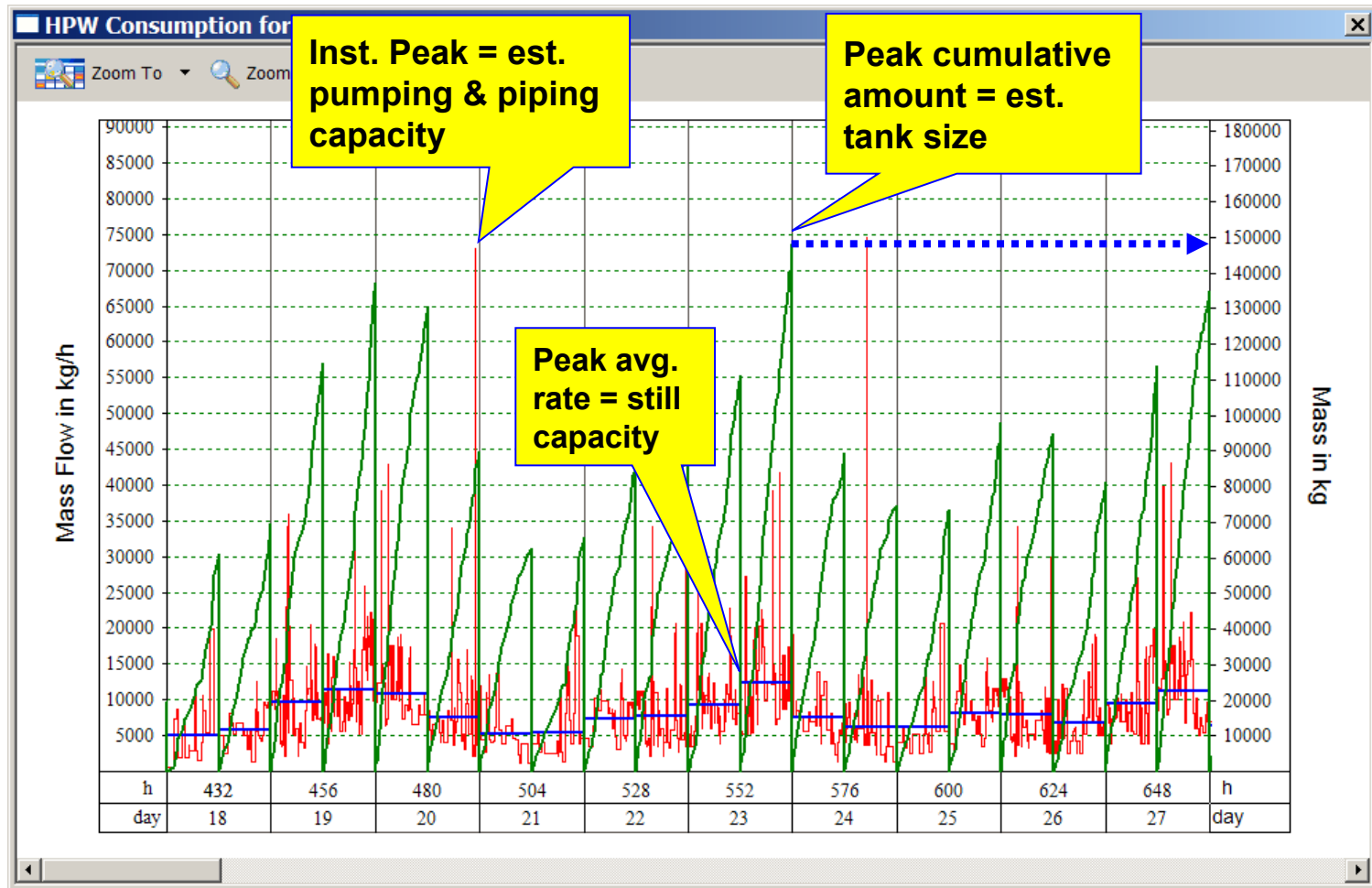


WFI Demand as a Function of Time

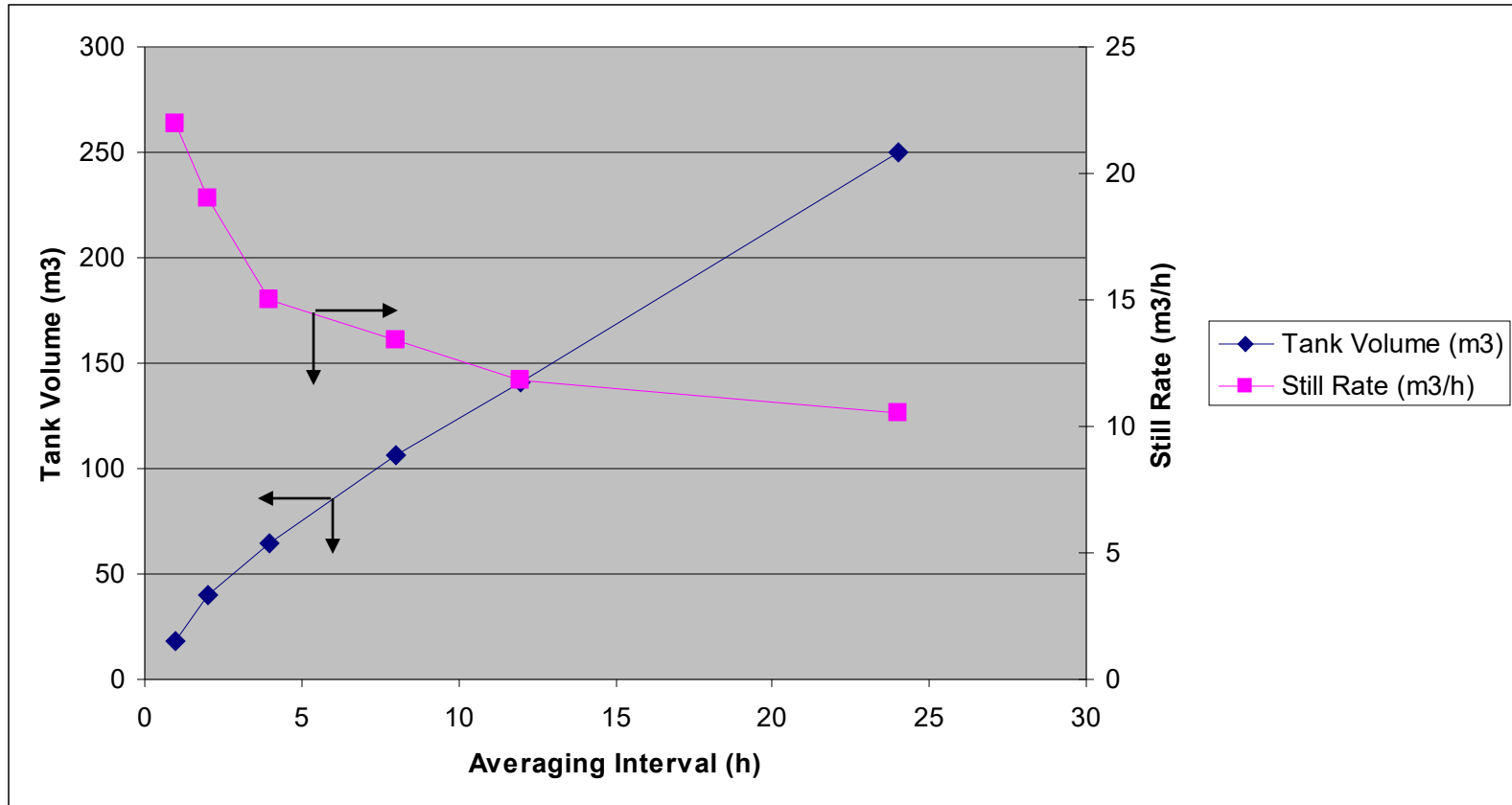


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WFI Demand as a Function of Time

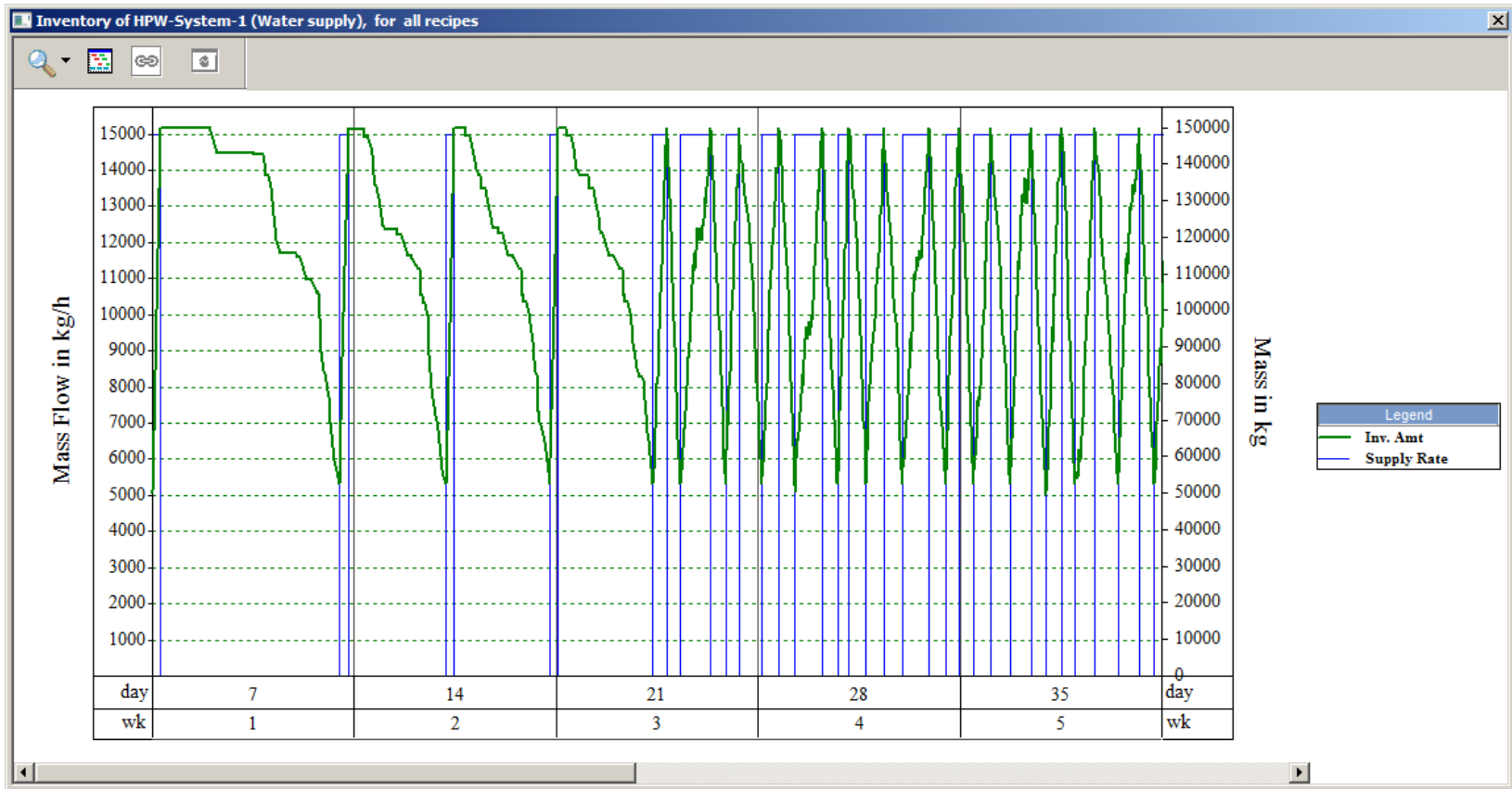


Tank Volume versus Still Rate



- Max Instantaneous Demand = 79 m3/h
- Long Term Average Rate = 7.5 m3/h

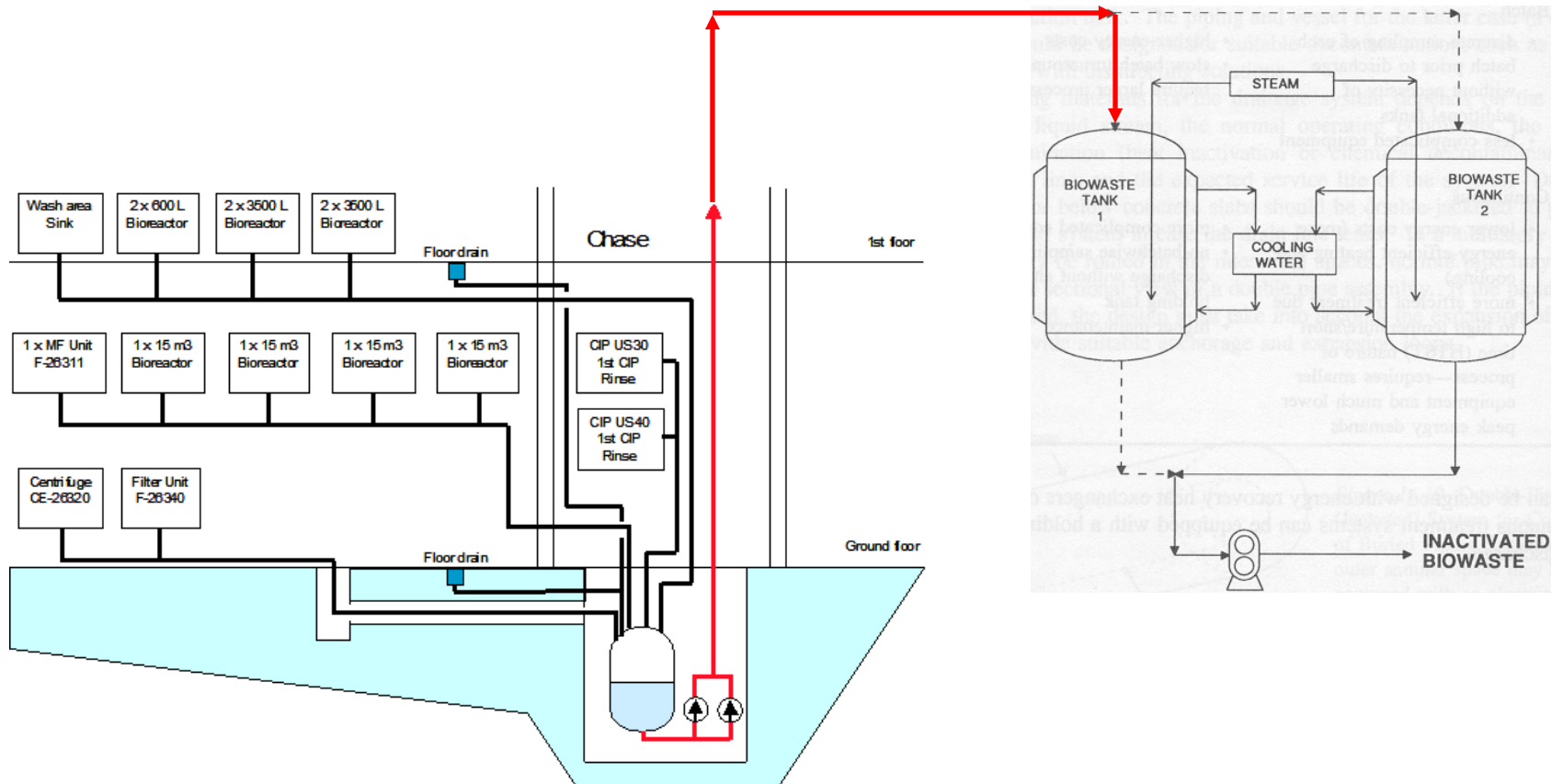
WFI Inventory



Tank Size = 150,000 L; Still Capacity = 15,000 L/h
Still On/Off Limits = 35 and 100%

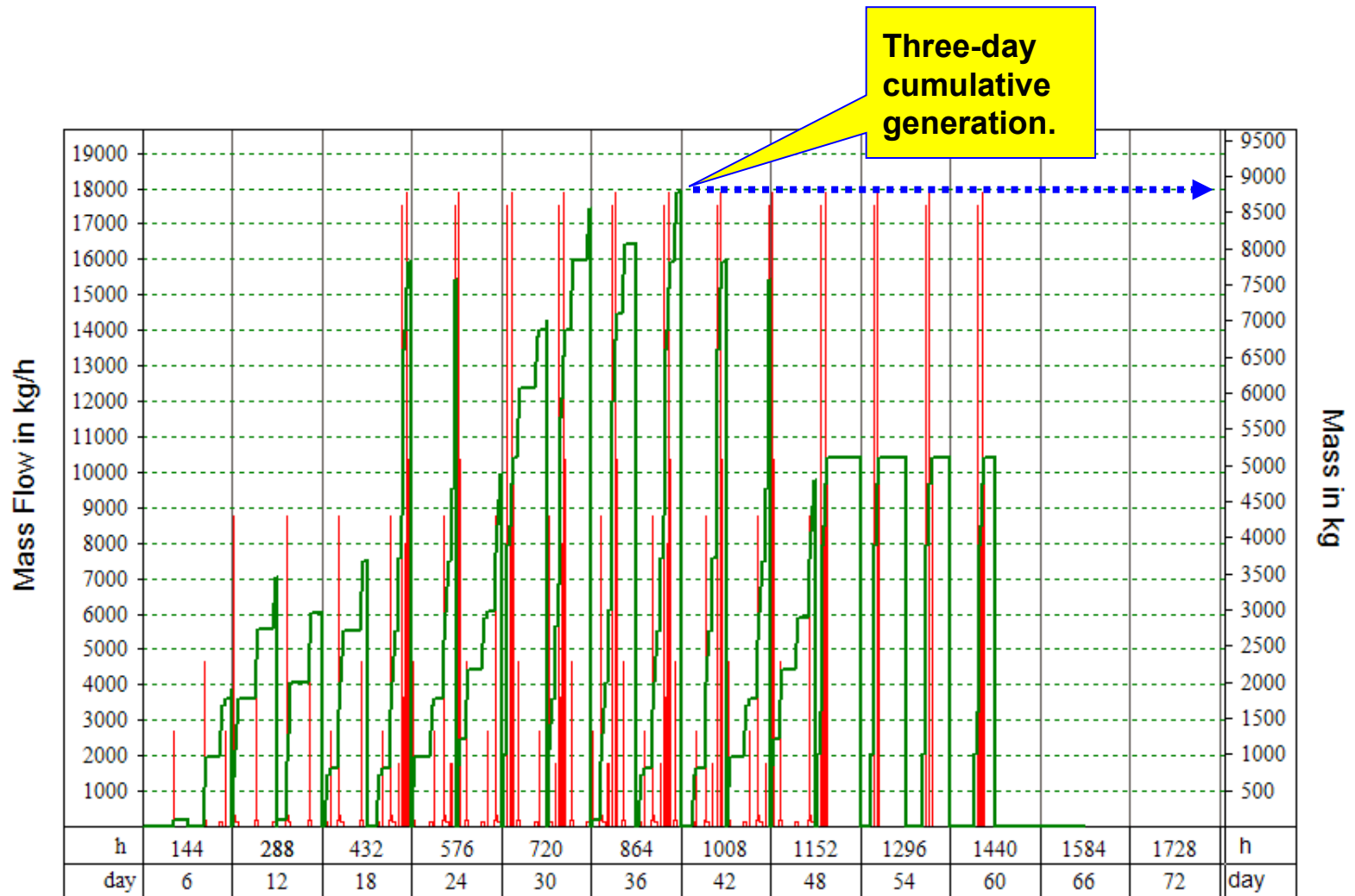
Sizing of Wastewater Systems

Bio-Waste Collection and Treatment



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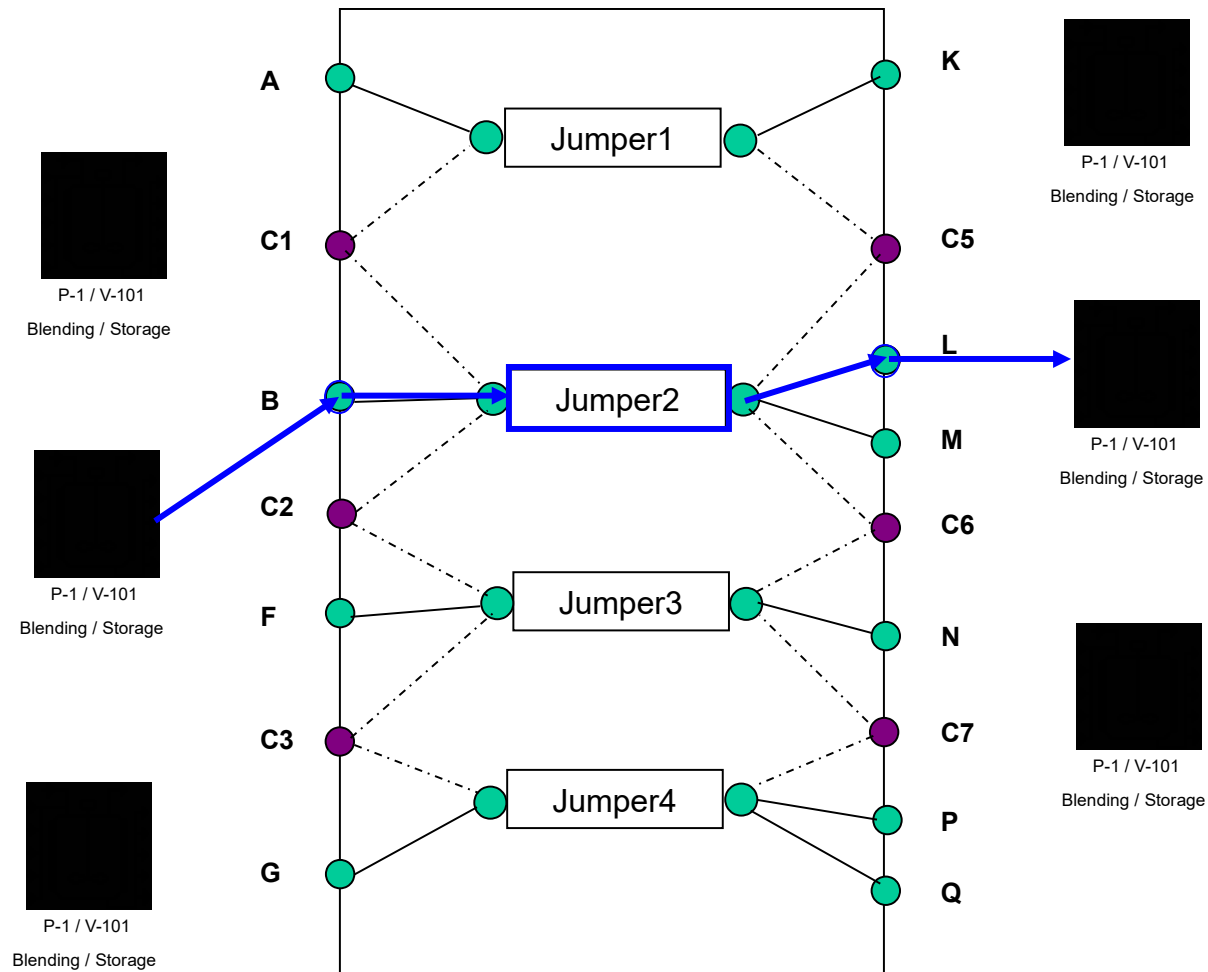
Generation of Bio-Waste



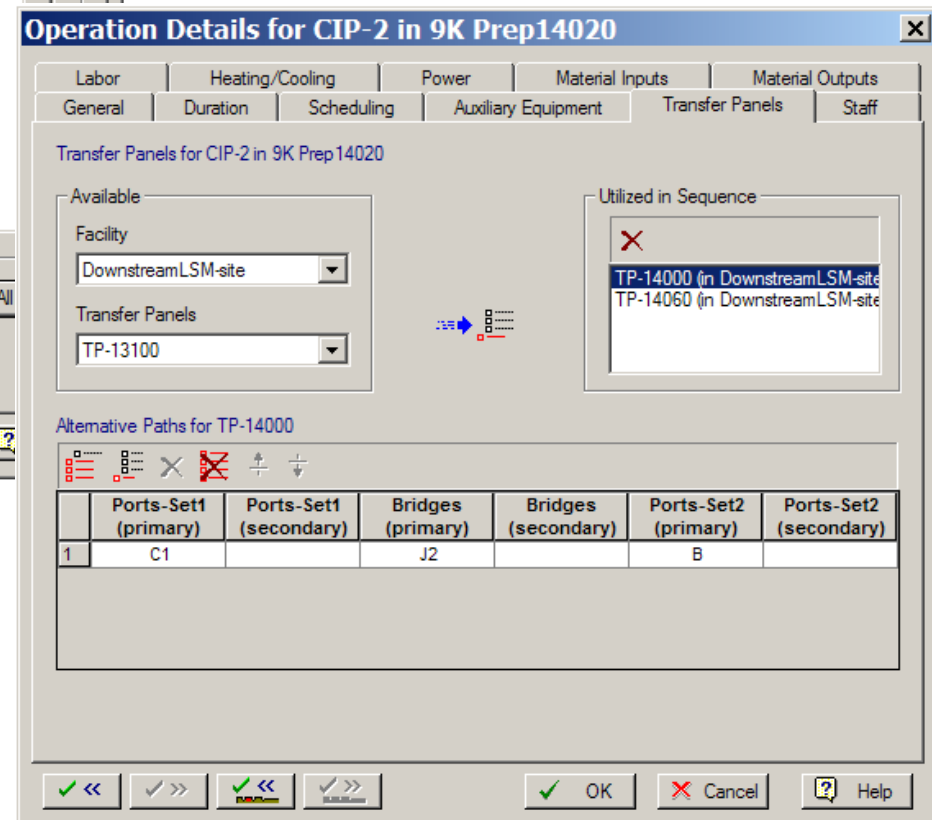
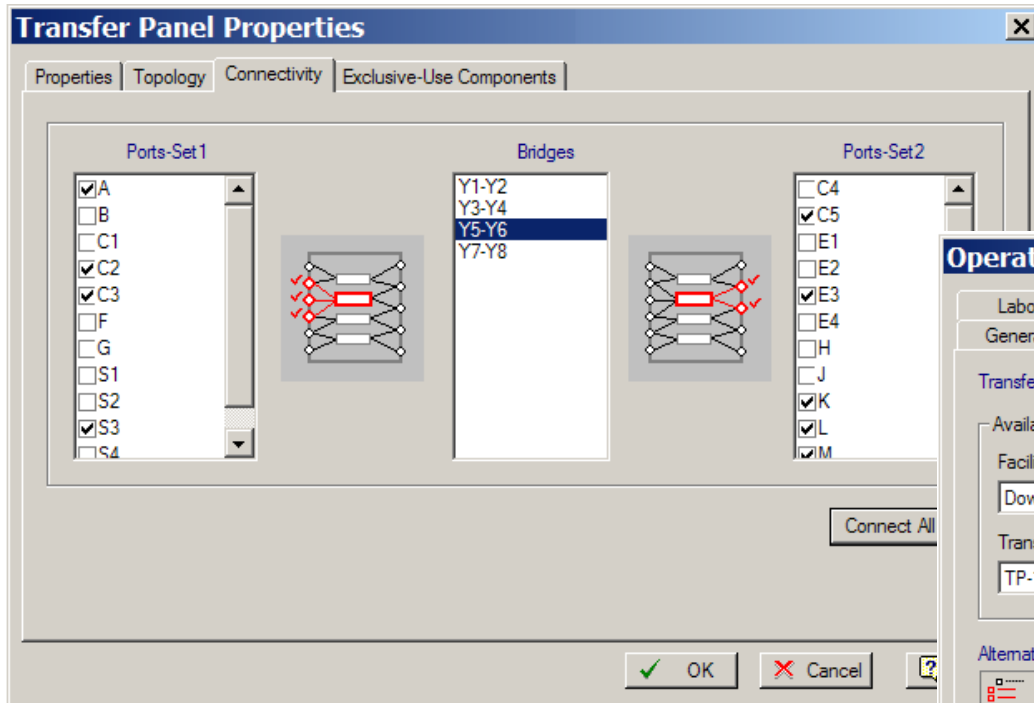
Intelligen, Inc.

Accounting for Transfer Panels

Transfer Panel Constraints

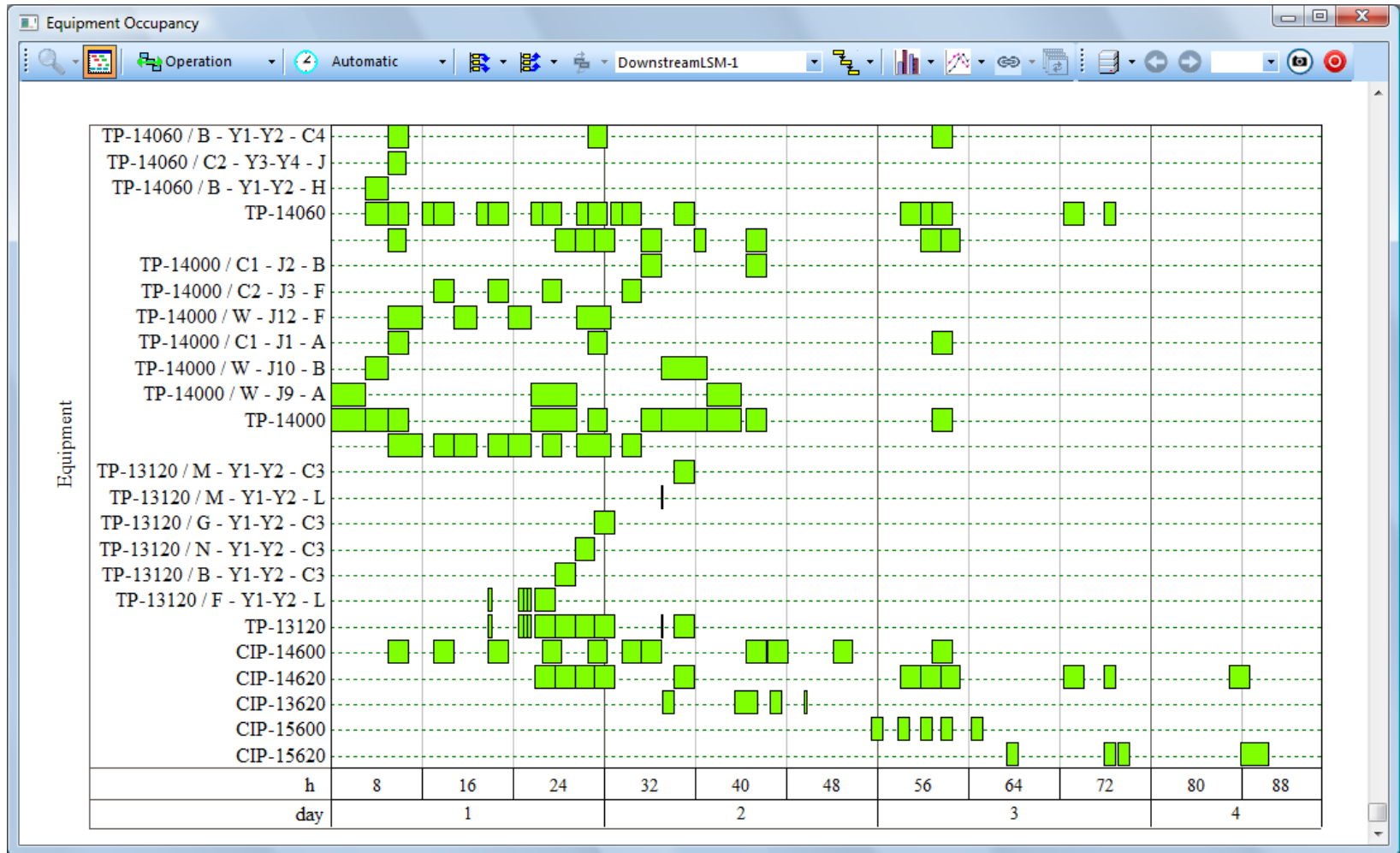


Detailed Representation of Transfer Panel



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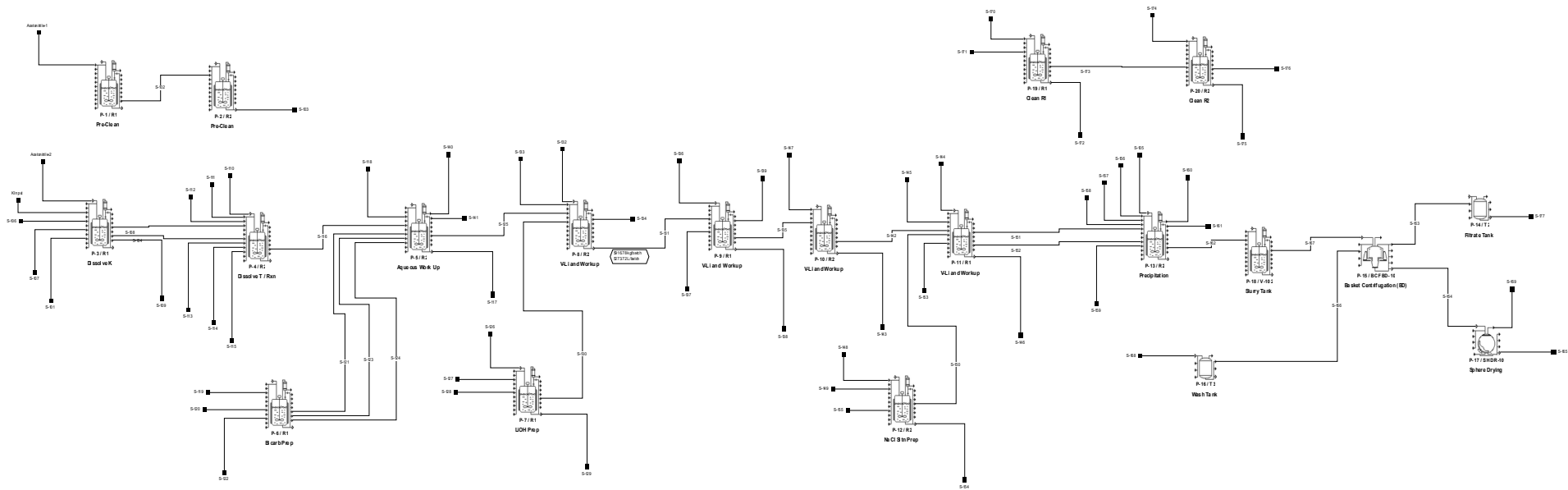
Use of Transfer Panels



SchedulePro Example

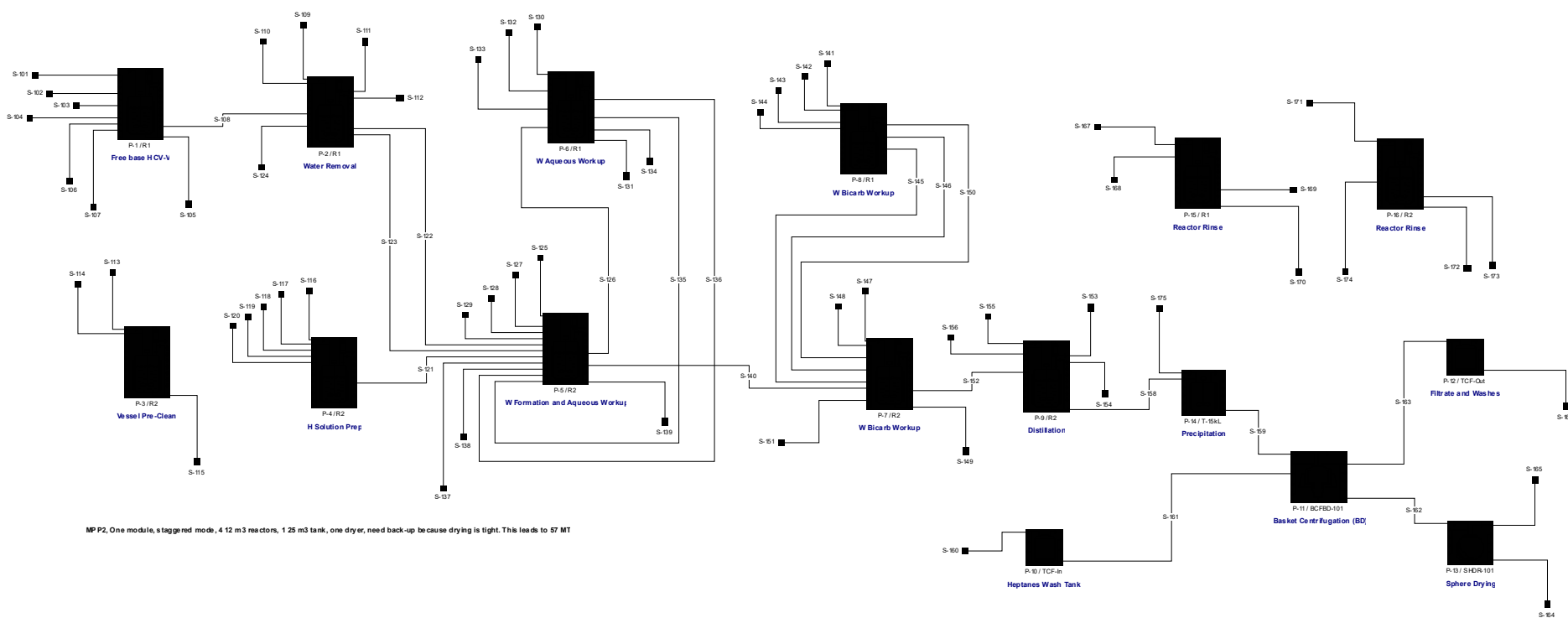
Capacity Analysis for an API Manufacturing Facility

Chemical Step 1



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Chemical Step 2

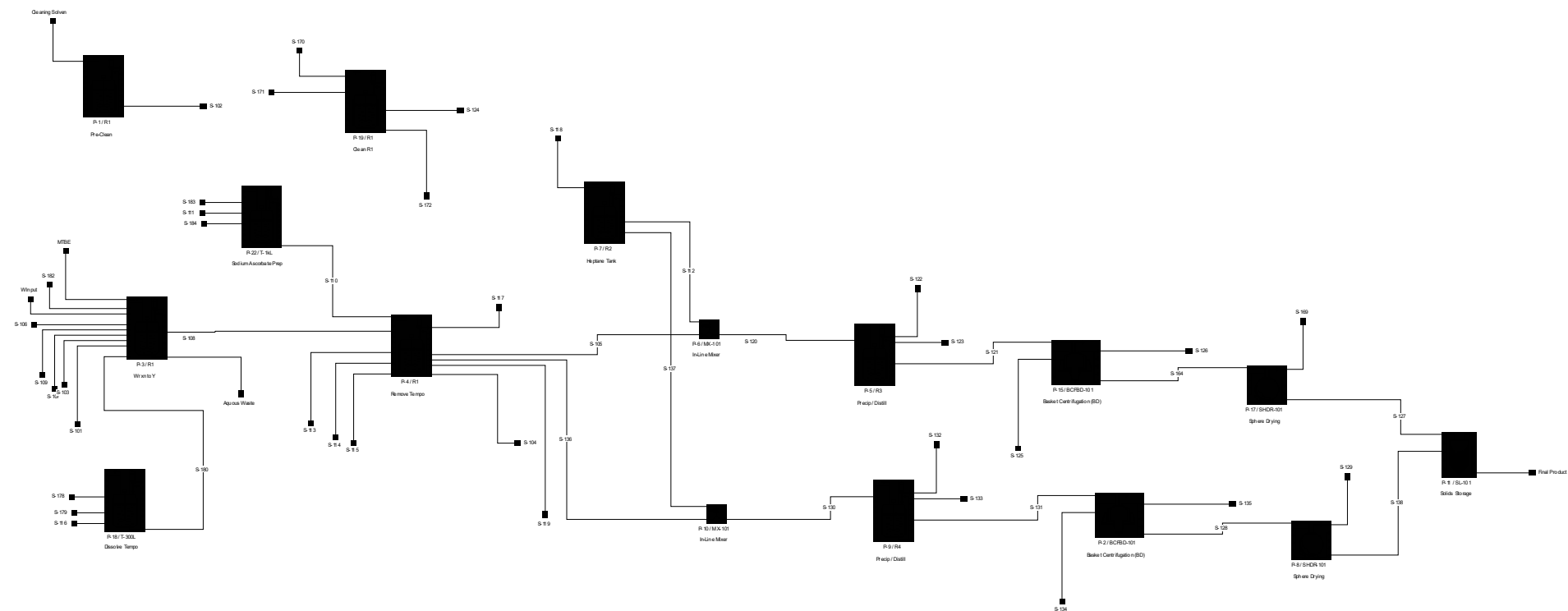


MP P2, One module, staggered mode, 4 12 m3 reactors, 1 25 m3 tank, one dryer, need back-up because drying is tight. This leads to 57 MT



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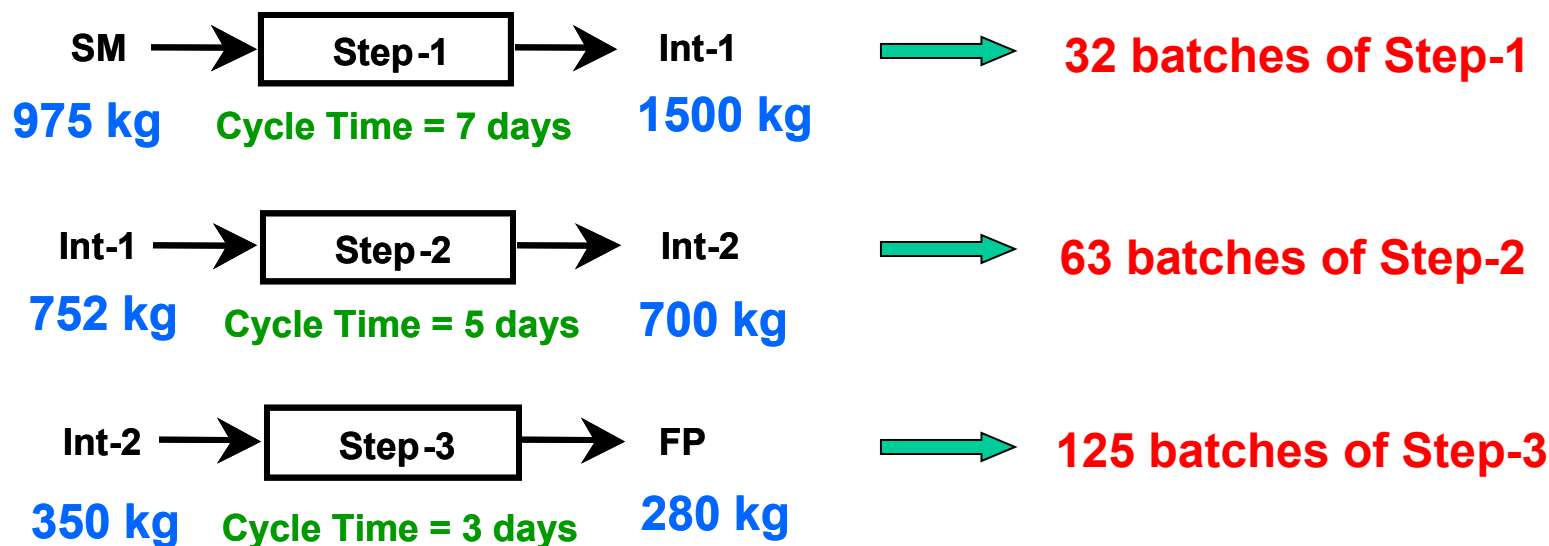
Chemical Step 3



Intelligen, Inc.

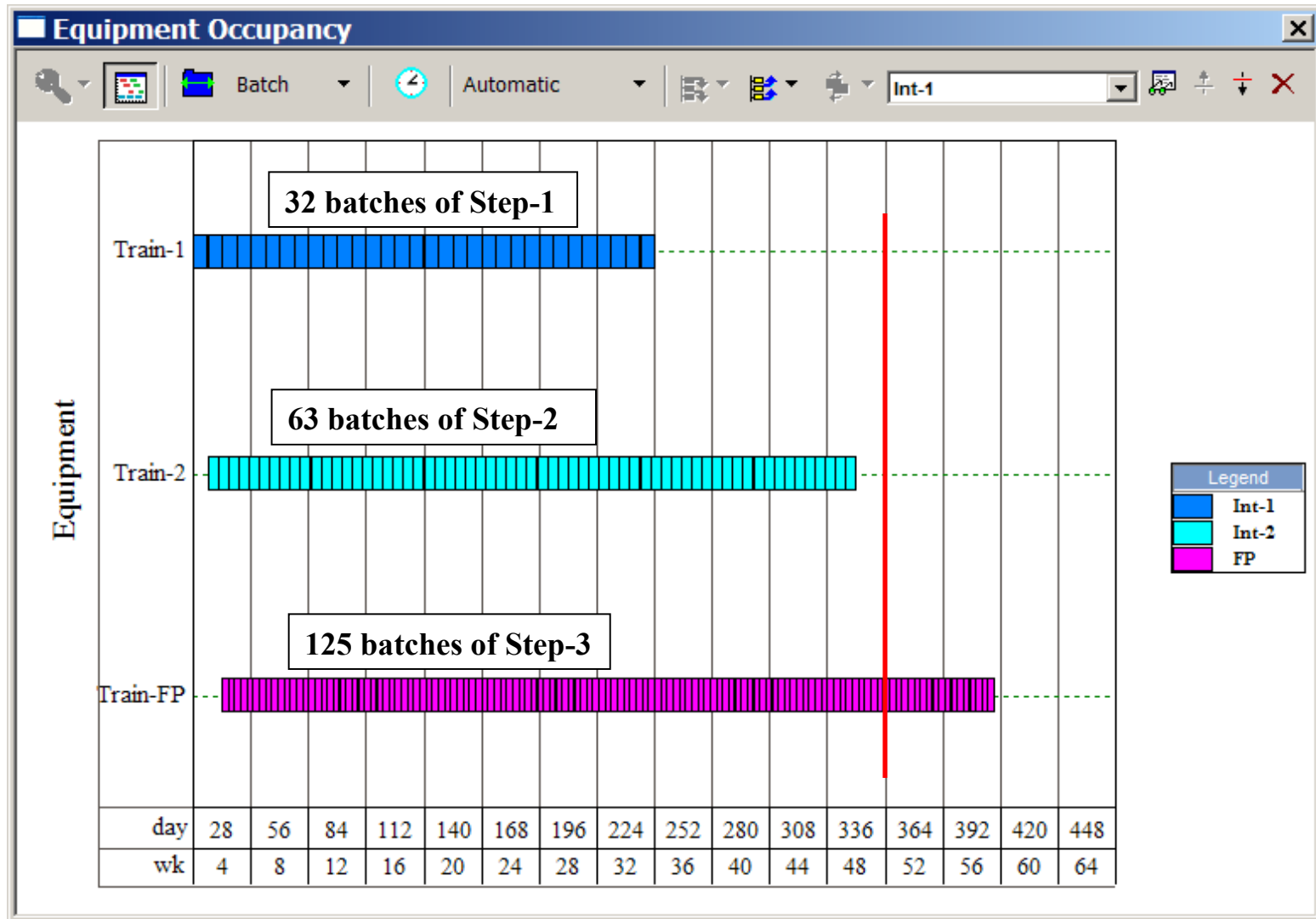
Balancing the Synthesis Route

Batches Required for 35,000 kg of FP



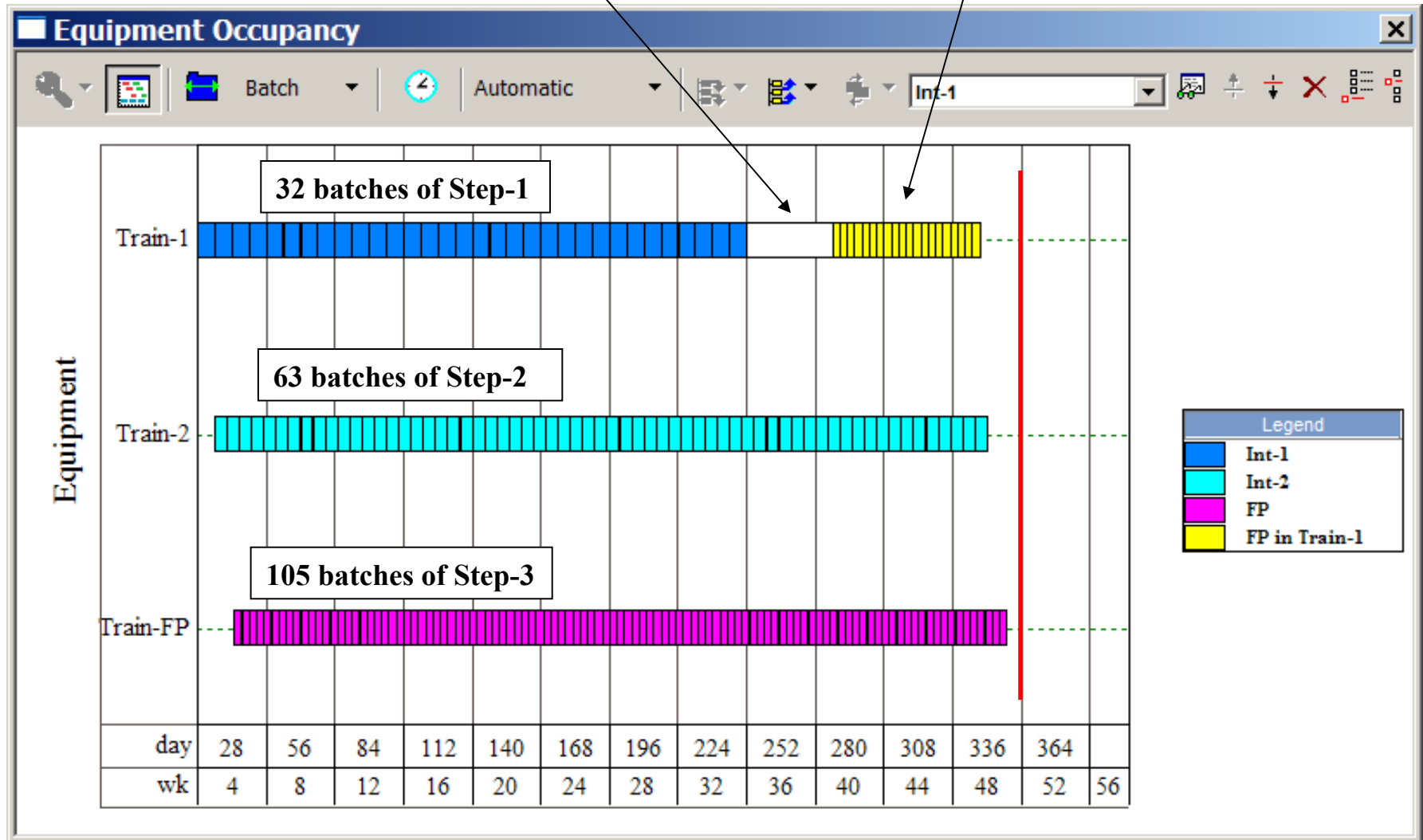
Max Annual Operation = 48 weeks

Annual Campaigns for the three Steps



5 weeks of
changeover time

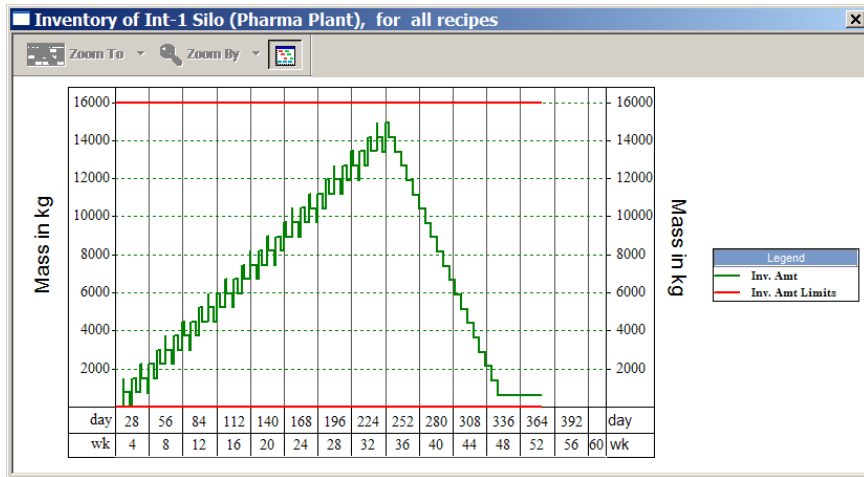
20 batches of Step-3 in Train-1



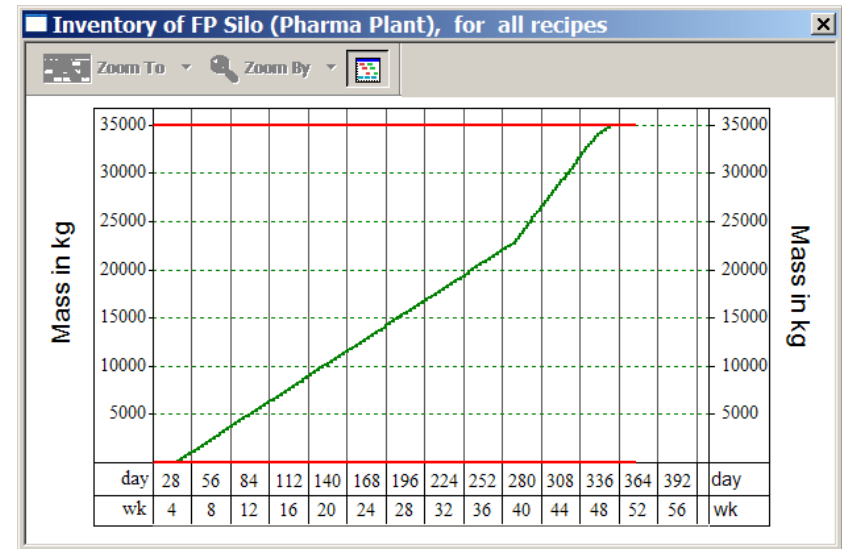
Intelligen, Inc.

Inventory of Intermediates and Final Product

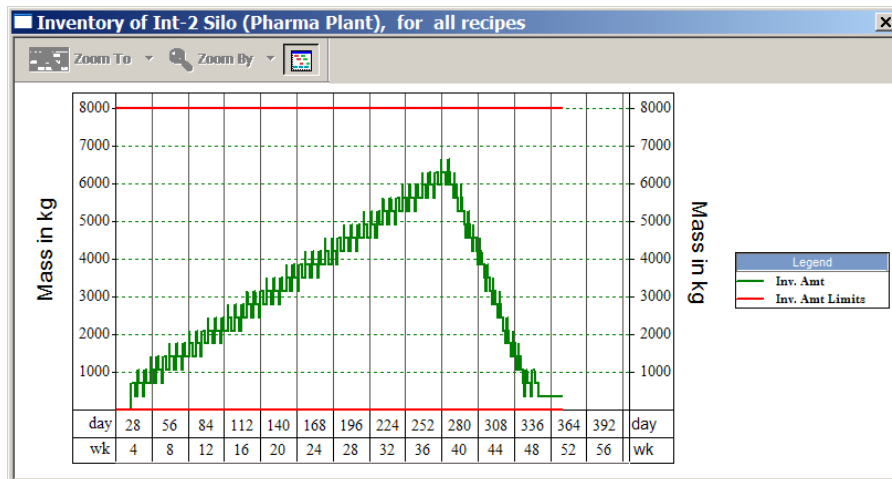
Int-1 inventory



FP inventory

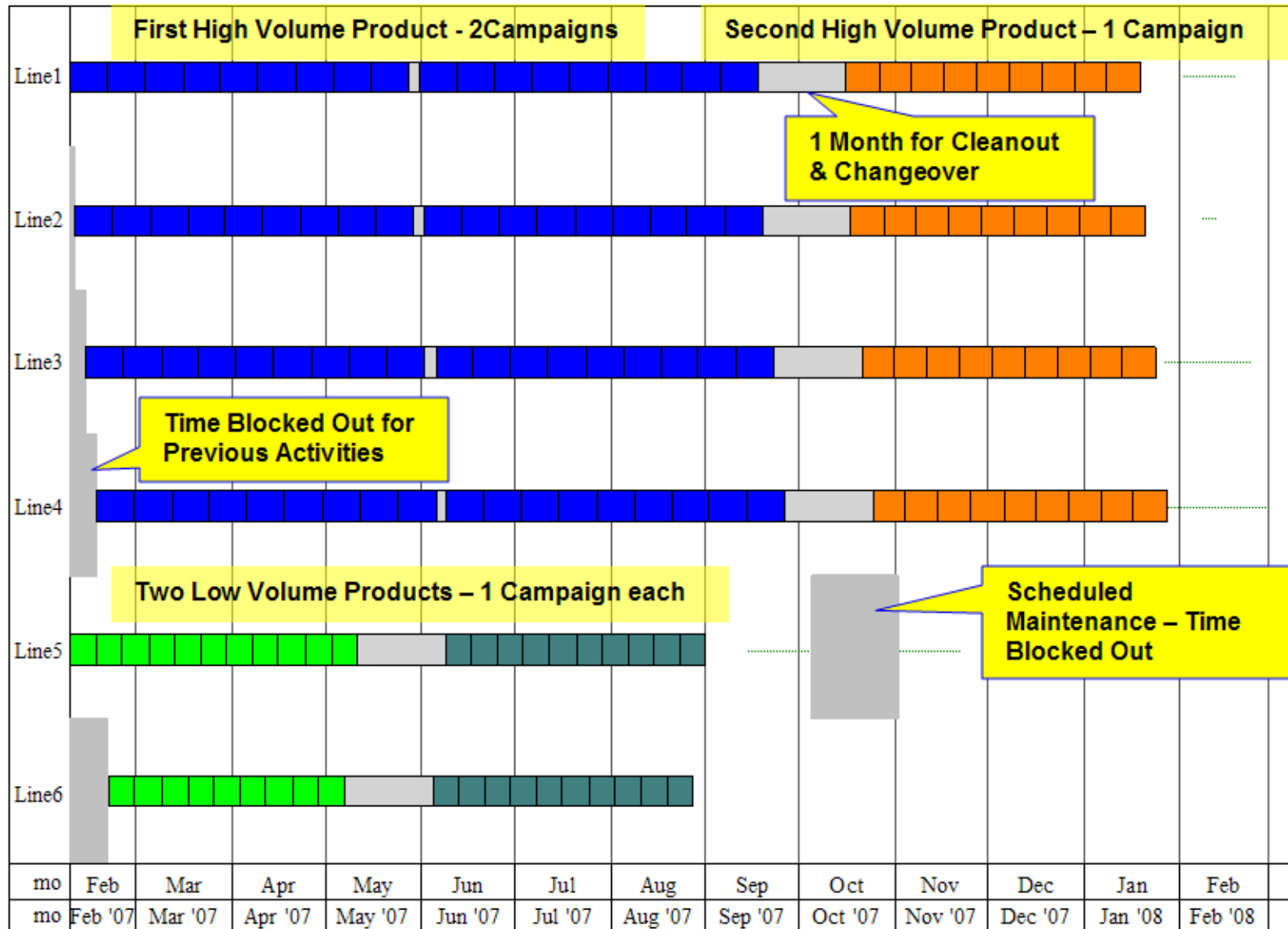


Int-2 inventory



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Long-Term Planning Using Simplified Recipe Representations



SuperPro Example

Cycle Time Reduction and Uncertainty Analysis

Overall Chemistry

Quinaldine + Hydroquinone $\Rightarrow$ Product

Pilot Plant Scale

55 kg/batch

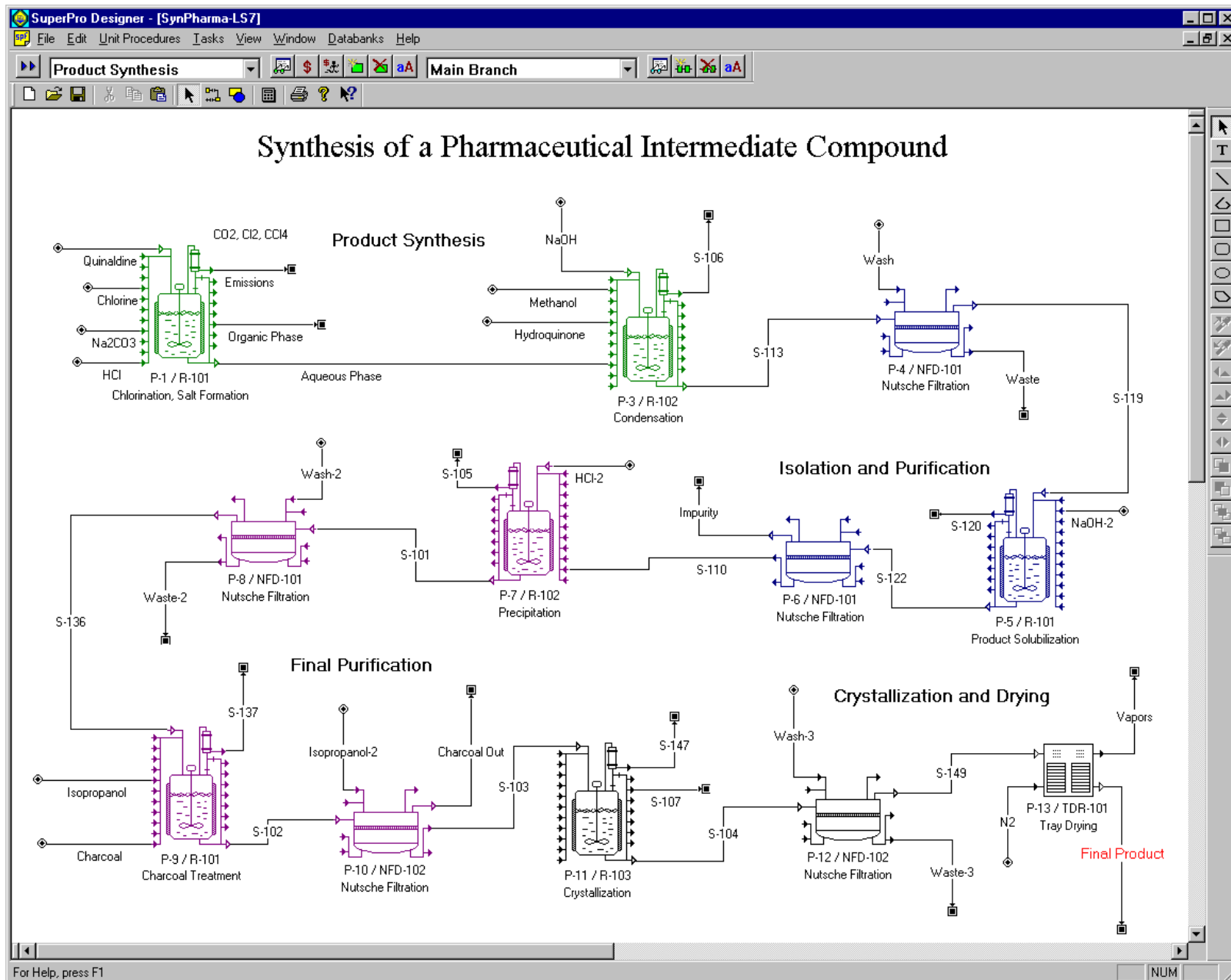
Project Objectives

Annual Throughput $\geq$ 36,000 kg

Manufacturing Cost $\leq$ \$250/kg



Intelligen, Inc.



Scenario 1

Equipment Available

Two 1,500 gal reactors (R-101 and R-102)

One 4 m² Nutsche filter

One 10 m² Tray Dryer (1 kg/m²-h drying capacity)

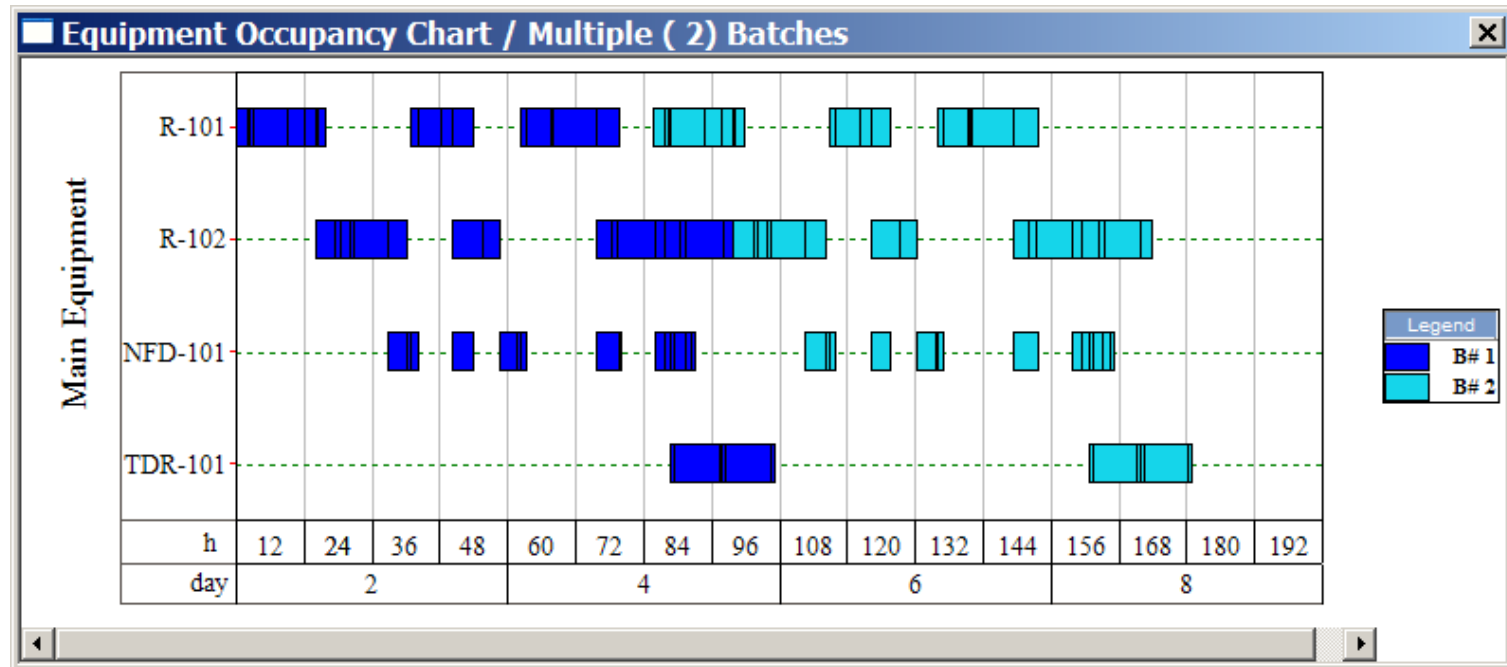
Annual Operating Time $\leq (330 \text{ days/yr})(3 \text{ shifts/day})(8 \text{ h/shift})$

Are they Adequate?



Intelligen, Inc.

Scenario 1 (continued)



Batch Size

246 kg

Number of Batches per Year

116

Annual Throughput

28,536 kg < 36,000 kg

Scheduling (Time) Bottleneck

R-102 (74 h cycle)



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Scenario 2

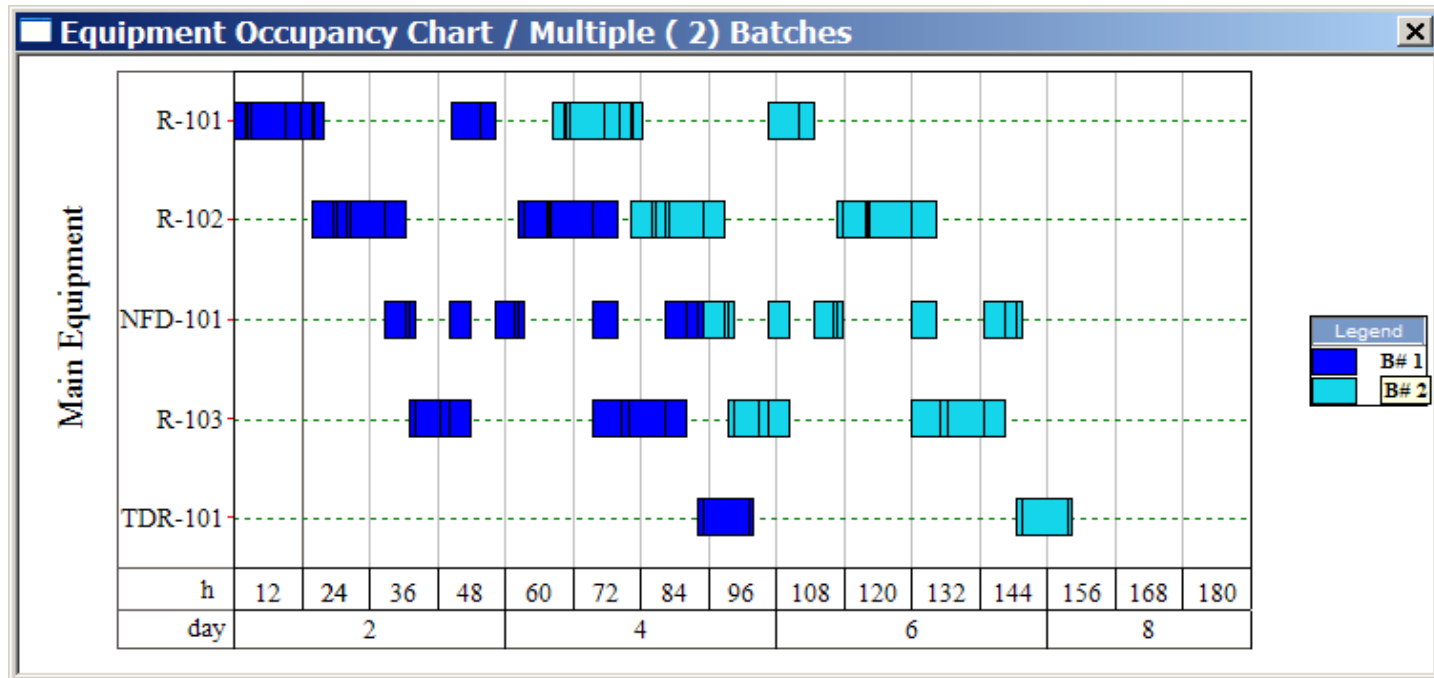
Equipment Available

Three 1,500 gal reactors (R-101, R-102, R-103)

One 4 m² Nutsche filter

One 10 m² Tray Dryer (1 kg/m²-h drying capacity)

Scenario 2 (continued)



Batch Size

246 kg

Number of Batches per Year

139 (116 => 139)

Annual Throughput

34,190 kg < 36,000 kg

Scheduling (Time) Bottleneck

NFD-101 (56.4 h cycle)



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Scenario 3

Equipment Available

Three 1,500 gal reactors (R-101, R-102, R-103)

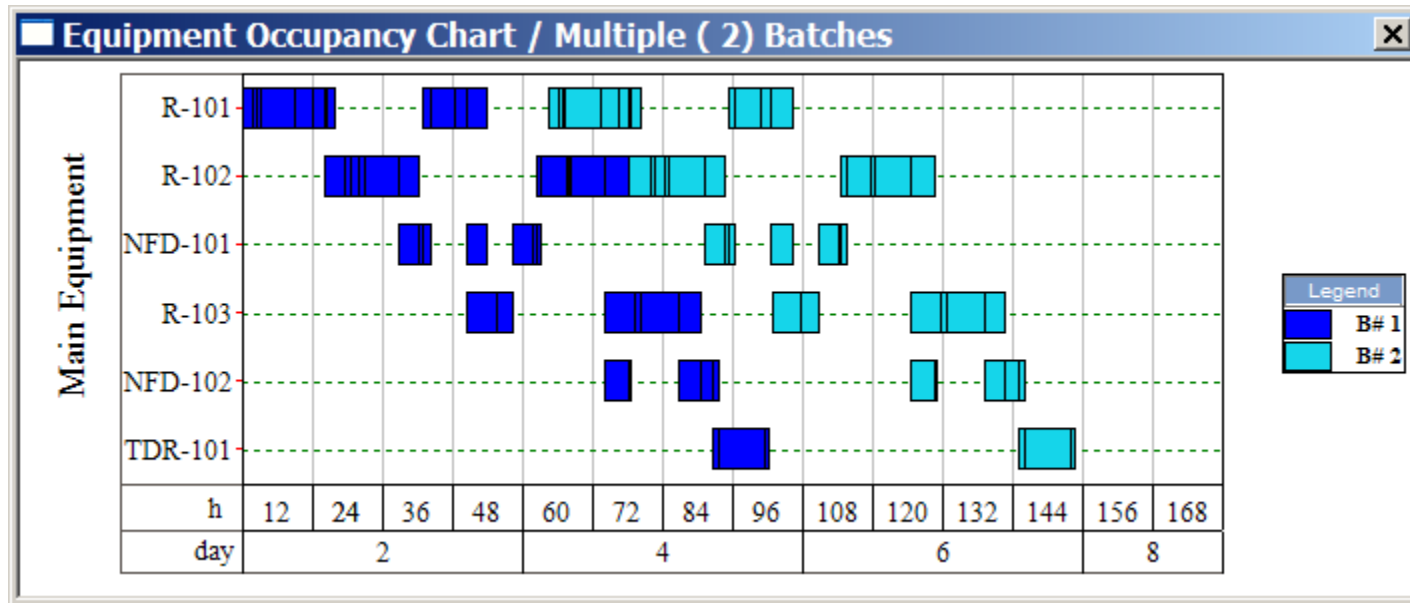
Two 4 m² Nutsche filters

One 10 m² Tray Dryer (1 kg/m²-h drying capacity)



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Scenario 3 (continued)



Batch Size

246 kg

Number of Batches per Year

150 (116 => 139=>150)

Annual Throughput

36,900 kg > 36,000 kg

Scheduling (Time) Bottleneck

R-102 (52.4 h cycle)



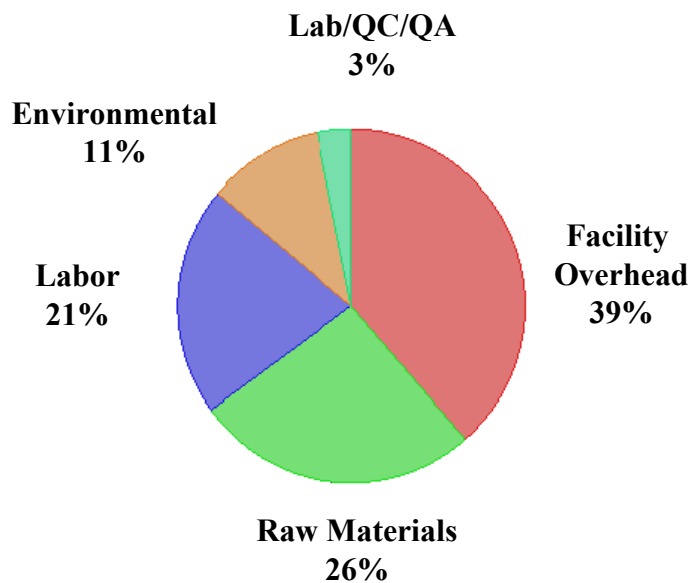
Intelligen, Inc.

Cost Analysis Results – Base Case

Unit Production Cost: \$237/kg < \$250/kg

Annual Production: 36,900 kg > 36,000

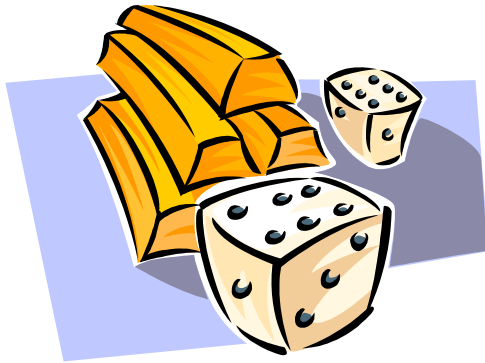
Cost Distribution



Raw Material Cost Distribution	%
Chlorine	2.72
Na ₂ CO ₃	6.30
Water	2.73
HCl (20% w/w)	0.49
NaOH (50% w/w)	0.28
Methanol	1.22
Hydroquinone	6.32
Carb. TetraCh	3.67
Quinaldine	43.85
Sodium Hydroxide	1.37
Isopropanol	20.13
charcoal	0.32
HCl (37% w/w)	0.34
Nitrogen	10.24
TOTAL	100.00



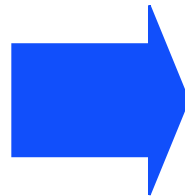
Intelligen, Inc.



Uncertainty in the Pharmaceutical Industry

Uncertainty and Variability in:

Operational Parameters
Resource Availability
Raw Materials
Market Demand
Regulatory Approvals



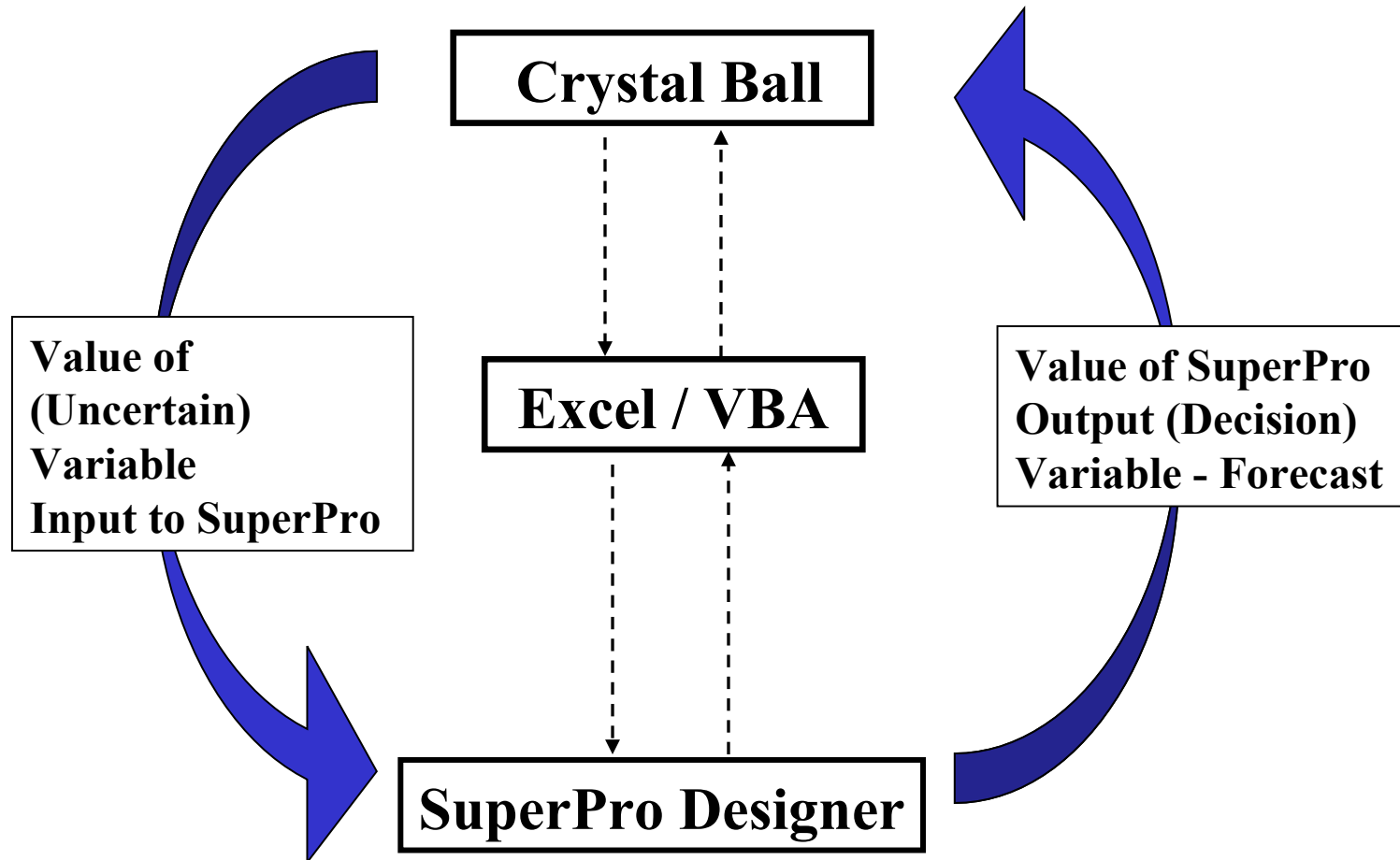
Affecting Process Evaluation Indices

Plant Throughput
Product Quality
Manufacturing Cost
Profitability
Environmental Impact



Intelligen, Inc.

Monte Carlo Simulation

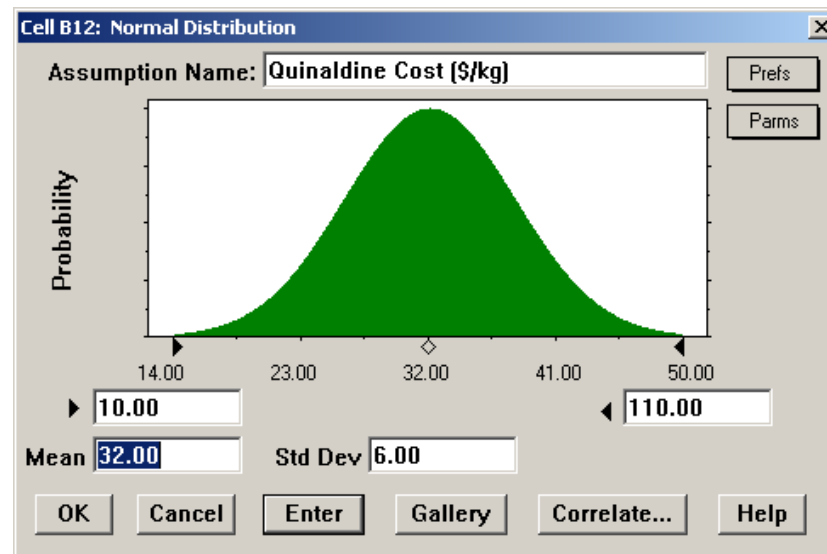


Selection of Uncertain Variables

- 1) Purchasing Price of the Key Raw Material (Quinaldine).**
- 2) Operating Parameters that Have an Impact on the Time Bottleneck.**

Uncertain Variables: Raw Material Cost

<i>Variable</i>	<i>Base Case</i>	<i>Distribution</i>	<i>Variation</i>
Quinaldine Cost (\$)	32 Normal	S.D. = 6	

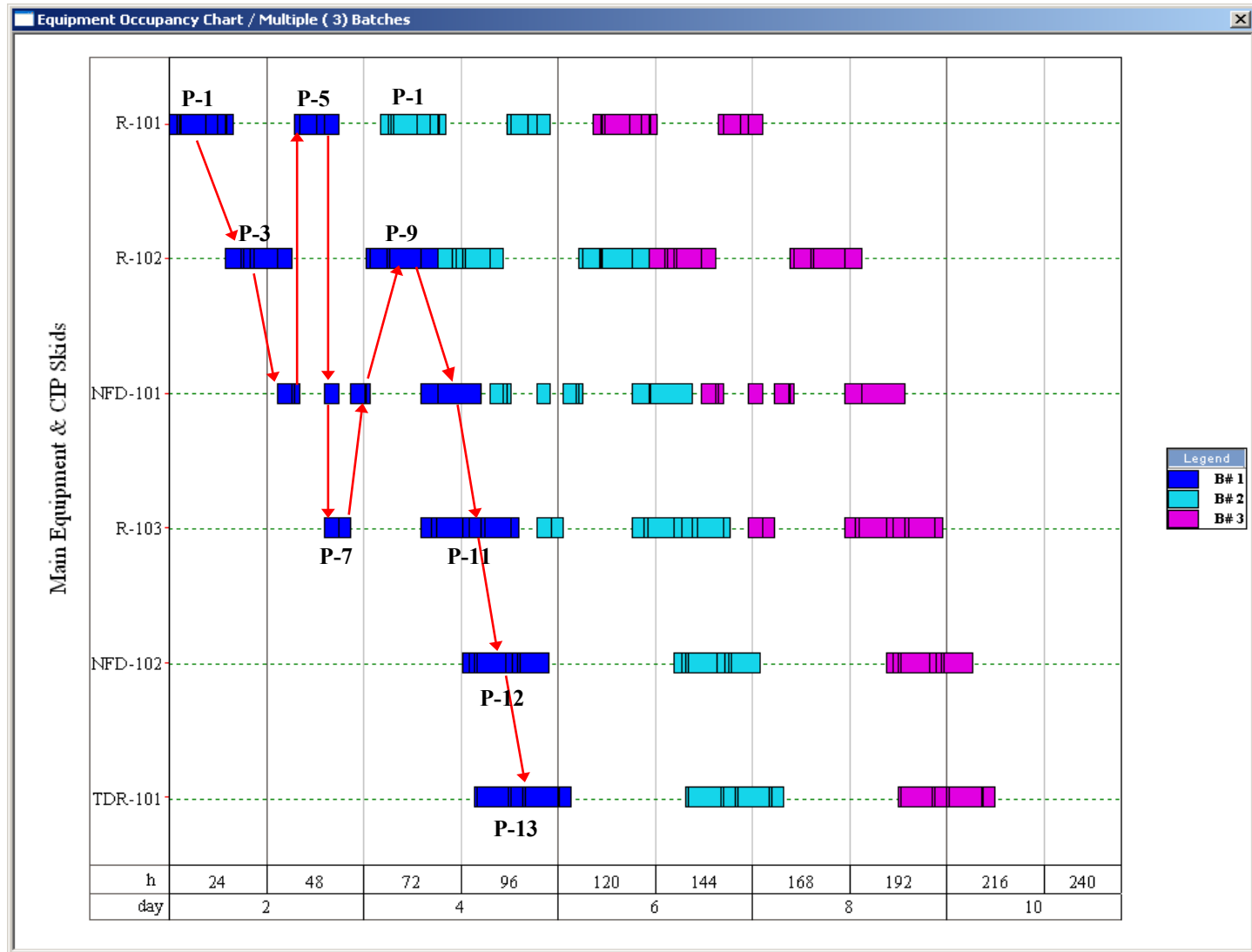


❖ *Quinaldine is the most expensive raw material*



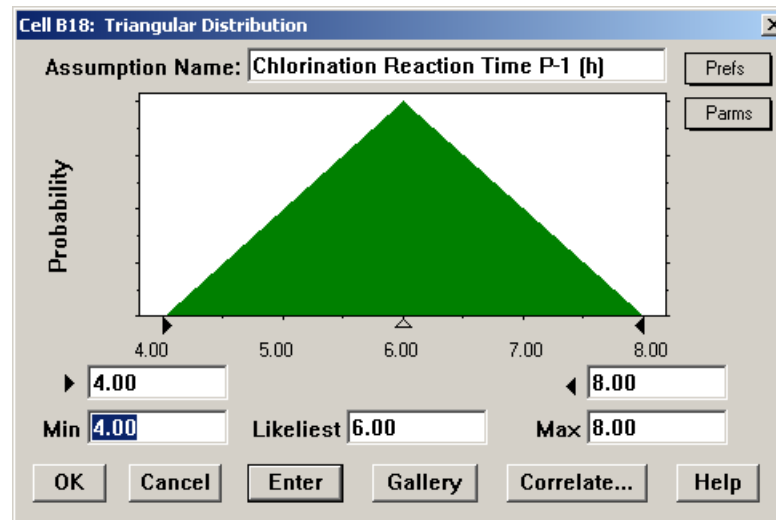
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Equipment Occupancy and Material Flow



Uncertain Variables: Reaction Times

<i>Variable</i>	<i>Base Case</i>	<i>Distribution</i>	<i>Variation</i>
Chlorination Time in P-1 (h)	6	Triangular	4-8
Condensation Time in P-3 (h)	6	Triangular	4-8

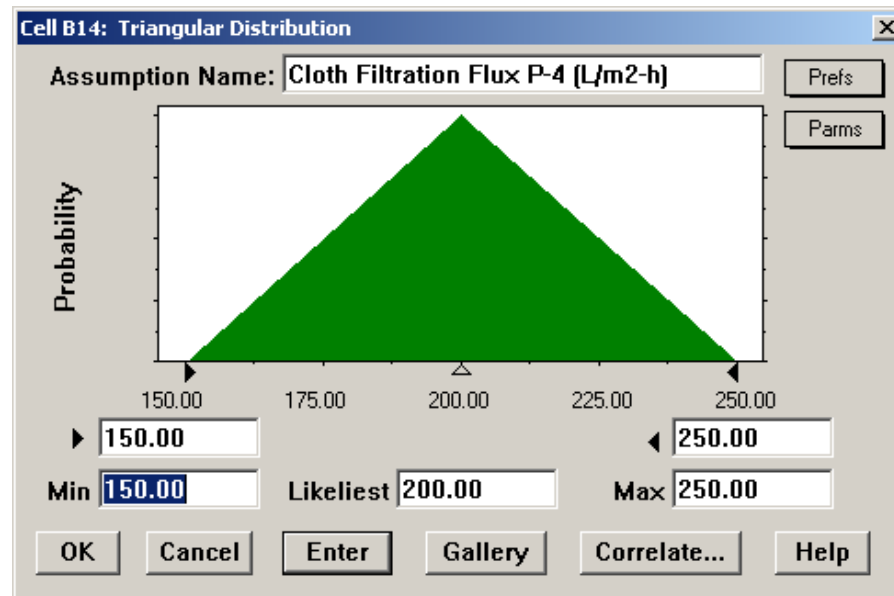


❖ *Variation in Reaction durations can affect the process cycle time and consequently the annual throughput and unit product cost.*



Uncertain Variables: Filtration Fluxes

<i>Variable</i>	<i>Base Case</i>	<i>Distribution</i>	<i>Variation</i>
Filtration Fluxes in NFD101			
In P-4, P-6, P-8, P-10	200 (L/m ² hr)	Triangular	150-250

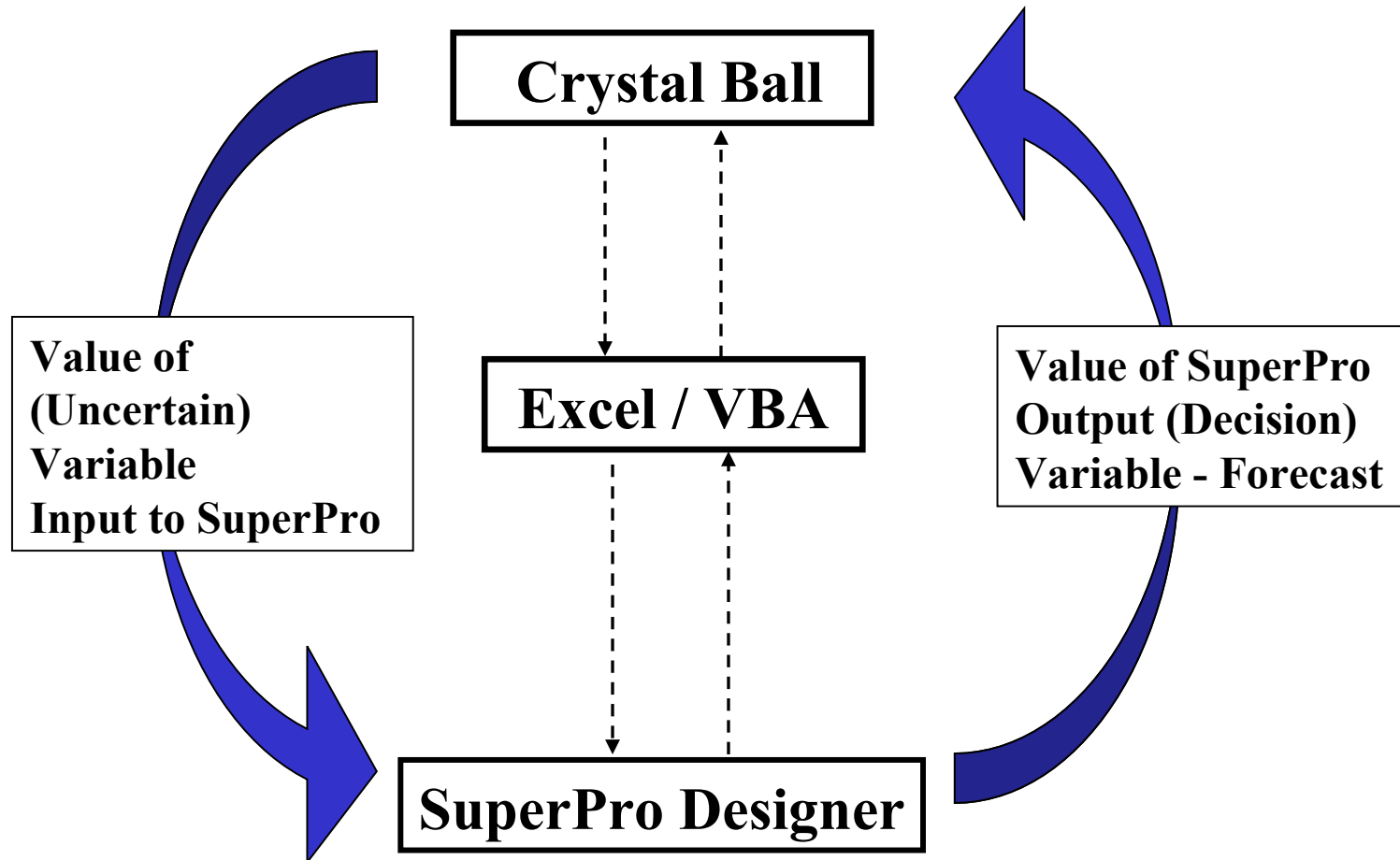


❖ *Variability in filtration fluxes can affect the cycle time and annual throughput of the process.*

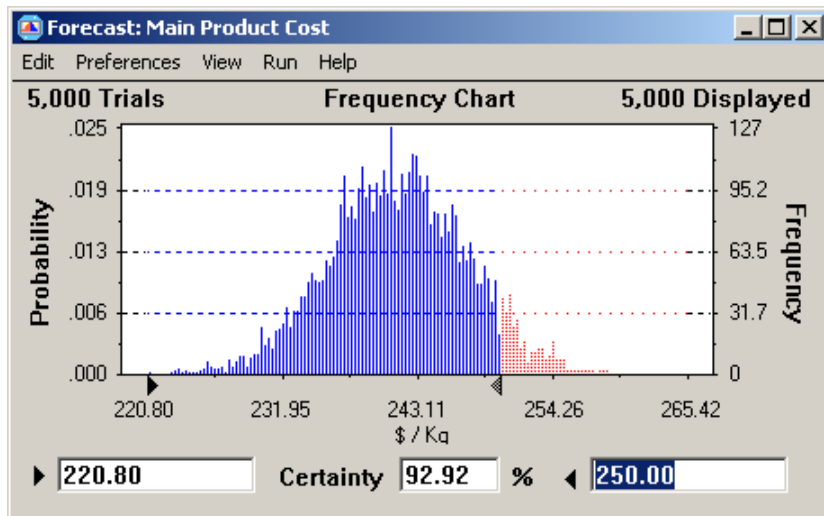


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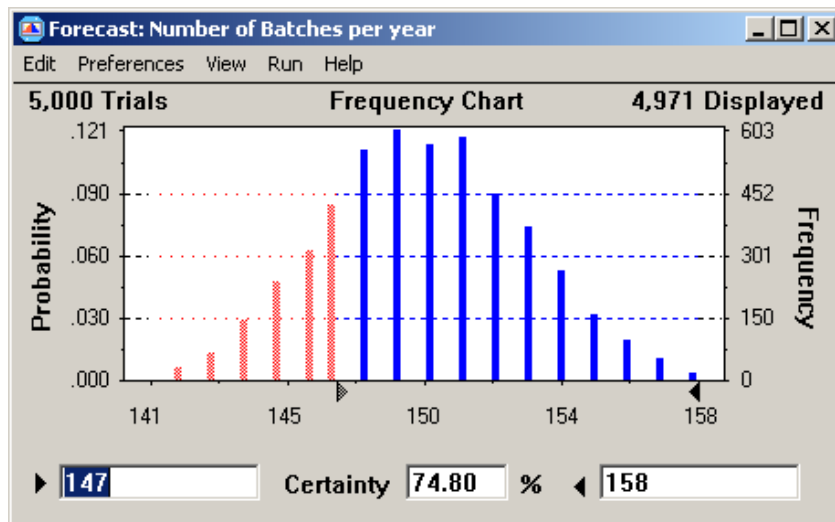
Monte Carlo Simulation



Forecasts: Determining the Certainty of the objective



❖ *The main product cost will be below \$250/kg within 93 % certainty*



❖ *The number of batches will be above 147 (corresponding to 36,000 kg/yr) within 74.8 % of certainty*



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SuperPro and SchedulePro Suite: Process Modeling Applications and Benefits

- **Engineering calculations performed for you – don't have to write all the formulas yourself.**
- **Generate equipment schedules and resource charts**
- **Enter data in one place, generate many outputs**
- **Update in one place and all outputs of that application are updated**
- **Easy to perform throughput analysis, what-if scenarios**
- **Financial calculations built-in, including equipment sizing and costing**
- **Facilitates analysis of capital and operating cost trade-offs to optimize profitability**
- **Track current production, plan future production and resource requirements, update plans as needed**
- **Comprehensive communication platform**