2.2 The Synthetic Pharmaceutical Design Case

This example analyzes the production of a synthetic pharmaceutical intermediate, which is formed by condensation of quinaldine and hydroquinone. This example is recommended for users in the pharmaceutical, agrochemical, and specialty chemical industries.

2.2.1 Process Description

Several reaction and separation steps are required to synthesize and purify the product. The generation of the flowsheet was based on information available in the patent and technical literature. The seven Pro-Designer files that are included in this example can be found in the **Examples \ Synpharm** subdirectory:

File SPhr5_0L: This process is based on lab-scale data which has been scaled up to pilot plant production volumes. At this point all equipment is in Design Mode. In other words, the equipment capacities have not yet been fixed.

File SPhr5_0a: This process was designed based on pilot plant volumes of reagents in manufacturing scale equipment. It is the same as SPhr5_0L except that the calculation mode for all process steps has been switched to Rating Mode. In addition, the reactors and filter are used for multiple unit procedures. Two 1000 gal reactors, one 4 m^2 filter and one 10 m^2 tray dryer are utilized.

File SPhr5_0b: This process is the same as SPhr5_0a, but the throughput has been scaled to 100% capacity utilization of the limiting-size reactor (R-102).

File SPhr5_0c: This process is the same as SPhr5_0b, except that THREE reactors are used in order to decrease the plant's effective batch time (so that more cycles can be run per year).

File SPhr5_0d: This process is the same as SPhr5_0c except that a second filter (NFD-102) has been added.

File SPhr5_0e: This is the same as SPhr5_0d except that procedure P-11 in R-103 (and subsequent procedures) have been split into two cycles, and the batch throughput has been increased to 100% in the new capacity-limiting piece of equipment (R-102).

File SPhr5_0f: This is the same as SPhr5_0e except that the utilization of several reactors has been rearranged. Specifically, the reactors for procedures P-5 and P-7 have been switched. This allows more cycles to be run per year because the batch cycle time of reactor R-103 is decreased. The SPhr5_0f file is described in more detail below.

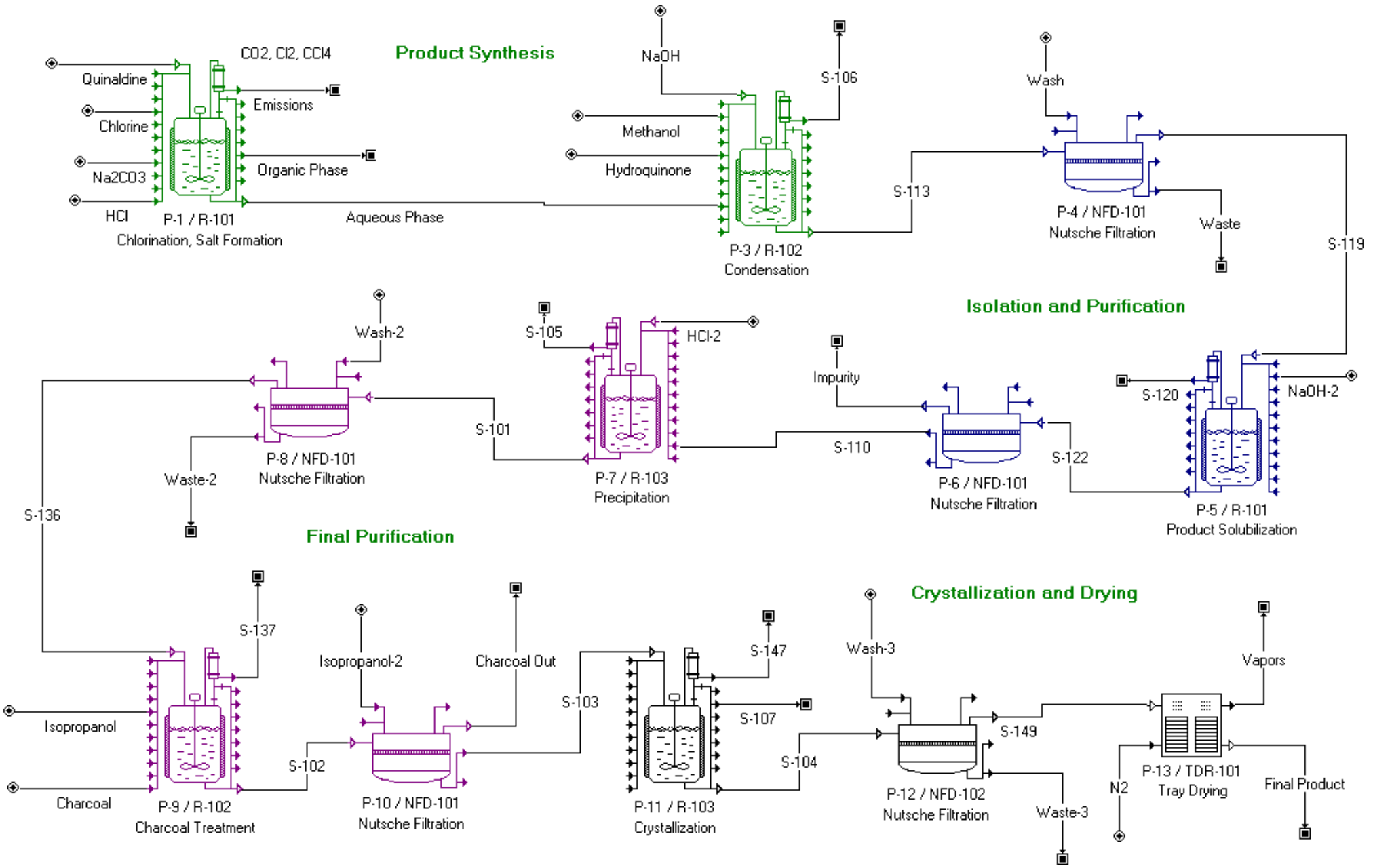
The description that follows corresponds to SPhr5_0f (see Figure 2.2-a). Please open this file now. The objective is to produce at least 33,000 kg of this intermediate per year in a plant that has the following equipment items:

1) three stirred-tank reactors each having a total volume of 1000 gallons,

2) two nutsche filters each with an area of 4 m^2, and

3) a tray dryer with a total tray area of 10 m^2.

Fig. 2.2a: Synthesis of a Pharmaceutical Intermediate Compound



The first reaction step involves the chlorination of quinaldine. Quinaldine is dissolved in carbon tetrachloride (CCl_4) and reacts with gaseous Cl_2. The yield of the reaction is around 98%. The generated HCl is neutralized using Na_2CO_3. The stoichiometry and yield of the three reactions follows:

$$\text{Quinaldine} + Cl_2 \;\; ===> \;\; \text{Chloroquinaldine} + HCl \quad \text{Yield} = 98\ \%$$

$$Na_2CO_3 \;\; + \;\; HCl \;\; ===> \;\; NaHCO_3 \;\; + \;\; NaCl \quad \text{Yield} = 100\ \%$$

$$NaHCO_3 \;\; + \;\; HCl \;\; ===> \;\; NaCl \;\; + H_2O + CO_2 \quad \text{Yield} = 100\ \%$$

Small amounts of unreacted Cl_2, generated CO_2, and volatilized CCl_4 are vented. The above three reactions occur sequentially in the first reactor vessel (R-101).

The second reaction step involves the formation of Chloroquinaldine.HCl. The added HCl first neutralizes the remaining $NaHCO_3$ and then reacts with chloroquinaldine to form its salt. The stoichiometry and yield of the two reactions follows:

$$NaHCO_3 \;\; + \;\; HCl \;\; ===> \;\; NaCl \;\; + H_2O \;\; + CO_2 \quad \text{Yield} = 100\ \%$$

$$\text{Chloroquinaldine} \;\; + HCl \;\; ===> \;\; \text{Chloroquinaldine.HCl} \quad \text{Yield} = 100\ \%$$

Small amounts of generated CO_2 and volatilized CCl_4 are vented. The presence of water (added with HCl as hydrochloric acid solution) and CCl_4 leads to the formation of two liquid phases. The small amounts of unreacted quinaldine and chloroquinaldine remain in the organic phase while the salts Chloroquinaldine.HCl and NaCl move to the aqueous phase. After the reactor contents have been allowed to settle, the aqueous phase is transferred to R-102 for further processing. The organic phase is then discharged as waste. Approximately 15.8 hours are required for the chlorination and salt formation reactions above, along with all associated charges and transfers. (Note – the times given for other procedures below also include associated material transfers, etc.)

Condensation Reaction Step (P-3/R-102)

The third reaction step involves the condensation of chloroquinaldine and hydroquinone. First, the salt chloroquinaldine.HCl is converted back to chloroquinaldine using NaOH. Then, hydroquinone reacts with NaOH and yields hydroquinone.Na. Finally, chloroquinaldine and hydroquinone.Na react and yield the desired intermediate product. Along with product formation, a small amount of chloroquinaldine dimerizes and forms an undesirable by-product (Impurity) that needs to be removed from the product. The stoichiometry and yield of the four reactions follows:

$$\text{Chloroquinaldine.HCl} + NaOH \;\; ===> NaCl + H_2O \;\; + \text{Chloroquinaldine} \quad \text{Yield} = 100\ \%$$

$$2\text{Chloroquinaldine} \;\; + \;\; 2NaOH \;\; ===> 2H_2O + 2NaCl + \text{Impurity} \quad \text{Yield} = 2\ \%$$

$$\text{Hydroquinone} \;\; + \;\; NaOH \;\; ===> \;\; H_2O + \text{Hydroquinone .Na} \quad \text{Yield} = 100\ \%$$

$$\text{Chloroquinaldine} + \text{Hydroquinone.Na} \;\; ===> \;\; \text{Product} \;\; + \;\; NaCl \quad \text{Yield} = 100\ \%$$

This step takes a total of 16.3 hours to complete.

Filtration Step #1 (P-4/NFD-101)

Both the product and impurity molecules formed during the condensation reaction precipitate out of solution and are recovered using a nutsche filter. The product

recovery yield is 90%. The total filtration and cake discharge time is 5.4 hours assuming an average filtrate flux of 200 L/m^2-h.

Solubilization Reaction Step (P-5/R-101)

The Product/Impurity cake recovered by filtration is added into a NaOH solution. The Product molecules react with NaOH forming Product.Na which is soluble in water. The Impurity molecules remain in solid phase. The stoichiometry and yield of the solubilization reaction follows:

Product + NaOH ===> H_2O + Product.Na Yield = 100 %

This step takes a total of 10.9 hours.

Filtration Step #2 (P-6/NFD-101)

Next the Impurity is removed using another filtration step (NFD-101). The total filtration and cake discharge time is 3.5 hours assuming an average filtrate flux of 200 L/m^2-h.

Precipitation Reaction Step (P-7/R-103)

The excess NaOH is neutralized using HCl and then Product.Na is converted back to Product. The stoichiometry and yield of the two reactions follows:

HCl + NaOH ===> H_2O + NaCl Yield = 100 %

HCl + Product .Na ===> NaCl + Product Yield = 100 %

The Product, which is insoluble in water, precipitates out of solution. This step takes around 8.1 hours.

Filtration Step #3 (P-8/NFD-101)

Next the Product is recovered using another filtration step. The Product cake is washed with water to remove impurities. The product recovery yield is 90%. The filtration and cake discharge time is 4.8 hours assuming an average filtrate flux of 200 L/m^2-h.

Charcoal Treatment (P-9/R-102)

The recovered Product cake is dissolved in isopropanol and treated with charcoal for discoloration. This step takes a total of 17.6 hours.

Filtration Step #4 (P-10/NFD-101)

After charcoal treatment, the solid carbon particles are removed using another filtration step. The filtration and cake discharge time is around 14.8 hours assuming an average filtrate flux of 200 L/m^2-h, and a hold time of 10.4 hours (to account for the extra time spent waiting for the second filtration cycle to get underway).

Crystallization Step (P-11/R-103)

In this step, the product solution is distilled to one third of its initial volume. Then it is crystallized with a yield of 97%. Crystallization is represented by the following reaction:

Product ===> Product-Cryst Yield = 97 %

In other words, a new component (Product-Cryst) is used to represent the crystalline form of product. This step is performed in two 12.1 hour cycles.

Filtration Step #5 (P-12/NFD-102)

The crystalline product is recovered using another filtration step with a yield of 90%. The filtration and cake discharge takes place in two 12.1 hour cycles, assuming an average filtrate flux of 50 L/m^2-h, and an 8.5 hour hold time (the hold time is necessary to synchronize these cycles with the P-11 crystallization step cycles).

Drying Step (P-13/TDR-101)

The recovered product crystals are dried in a tray dryer. The drying is done in two 12.1 hour cycles, which includes a 3.02 hour hold time (to synchronize these cycles with P-11 and P-12). Approximately 246 kg of dried product is produced per batch.

2.2.2 Flowsheet Sections

A flowsheet section is a group of processing steps that have something in common. The flowsheet of this example was divided into four sections: 1) Product Synthesis, 2) Isolation and Purification, 3) Final Purification, and 4) Crystallization and Drying. All unit procedure icons of the Product Synthesis section are displayed in green. The icons in the Isolation and Purification, Final Purification, and Crystallization and Drying sections are displayed in blue, purple, and black, respectively.

Many economic factors in pro-Designer are section-dependent and that is one reason to break-up your flowsheeet into more than one sections. Another reason is that you can allocate sections to different physical sites declared in the databank and thus make use of equipment and resources of specific sites. To use this feature you will first need to declare the sites in the databank through the **Databanks/Sites and Resources…** menu option from the main menu. There you are able to define new sites in a parent-child hierarchy (i.e. sites with their sub-sites or facilities) and declare their equipment, utility and labor resources as well as site-related economic data (see Chapter 5 for details.)

To allocate a section to a databank site, first select the section through the drop-down menu of the section toolbar and then click on the "Edit Section" button (the button with the pair of glasses.), select the ‘Allocated’ option in the dialog that comes up and select the desired site from the drop-down tree of available sites. Once you allocate a section to a site, you can allocate equipment of this section to site equipment and also make use within each operation of site utilities and labor. Following the instructions in Chapter 5, the Help Facility or the User’s guide, you might want to go through the exercise of declaring new site in the User databank and allocating one or more sections of this example.

In the same dialog that comes up when you press the “Edit Section” button you can also define and see the main starting material and product of the section along with the calculated yields. If you go to the Yields tab, you can see the molar yields of the Product Synthesis, Isolation and Purification, Final Purification, and Crystallization and Drying sections are 93.9%, 89.9%, 90.0%, and 87.3%, respectively.

2.2.3 Equipment Sharing

In a batch plant, it is common to utilize the same piece of equipment for carrying out multiple processing steps. For instance, in this example process, vessel R-101 handles steps P-1 and P-5. By default, whenever a unit procedure is introduced in the flowsheet, the system assumes that the procedure is carried out in its own piece of

equipment. However, you also have the option of selecting one of the existing equipment items that are compatible with this procedure through the Equipment Data dialog (right-click on a unit procedure icon and choose the **Equipment Data**… option).

Figure 2.2-b displays the equipment data dialog of procedure P-5. Instead of using a unique vessel for this procedure, the user decided to reuse R-101, which also handles procedure P-1. Starting with version 4.0, equipment sharing is available in Design as well as in Rating mode. Equipment sharing is also implied when two or more procedures use equipment allocated to the same databank site equipment. The site equipment databank, therefore, provides you the means to declare that the same equipment is used for multiple tasks not only in the same recipe but across recipes as well.

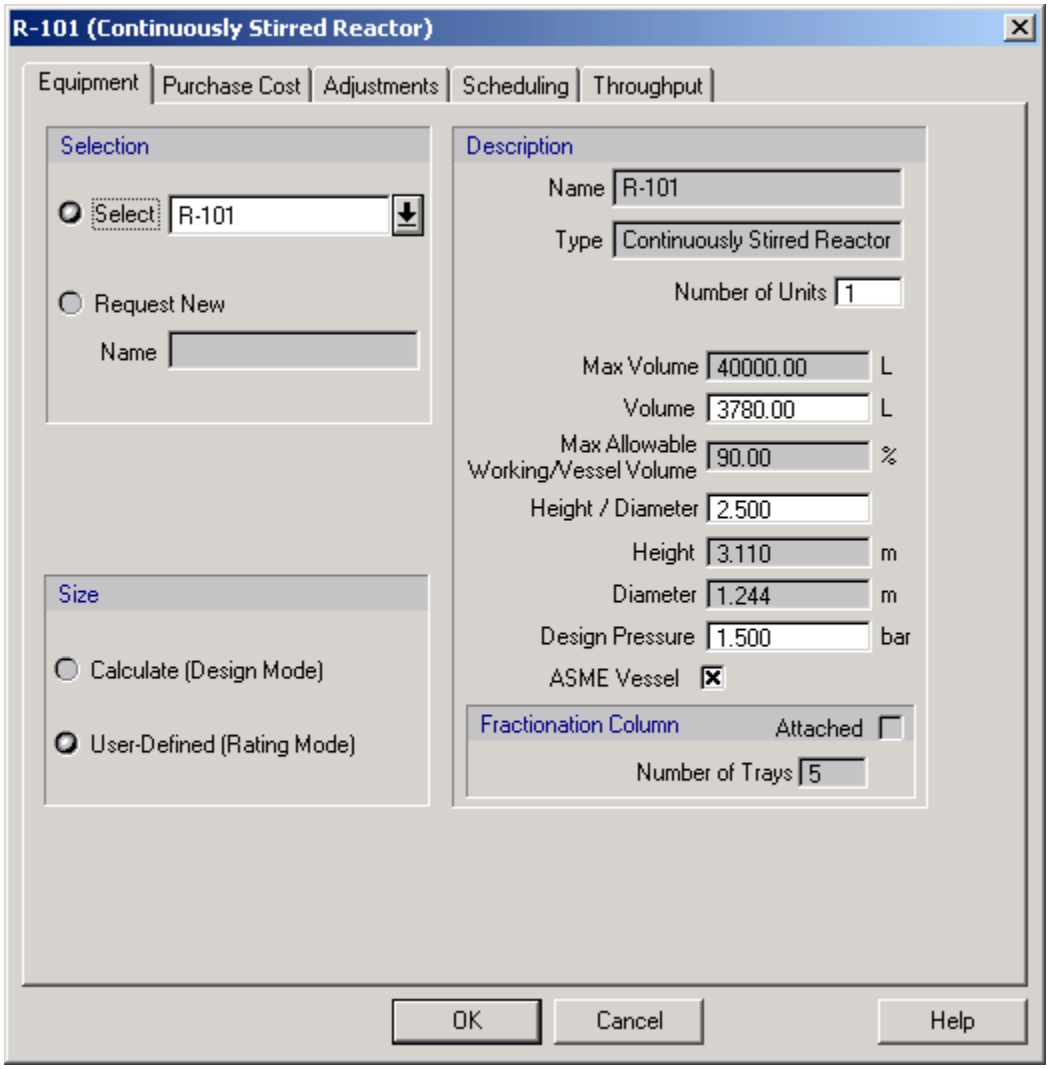


Figure 2.2-b: Equipment Data Dialog of a Stirred-Tank Reactor.

When multiple procedures share a piece of equipment that is in Design mode (unspecified size), each procedure recommends its own sizing and Pro-Designer selects the maximum. If the calculated equipment size exceeds the maximum possible

value, then Pro-Designer assumes multiple (identical) equipment items with a total size equal to the calculated total capacity requirement and an individual size that is smaller than or equal to the maximum. For example, if the maximum size of an individual filter in Design mode is 5 m^2, and your process requires 12 m^2 of filter area to achieve the necessary throughput, three 4 m^2 filters will be used by Pro-Designer. In Rating mode, the user specifies the equipment size as well as the number of equipment items employed by a unit procedure. In other words, in Pro-Designer a single unit procedure icon may correspond to multiple equipment items that operate in parallel, or multiple unit procedure icons may correspond to a single piece of equipment (if the flowsheet is in Batch mode and those procedures share equipment).

When the equipment is allocated, its mode is set by default to Rating (with the Design Mode option deactivated), all its data are set according to the corresponding site equipment and become non-editable. This signifies the fact that the equipment shown in the recipe is actually the one declared in the site databank and has therefore fixed specifications that cannot be changed unless you visit the site databank and change them from there.

Equipment sharing reduces the number of equipment items required for a batch process and consequently saves money in terms of capital expenditures. However, it also introduces scheduling constraints that may reduce the number of batches that can be processed per year. Information on visualization of equipment sharing can be found in section 2.2.5. For detailed information on the impact of equipment sharing on plant throughput please see Chapter 10 or search for Debottlenecking in the Help Facility.

2.2.4 Initialization of Reaction Operations

Batch reactions constitute the most common operation in synthetic pharmaceutical processes. Pro-Designer is equipped with three different batch reaction operation models: stoichiometric, kinetic, and equilibrium. The stoichiometric is used if no kinetic and equilibrium data are available. If kinetic data are available, the kinetic model can be used to calculate composition, temperature, and utility profiles as a function of time. All reaction operations share the same “Oper.Cond’s” tab (see Figure 2.2-c) through which the user can specify the duration of the operation, the thermal mode, the power consumption, etc.

Similarly, all reaction operations share the same “Volumes” tab (see Figure 2.2-d). In Design Mode (equipment size unspecified), the Maximum Allowable Working / Vessel Volume (%) value is used for sizing the vessel. If multiple operations in the same unit procedure require different capacity values, the maximum capacity requirement of these operations is selected as the equipment size. In Rating mode (equipment size specified), the Maximum Allowable (%) acts as a constraint that generates a warning when it is violated. The Minimum Allowable (%) value also acts as a constraint. The same logic applies to other vessel operations.

Figure 2.2-e displays the “Reactions” tab of a stoichiometric reaction operation. Through this tab the user specifies the stoichiometry and other data associated with the various reactions in this operation. Please note that a reaction operation can handle any number of reactions.

The “Extent” of a stoichiometric reaction represents the fractional conversion of its limiting component. By default, the limiting component is identified by the model based

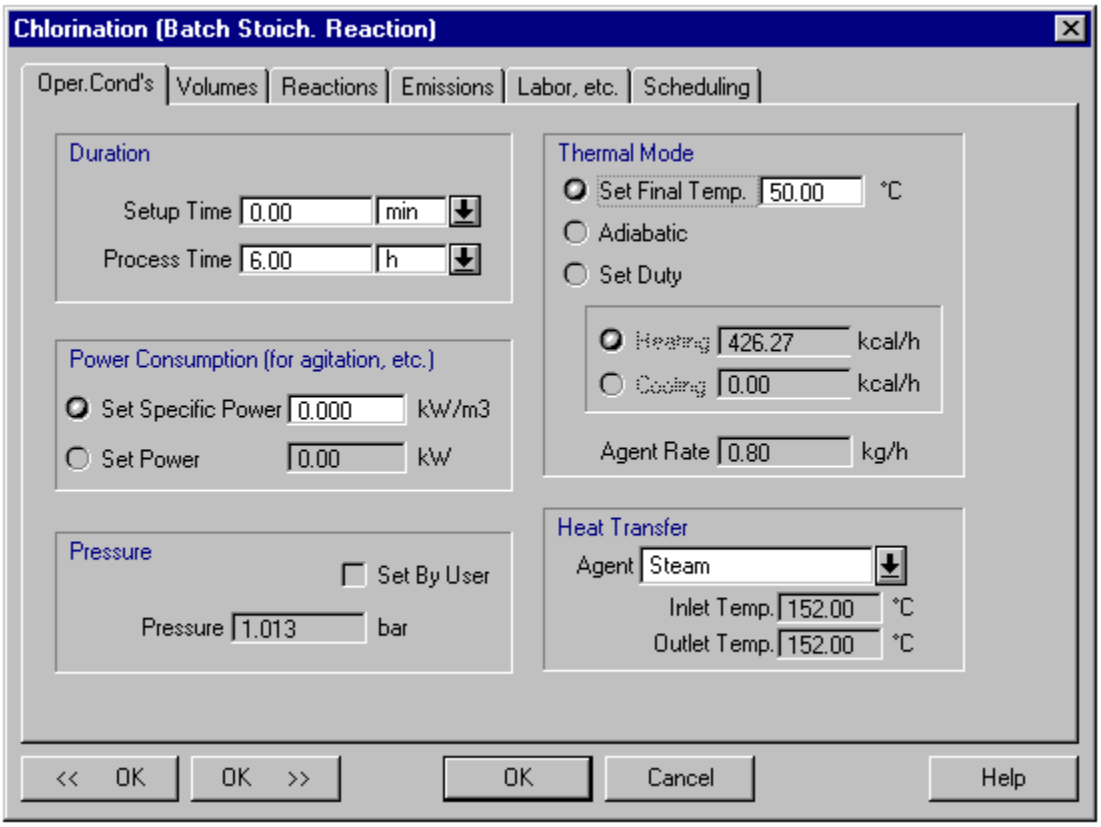


Figure 2.2-c: Oper. Cond’s tab of a reaction operation.

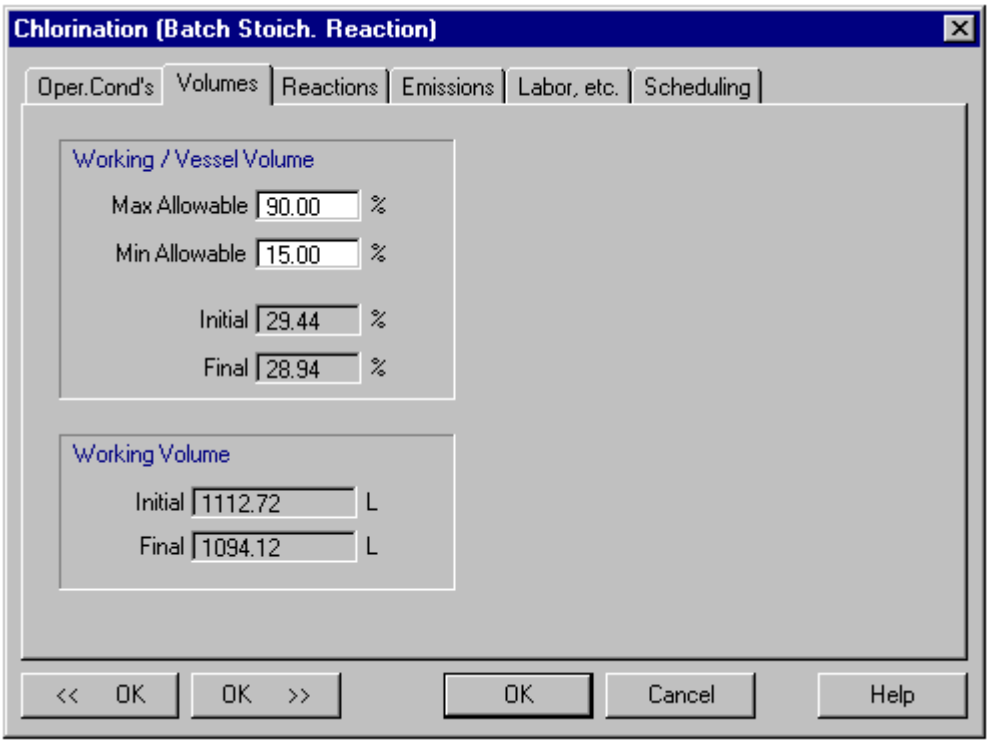


Figure 2.2-d: Volumes tab of a reaction operation.

on the stoichiometric coefficients and the feed composition. The user has the option to specify a reference component for the extent of reaction. In that case, if the specified value of the extent of reaction is not feasible, the model adjusts its value to the maximum possible. The user also has the option to specify the desired final concentration of a reactant or product and have the model estimate the extent of reaction. Again, in this case if the specified concentration is not feasible, the model adjusts its value to the maximum (or minimum) possible.

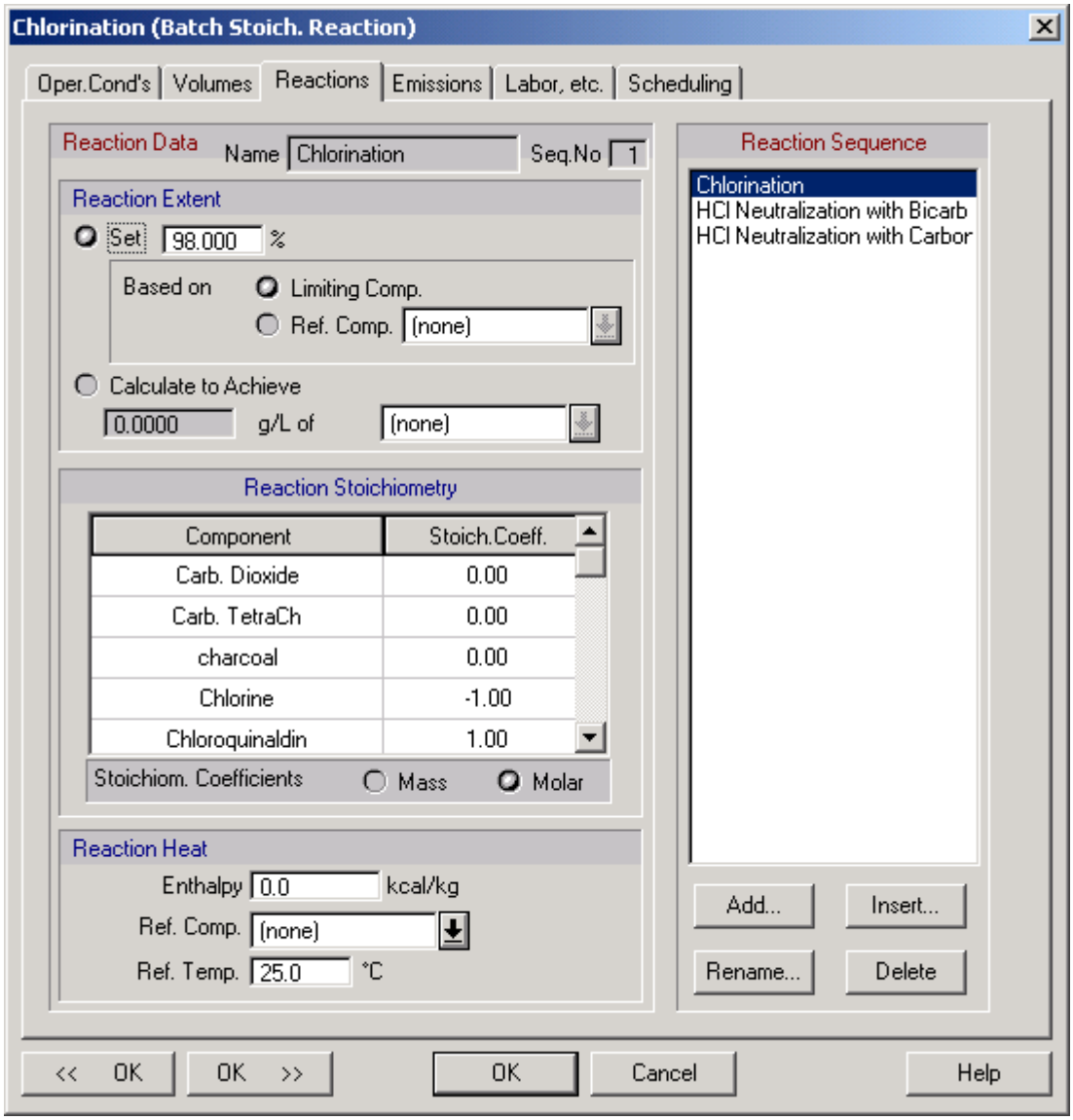


Figure 2.2-e: Reactions tab of a stoichiometric reaction operation.

The “Reactions” tab of kinetic and equilibrium batch reactions is quite similar to that of Figure 2.2-e. The main difference is that instead of the extent of reaction variables, it has a button through which the user can bring up the kinetic data dialog of a reaction (see Figure 2.2-f). Through this dialog the user specifies the kinetics of a reaction. Furthermore, clicking on the “Start/End Criteria” buttons brings up other dialogs through which the user can specify when or under what conditions a reaction is initiated or terminated.

Important Note about Stoichiometric Reactions

Several different methods can be used to specify multiple reactions within a single Reaction Operation. For instance, each reaction could be written individually (as was done for the Chlorination and HCL Neutralizations listed in the Reaction Sequence box of the above dialog.) In this case, mass balances for each reaction are performed sequentially. In other words, first the Chlorination Reaction proceeds to its specified Extent of Reaction. Then the first Neutralization proceeds to its specified Extent of Reaction. Finally, the second Neutralization occurs. In other situations, you may wish to specify reactions that occur simultaneously. This can be done in several ways. In the first method, you can specify all stoichiometric coefficients in one reaction. Consider the following example: 90% of your Starting Material reacts with your Reagent to produce the Desired Product, while the other 10% self-couples to form a Byproduct (made of two reagent molecules):

1) Starting Material + Reagent → Desired Product (90% yield)
2) Starting Material + Starting Material → Byproduct

These two scenarios would happen simultaneously, and the extent of reaction for this system would be 100% (100% of the Starting Material would react). In this situation, the relative stoichiometric coefficients (on a molar basis) of Starting Material, Reagent, Desired Product, and Byproduct would be: -1, -0.9, 0.9, and 0.05, respectively. In other words, for every 1 mole of Starting Material used, 0.9 moles of Reagent are used, 0.9 moles of Desired Product is produced, and 0.05 moles of Byproduct is produced.

Sometimes it is clearer to specify stoichiometric coefficients on a mass basis (as opposed to molar.) In the above example, let's assume that the molecular weights of Starting Material, Reagent, Desired Product, and Byproduct are: 200, 50, 250, and 400 g/mole, respectively. Assuming a 200 kg basis for the amount of Starting Material and a 50 kg basis for the amount of Reagent, the mass of Reagent consumed would be 45 kg (50*0.9), and the masses of Desired Product and Byproduct generated would be 225 kg (250*0.9) and 20 kg (400*0.05). Notice that the mass balance here is complete: initially there is 200 kg of Starting Material and 50 kg of Reagent (250 kg total). After the reactions are complete, there are 225 kg of Desired Product, 20 kg of Byproduct, and 5 kg of unreacted Reagent (250 kg total).

Another method that could have been used to model these simultaneous reactions is the following: Create two distinct reactions within your Reaction Operation (similar to the three distinct reactions shown in Figure 2.2-e). Then specify the following:

1) Starting Material + Reagent → Desired Product (90% extent of reaction)
2) Starting Material + Starting Material → Byproduct (100% extent of reaction)

When modeled as <u>separate</u> reactions, the computer will first calculate the results for Reaction 1 above. In other words, it will determine that 180 kg (200*0.9) of Starting Material and 45 kg (50*0.9) of Reagent has been consumed, and 225 kg (250*0.9) of Desired Product has been generated. Next, the computer will simulate the second reaction, in which <u>all</u> of the <u>remaining</u> 20 kg of Starting Material is transformed into 20 kg of Byproduct.

2.2.5 Process Analysis

At this point you may return to the synthetic pharmaceutical example.

Do not hesitate to change the values of certain parameters and redo the calculations (by selecting **Tasks/Solve M&E Balances**). The calculated flowrates and compositions of intermediate and output streams can be viewed by revisiting the input/output dialog windows of each stream (double click on a stream line or click with the right mouse button and select **Simulation Data…).** In addition, a report containing information on raw material requirements, stream compositions and flowrates, as well as an overall material balance, can be generated by selecting the **Tasks: Generate Stream Report (SR)...** option from the main menu. The resulting report can be viewed by selecting the **View: Stream Report** option of the main menu. Tables 2.2a,b, and c display portions of the stream report. These tables were extracted from the spreadsheet version of the Stream Report, which was generated by selecting **File : Export Reports to Excel**. They were then edited in Excel and pasted into Pro-Designer as a MS Excel worksheet.

The detailed equipment contents during a processing step can be viewed by right clicking on the appropriate unit procedure and selecting **Equipment Contents**. Right clicking and selecting **Operation Sequence** displays related information.

Table 2.2a: OVERALL PROCESS DATA

Annual Operating Time	7890.88	h
Annual Throughput	35185.06	kg MP
Batch Throughput	246.05	kg MP
Plant Batch Time	101.07	h
Effective Plant Batch Time	55	(h)
Number of Batches Per Year	143	

MP = Main Product

Table 2.2b: STARTING MATERIAL REQUIREMENTS

Section Name	Starting Material	Active Product	Gross Yield (%)	Amt Needed kg Sin/kg MP
Product Synthesis	Quinaldine	Product	164.87	0.86
Isolation and Purification	Product	Product.Na	97.74	1.41
Final Purification	Product.Na	Product	82.78	1.38
Crystallization and Drying	Product	Product_cryst	87.30	1.14

Table 2.2c: RAW MATERIAL REQUIREMENTS – ENTIRE FLOWSHEET

Raw Material	kg/Year	kg/Batch	kg/kg MP
Chlorine	18,184.94	127.17	0.52
Na2CO3	21,342.04	149.25	0.61
Water	602,443.05	4,212.89	17.12
HCl (20% w/w)	72,613.46	507.79	2.06
NaOH (50% w/w)	41,547.53	290.54	1.18
Methanol	112,393.00	785.97	3.19
Hydroquinone	34,829.20	243.56	0.99
Carb. TetraCh	101,027.42	706.49	2.87
Quinaldine	30,194.57	211.15	0.86
Sodium Hydroxide	15,065.71	105.36	0.43
Isopropanol	403,267.87	2,820.06	11.46
charcoal	3,220.25	22.52	0.09
HCl (37% w/w)	44,199.50	309.09	1.26
Nitrogen	225,592.28	1,577.57	6.41
Flowsheet Total	**1,725,920.80**	**12,069.38**	**49.05**

Scheduling, Equipment Utilization, and Resource Demand Graphs

Pro-Designer generates **Operations** and **Equipment Gantt charts** for single and multiple batches. Figure 2.2-g displays a portion of the operations Gantt chart for a single batch of this example process.

The left view (spreadsheet view) displays the name, duration, start time, and end time for each activity (e.g. each operation, unit procedure, cycle, batch, etc). You can use

the left view to expand or collapse the activity summaries by clicking on the + or – signs in the boxes to the left of the activity names.

The right view (chart view) displays a bar for each activity in the overall process recipe. To edit the scheduling data (or any other data affecting an activity), simply right-click on a bar and a relevant command menu will appear. Selecting the uppermost entry on this menu will bring up a dialog that will allow you to edit the information associated with that particular activity bar. In fact, anything you can accomplish with the other scheduling interfaces, you can also accomplish from the Gantt chart interface. Furthermore, you can redo the M&E balances and have the Gantt Chart updated to reflect the new (calculated) scheduling settings for the recipe by clicking on the Update Chart entry in the main menu of the interface.

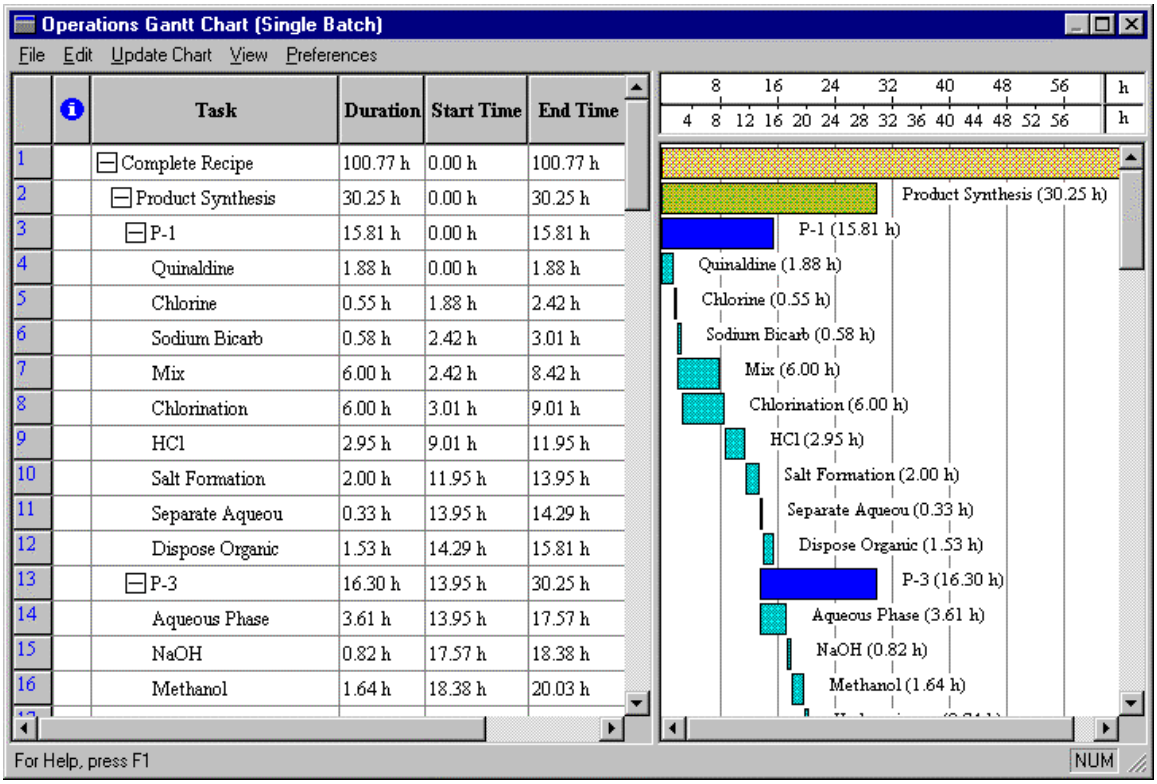


Figure 2.2-g: Operations Gantt Chart for a Single Batch.

Another way of visualizing the execution of a batch process as a function of time is through the Equipment Occupancy chart (select **View : Equipment Occupancy Chart**). Figure 2.2-h displays the equipment occuapancy chart for two consecutive batches of this example process. Multiple bars on the same line (e.g., for R-101, R-102, NFD-101, and R-103) represent reuse (sharing) of equipment by multiple procedures. White space represents idle time. The equipment with the least idle time between consecutive batches is the **time (or scheduling) bottleneck** (R-102 in this case) that determines the maximum number of batches per year. Its occupancy time (approximately 54 hours) is the minimum possible time between consecutive batches (also known as Min. Effective Plant Batch Time). The actual time between consecutive

batches (also known as Effective Plant Batch Time) is approximately 55 hours. The plant batch time (the time required to complete a single batch) is roughly 101 hours.

Note: If your Gantt chart does not appear exactly as shown, you may want to change some of its display options. Select **Preferences: Styles: Gantt chart**. The resulting dialog will allow you to display or hide the branch and section bars and to configure the text displayed with the bars.

Pro-Designer also generates occupancy charts for auxiliary equipment, such as clean-in-place (CIP) and steam-in-place (SIP) skids.

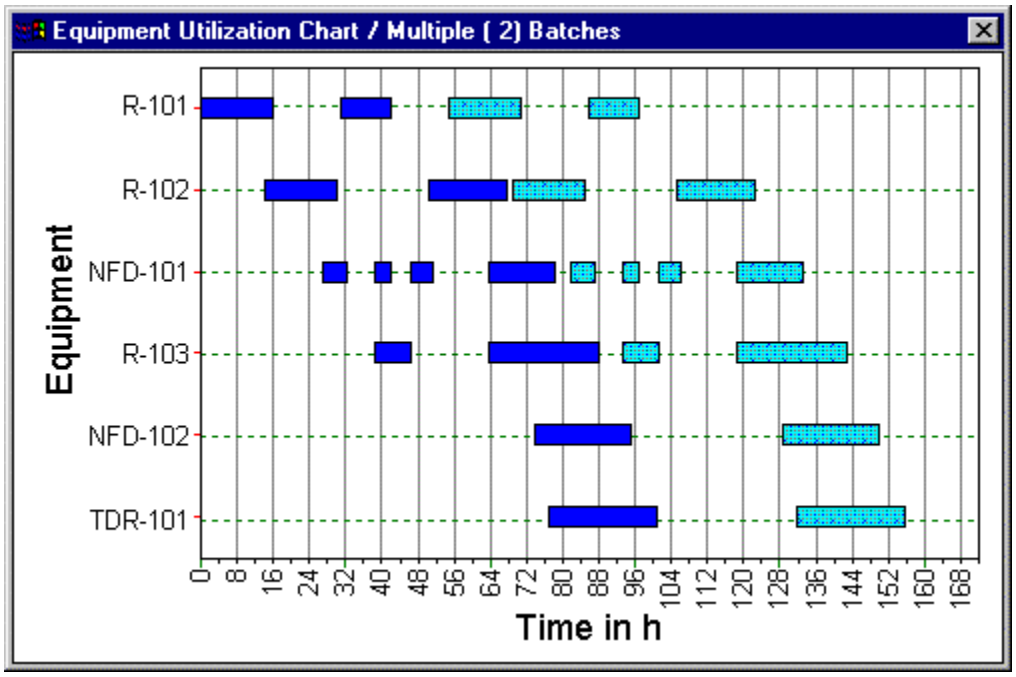


Figure 2.2-h: Equipment Occupancy Chart (two consecutive batches).

In addition to creating Gantt charts for equipment occupancy and operations, Pro-Designer automatically generates graphs of resource demand as a function of time for such things as heating and cooling utilities, power, labor, and raw materials. To view these graphs, select **View: Resource Consumption Tracking Chart**, choose the resource type from the drop-down menu and from the pop-up dialog select the desired resource. Figure 2.2-i displays the total labor demand graph for four consecutive batches. Note that for short periods of time there is a need for up to seven operators. If this exceeds the actual number of operators available, then certain operations will need to be delayed to accommodate the labor constraint. Inventory graphs for heat transfer agents and raw materials can also be generated in a similar way by using the **View: Inventory Chart** menu item.

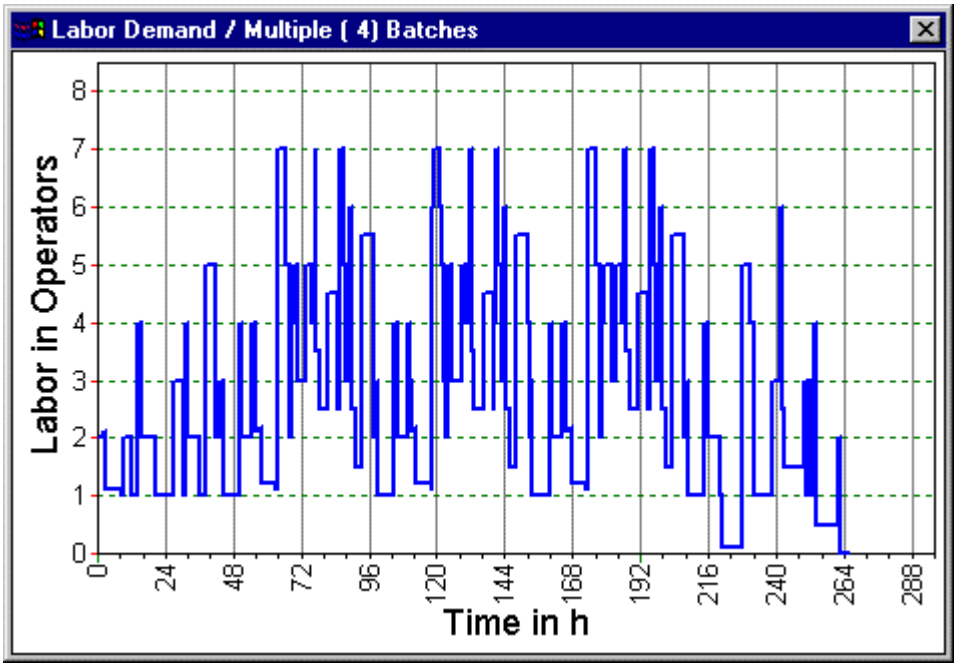


Figure 2.2-i: Labor Demand Chart (four consecutive batches).

Throughput Analysis and Debottlenecking

Pro-Designer is equipped with powerful throughput analysis and debottlenecking capabilities. The objective of these features is to allow the user to quickly and easily analyze the capacity and time utilization of each piece of equipment, and to identify opportunities for increasing throughput with the minimum possible capital investment. For a detailed throughput analysis example (based on this process), please see Chapter 9 or search for Debottlenecking in the Help Facility.

To see the analysis results for this example, select **View: Throughput Analysis Charts: Utilization**. The utilization chart will appear showing the capacity, time, and combined utilizations for each procedure. If the equipment is shared, the time utilization is based on the entire time the equipment is used.

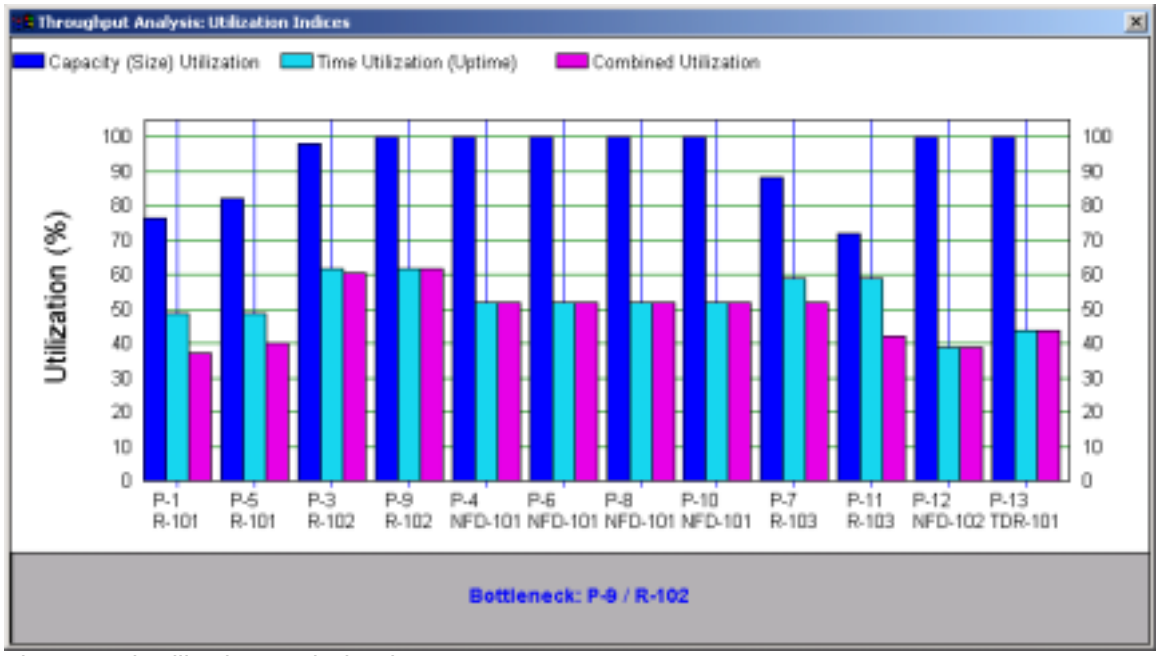


Figure 2.2-j Utilization Analysis Chart

Select **View: Throughput Analysis Charts: Potential** to view the throughput potential chart below. This chart shows the potential batch size increase for each unit procedure. The actual batch size is indicated by the red dashed line behind the bars.

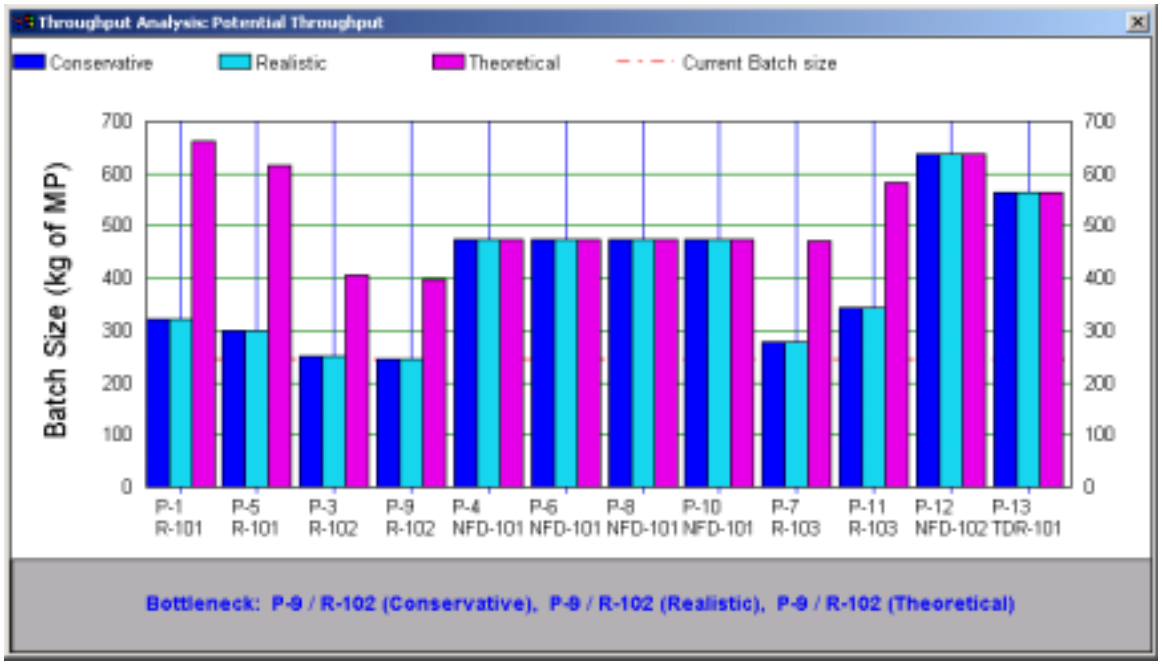


Figure 2.2-k Throughput Potential Chart

Note: The current batch size line is easier to see if you edit the chart style (right-click) and set the chart style a pattern rather than a solid color.

2.2.6 Cost Analysis and Economic Evaluation

Below are the key results of cost analysis for a plant producing 35,200 kg of this intermediate per year. The Table 2.2d gives an overview of the total economic impact of the plant, including the total capital investment, yearly revenues, and rate of return. This table was extracted from the spreadsheet version of the Economic Evaluation Report (EER). The full EER can be generated by selecting **Tasks: Generate Economic**

Table 2.2d: Executive Summary

TOTAL CAPITAL INVESTMENT	10,633,000	$
OPERATING COST	6,747,000	$/year
PRODUCTION RATE	35,185	kg/year
UNIT PRODUCTION COST	192	$/kg
TOTAL REVENUES	17,593,000	$/year
GROSS MARGIN	61.65	%
RETURN ON INVESTMENT	69.88	%
PAYBACK TIME	1.43	years
IRR AFTER TAXES	51.33	%
NPV (at 7.0 % interest)	40,405,000	$

Evaluation Report (EER)... from the main menu. The resulting report can be viewed by selecting the **View: Economic Evaluation Report** option of the main menu.

Tables 2.2e and 2.2f provide breakdowns of the annual operating and raw materials costs. They were extracted from the spreadsheet version of the Itemized Cost Report (ICR). The full ICR can be generated by selecting **Tasks: Generate Itemized Cost Report (ICR)...** from the main menu. The resulting report can be viewed by selecting the **View: Itemized Cost Report** option of the main menu. The ICR enables the user to readily identify the cost sensitive sections of a flowsheet – the economic hot-spots. For instance, a quick look at Table 2.2e reveals that 32.7% of the operating cost is associated with raw materials, especially quinaldine (Table 2.2f). If a lower-priced quinaldine vendor could be found, the overall process cost would be reduced significantly. Another large cost in this example is the Equipment-Dependent expenses, which account for roughly 27% of the operating cost. Increased equipment sharing may reduce this cost but may also reduce the annual throughput. Labor and Waste Treatment/Disposal occupy the 3rd and 4th positions, respectively. Labor can be reduced through increased automation. The environmental cost can be reduced through solvent recovery, purification, and reuse.

Table 2.2e: Breakdown of Operating Costs

Cost Item	Product Synthesis	Isolation & Purification	Final Purification	Crystal lization	Subtotal	%
	$/year	$/year	$/year	$/year	$/year	
Raw Materials	1,444,491	69,389	408,683	280,795	2,203,358	32.66
Equipment	466,923	246,656	486,226	616,698	1,816,503	26.92
Labor	298,863	295,765	450,735	538,390	1,583,753	23.47
Lab/QC/QA	44,829	44,365	67,610	80,758	237,563	3.52
Waste Trt/Dsp	256,375	5,653	10,600	632,901	905,528	13.42
Utilities	63	4	48	95	211	0.00
Subtotal	**2,511,544**	**661,832**	**1,423,902**	**2,149,638**	**6,746,916**	**100.00**
Contribution (%)	**37.23**	**9.81**	**21.10**	**31.86**	**100.00**	

Table 2.2f: Breakdown of Raw Materials Costs

Raw Material	Product Synthesis	Isolation & Purification	Final Purification	Crystal lization	Subtotal	%
Chlorine	60,010	0	0	0	60,010	2.72
Na2CO3	138,723	0	0	0	138,723	6.30
Water	15,294	39,258	5,692	0	60,244	2.73
HCl (20% w/w)	10,892	0	0	0	10,892	0.49
NaOH (50% w/w)	6,232	0	0	0	6,232	0.28
Methanol	26,974	0	0	0	26,974	1.22
Hydroquinone	139,317	0	0	0	139,317	6.32
Carb. TetraCh	80,822	0	0	0	80,822	3.67
Quinaldine	966,226	0	0	0	966,226	43.85
Sodium Hydroxid	0	30,131	0	0	30,131	1.37
Isopropanol	0	0	388,392	55,203	443,595	20.13
charcoal	0	0	7,085	0	7,085	0.32
HCl (37% w/w)	0	0	7,514	0	7,514	0.34
Nitrogen	0	0	0	225,592	225,592	10.24
TOTAL	**1,444,491**	**69,389**	**408,683**	**280,795**	**2,203,358**	**100.00**

The above analyses show how the economic reports can be used not only for estimation of the total cost of a process, but also as a tool to optimize the process through "what-if" scenarios. Would it make economic sense to use two reactors instead of three? It depends on how much the throughput would decrease if two reactors were used, and how much the third reactor adds to the total cost. Would a radically modified purification scheme be better than the current scheme? It depends on what equipment, reagents, etc. would be required for the modified purification, and what the overall yield of the product would be. This type of what-if analysis is quick and easy to perform using Pro-Designer.

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2.2.7 Environmental Impact

Pro-Designer generates two different reports that provide information on the environmental impact of a process. The **Emissions Report** provides information on emissions of volatile organic compounds (VOC's) and other regulated compounds. The **Environmental Impact Report** provides information on the amount and type of waste

generated by a manufacturing facility. It also provides information on the fate of a compound that enters an integrated manufacturing facility.

2.2.8 Product Formulation and Packaging

Pro-Designer contains a variety of formulation, packaging, and transportation unit procedures in order to capture the cost associated with such processes.

Product formulation and packaging processes often involve formation and use of discrete entities, such as tablets, bottles, boxes, etc. The flow of such entities is represented by discrete streams, which by default are displayed in blue. For more information on discrete streams and entities, please see Chapter 4 and/or consult the Help Facility.

To familiarize yourself with the formulation and packaging models and the concepts of discrete streams and entities, please open the **Bgal4_7c** design case and visit the simulation data and operation data dialog windows. As usual, you can open these dialogs by right-clicking on the various packaging unit procedure icons and their corresponding streams. Notice the different interface of discrete streams, which display the flow of discrete entities as well as the equivalent bulk flow (based on the bulk ingredients that compose the discrete entities.

GO TO TOP LEVEL CONTENTS