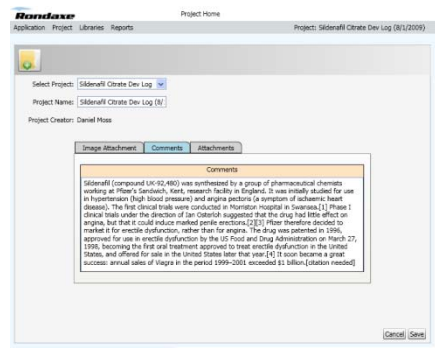


# Rondaxe

## FORMULATIONS -

### How to Guide

Rondaxe Formulations Development Log is a software application that allows you to manage all aspects of a drug product development project. The software allows the user to collect data and organize into interactive data display screens and reports. This allows a single source where data can be stored and managed in an intelligent way. It will allow users to dynamically interact with data in new ways.



This document is intended to provide an outline of the functionality and overview of instructions and includes additional information on new functionality that has been added.



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## General Guideline for Using

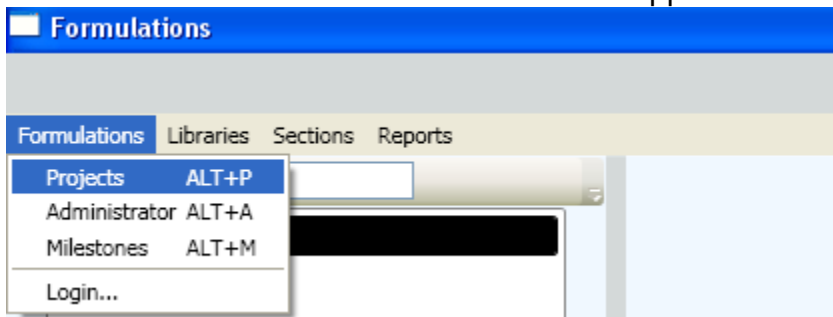
In order to populate the Development Log, the following guidelines are useful guide to follow in order to efficiently build the database.

1. Begin by populating the libraries with the basic information for your project: Materials (raw, starting, intermediates, API), Vendors & Impurities.
2. Build Process Steps
3. Build Processes
4. Build Material Specifications
5. Populate Batches & Results

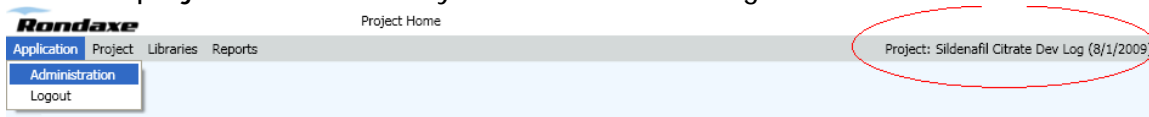
Remember to SAVE   your work at regular intervals and when moving between pages/tabs. This will avoid any inadvertent loss of your work.

## General Navigation

User the Main Menu Bar to move within the application



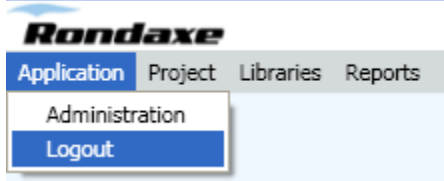
The navy color highlights the menu item that you are on. Note the project name is always indicated on the right side of the menu bar.





To Log Out follow the Menu Path: Application> Log Out

Or just click the X button to exit



## Icons

The following Icons are common within the application

Attach File	
Add / Remove Files	
Add Milestone	
Create a New Project	
Comments	
Create New Entry/Process	
Delete	
Export Table	
Open Attachment/File	
Paste from Clipboard	
Save	
Select a Date	
View / Zoom	



## Logging In

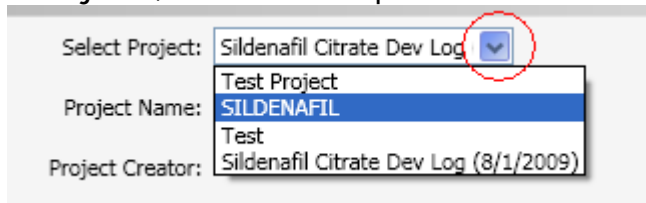
Point your browser to the link for Development Log  
Enter your name, password, and client.

Client:   
Username:   
Password:

Application brings you to the front page of the last Project you worked on.



To switch between Projects, select the drop down menu.



Your administrator will have access to create new projects in the application.  
To navigate between different projects select from the drop down menu and  
the application will navigate to the selected project.




## Project Home Page




The main Project page shows Project Name, Creator, Project Summary, Chemistry and attachments. Access to modify this page will be restricted by security to a project manager or super user. Summary information on project will be displayed here. Background documents (PowerPoint presentations, reports etc.) can be attached here. Click on the Tabs to see Image, Comments or Attachments associated with this project.



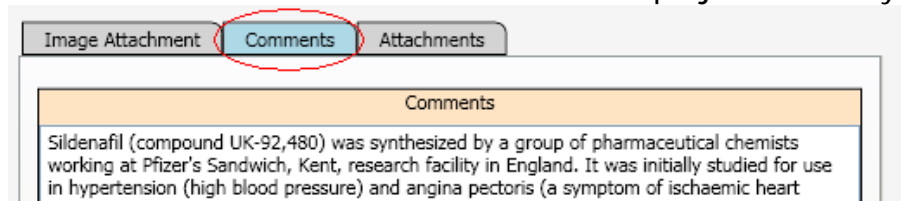
## Image Files

Image files can be uploaded to show chemistry using the Attach icon , select the Browse button to choose the file you want to display (jpeg, bmp format). Click the Attach Icon to display the image. To remove the image, click the Remove button. Click the Save button to save your changes. To view the image in a pop up window, click on the Attach icon.

## Attaching Documents

To attach documents to the project summary page, Click the Add File . Either select a file from the Attachments Library or click the Attach Icon  to add a file to the Library from your computer. Select the file on your computer, click open, enter any additional information you have and click Save. Select the ADD button to add to the attachments Library. Click SAVE. To remove any file, click the  icon.

The Comments tab is a useful area to record project summary information.

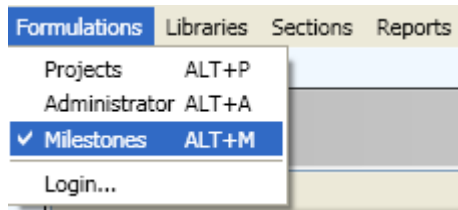


Click the Save button to save any changes before moving to a new page .



## Milestones Information

Click on the Milestones Info tab to see Milestone information for the project.



Use Add New Milestone button to add




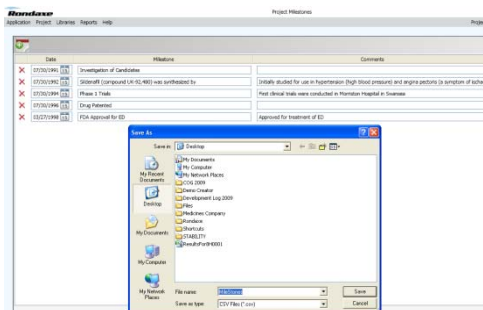
	Date	Milestone	
✗	07/30/1991 15	Investigation of Candidates	
✗	07/30/1992 15	Sildenafil (compound UK-92,480) was synthesized by	Initially

Add date information, Milestone Title, Description, attach relevant files etc.

To Edit a milestone select the line, make any adjustments and SAVE.

To delete a milestone, select the delete icon for that milestone.

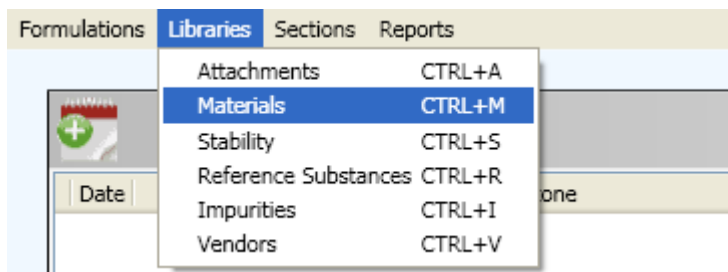
To Export the list to an excel worksheet click the Excel icon  and you will see a dialogue box to open or save the exported file.





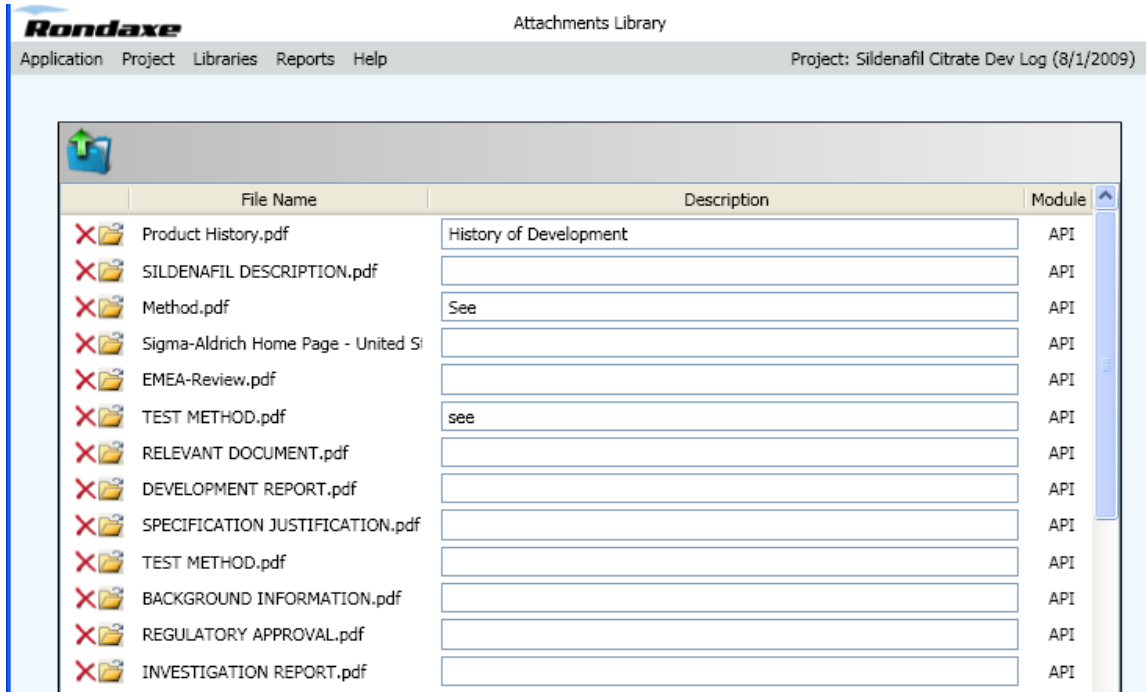
## Libraries

The Development Log data libraries are where the user will build the foundation data for the entire application. Access this from the main menu bar.



## Attachments Library

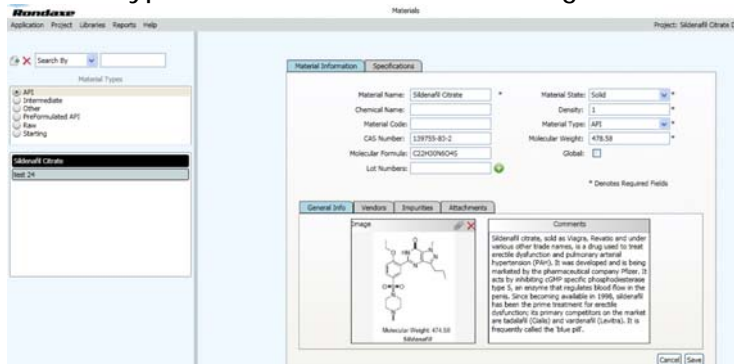
All attachments associated with particular projects can be found directly in the Attachments Library. Files can be attached, opened and reviewed from this area.



## Materials

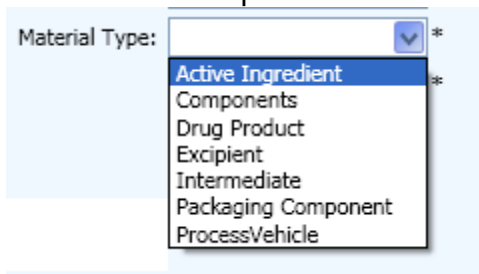


The Materials Library displays all the material in a project. The materials are displayed by material type API, Intermediate, Starting Material etc.



User can create new Material by clicking the Add New button. Complete information such as Name, Molecular Weight, and Density etc. Save to complete.

Note the Material Type selection is important for the application to build synthetic routes. Users are required to select Material Type before a material



can be saved.

Active Ingredient - API

Components - e.g. capsule shells

Drug Product - e.g. Bulk Tablets

Excipient - inactive ingredients used in formulation

Intermediate - e.g. granulation, blend, etc.

Packaging Component - e.g. bottles, cartons etc.

Process Vehicle - e.g. Purified Water used in process but not part of the formula



## Material Specifications

Material Specifications can be set up for any material.

Selected	Assay	Specification	Method ID	Method Description	Attach Method
<input type="checkbox"/>	Description	1	1		
<input type="checkbox"/>	IR Identifica	1			
<input type="checkbox"/>	HPLC Identif	1			

**Add Specification**

Assay:

Method ID:

Specification:

Method Description:

Assays can be set up and New Assays can be created. Click New. Add

**Add Specification**

Assay:

Method ID:

Specification:

Method Description:

Set up Specifications for a particular Assay.  
Attach appropriate documents. Click Add.

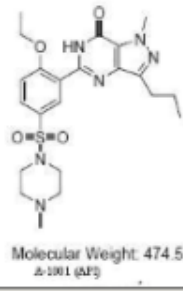


## Reference Substances

The Reference Substances Library allows the user to record information on any reference substances for a specific project. User can save information such as Name, Reference Substance Type, Material Type, Batch Number, Purity as well as any other image or text information.

Reference Substance Name:	<input type="text" value="Sildenafil Citrate"/>	Purity:	<input type="text" value="0.00"/>
Reference Substance Number:	<input type="text" value="00001111"/>	Lot Number:	<input type="text" value="8A0001"/>
Chemical Name:	<input type="text"/>		
Reference Substance Type:	<input type="text" value="Reference Material"/>	Global:	<input type="checkbox"/>
Reference Material Type:	<input type="text" value="API"/>		

Image



Molecular Weight: 474.5  
2-1001 (API)



## Impurities

The Impurities Library allows users to save information on impurities for a project. Name, Molecular Weight, Image, Comments and any Documents required can be associated and saved.

Impurity Name:

Molecular Weight:

Global:

Image Attachment | **Comments** | Attachments

Comments

The US Food and Drug Administration last week posted the final version of its Guidance for Industry, ANDAs: Impurities in Drug Substances. The document provides agency recommendations for establishing acceptance criteria for impurities in drug substances. It also provides recommendations on the chemistry, manufacturing, and controls (CMC) information to include the reporting, identification



## Vendors

The Vendors Library allows the user to store information on vendors. Note that Vendor information is global (will show in all projects for a client) - this avoids the requirement to input repeat information. Name, Address, Contact, Audit information can be input and saved. In addition the user can associate materials to a vendor to produce a list of all materials sourced from a particular vendor.

Company Name:	BASF	Contact:	Bob Smith
Address Line 1:	100 Campus Drive	Contact Email:	bsmith@basf.usa.com
Address Line 2:	Suite 1000	Contact Phone:	201 895 2323
City:	Florham Park	Contact Fax:	201 895 2323
State:	New Jersey	Last Audit Date:	06/22/2009 15
Country:	United States Of America	Next Audit Date:	06/24/2009 15
ZipCode:	08818		

Associated Materials	Comments	Attachments
----------------------	----------	-------------

Material	CAS Number	Chemical Name	Type	Molecular Weight	Density
Toluene	108-88-3	Toluene		92.14	0.8669
SOCI2	7719-09-7	Thionyl Chloride		118.97	1
NMP	109-01-3	n methyl piperazin		100.19	
Potassium tert-but	865-47-4]	865-47-4]		112.21	1
TEA	121-44-8	Triethylamine		101.19	1
tert-Butanol	75-65-0	2-methyl-2-propar		74.12	0.78
Sildenafil	139755-83-2	1-[4-ethoxy-3-(6,7		474.6	1



## Stability Information

The Stability Information Library allows the user to record information from Stability Studies within the application. Stability Name, Protocol #, Document # can be saved. User can associate specific materials and lot numbers with the study. All relevant information can be entered in the Study Objectives, Performance Conditions area.

Stability Study Criteria can be added by adding

Assay can be set up by clicking add new.

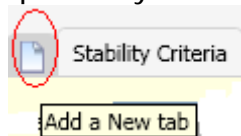
New Assays can be created. Click New Assay +.

Disable	Assay Name	Description
<input type="checkbox"/>	Assay & Impurities by HPLC	
<input type="checkbox"/>	Water Content by KF	
<input type="checkbox"/>	DSC (USP <891>)	
<input type="checkbox"/>	Appearance	Test Method 1
<input type="checkbox"/>	Assay & Impurities by HPLC	
<input type="checkbox"/>	Water Content by KF	
<input type="checkbox"/>	DSC (USP <891>)	

Set Specifications for a particular Assay.

Attach appropriate documents

Results can be recorded at time points by clicking.





NOTE YOU NEED TO SAVE THE STABILITY STUDY, EXIT and REOPEN BEFORE YOU CAN ENTER RESULTS.

Stability Criteria 1 MONTH x 3 MONTH x 6 MONTHS BATCH 4 x

Interval: 6 MONTHS BATCH 4 Date: 08/12/2009 15

Assay	Test	Method ID	Method Description	Attach Method	Results	Out Of Specification
Water by KF	less than 5%	1e	test		10%	<input type="radio"/>
Assay & Imp	complies to sta	1e	test		NOT COMPLIE!	<input checked="" type="radio"/>

Cancel Results Save Results

Remember to Save Results and Save the Stability Information as information is entered.

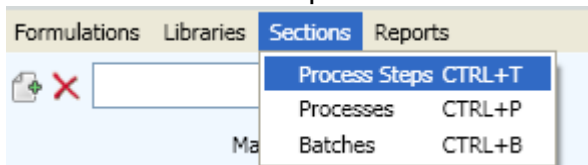


## Process Steps

A Process Step is used to represent a unit operation in the software e.g. Blending, Tableting, Milling etc. By breaking the Formulation Process into a number of Process Steps the user can collect information about and build the process in the application.

The user can select from a drop down menu of Step Types. The User defines specifies the output material, input materials and Step Controls.

### Sections> Process Steps



#### Add New Process Step

Complete the Step Name, Route of Admin, Step Type, Material Output.

Complete the items on the Bill of Materials

Specify the Equipment

Add information on Process Control Steps

Step Name:  \*

Route Of Administration:  \*

Step Type:  \*

Material Output:  \*

Equipment:

Icon Comments

**Material Inputs**

Material Name	Type
Simvastatin	Active Ingredient
ascorbic acid	Excipient
citric acid	Excipient
Butylated hydroxyanisole	Excipient
microcrystalline cellulose	Excipient
starch	Excipient
lactose	Excipient
magnesium stearate	Excipient

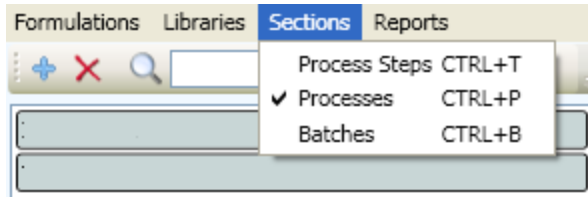
	Type	Text	Attachment
<input type="checkbox"/>	Step Control	Blend Time	click to attach file

Save



## Processes

Processes allows the user to link together various Process Steps to represent the overall manufacturing process for a particular formulation. This allows the user to collect in one place information on development, formula and process. It can be used to draw a Process Flow Diagram.



Create New

Enter Route of Admin, Drug Product Form and Final Product

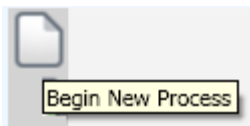
Attachments can be added

Hit Save

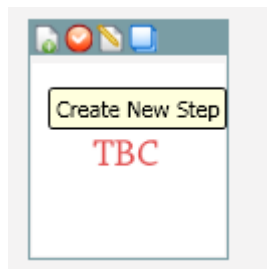
Toggle to the Process Diagram



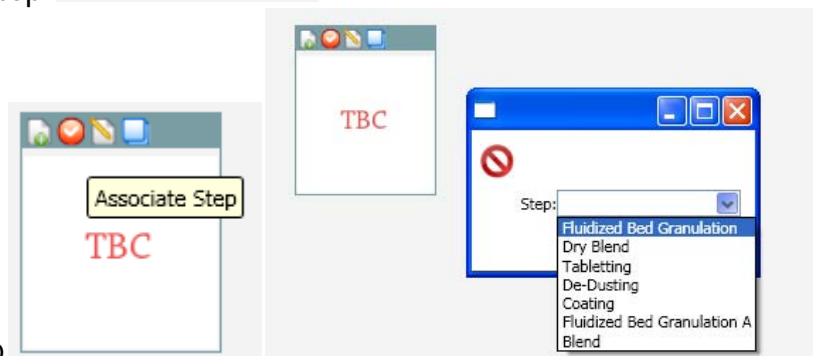
Begin New Process

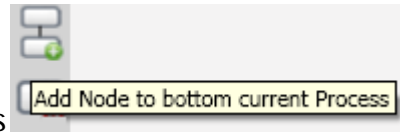


Create Next Step

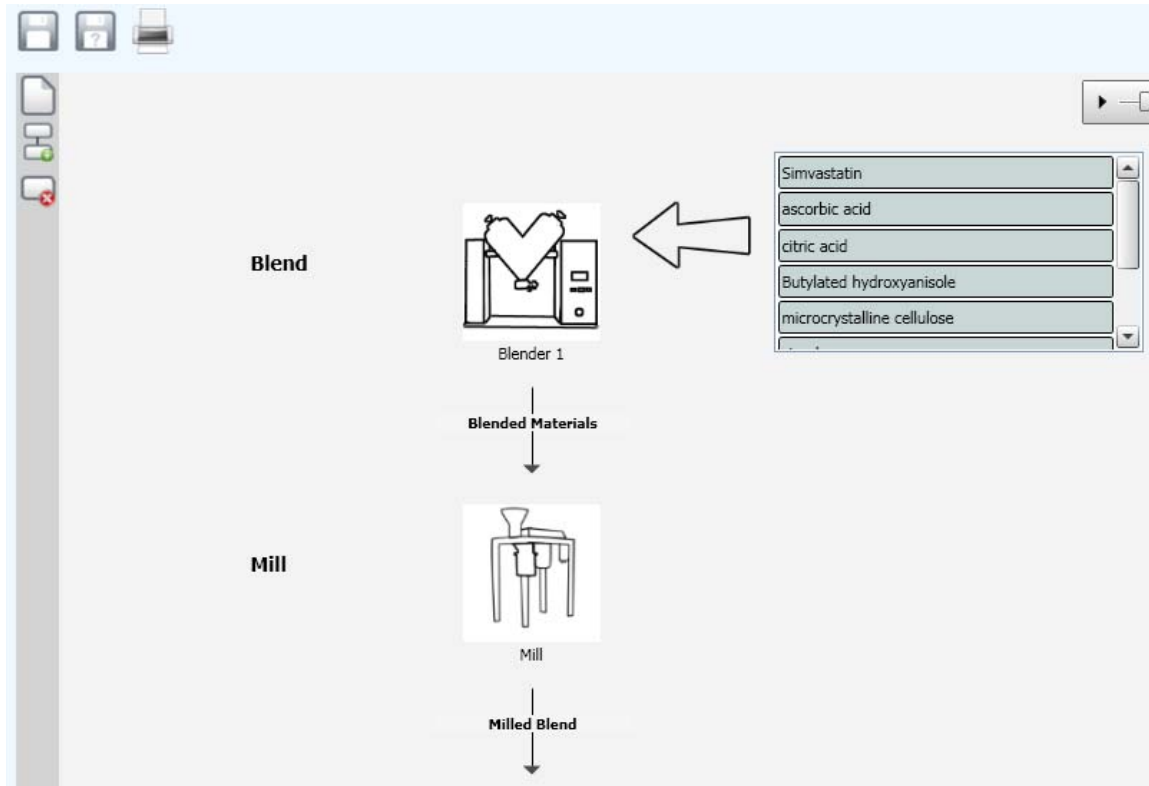


Associate Step





Add Node to Bottom of Current Process



Continue to Build the Process.

When completed hit SAVE

Toggle back to Process Page

Enter Formula

Complete the Theoretical Number of Units

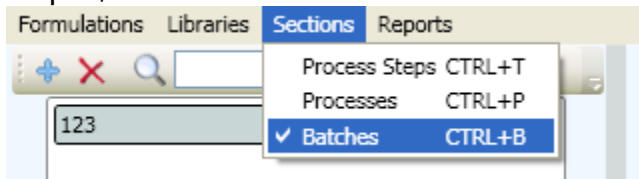
Complete the Formula Unit Content for each Tablet/Capsule

Click the Calculate Button to update the kg/Batch column.

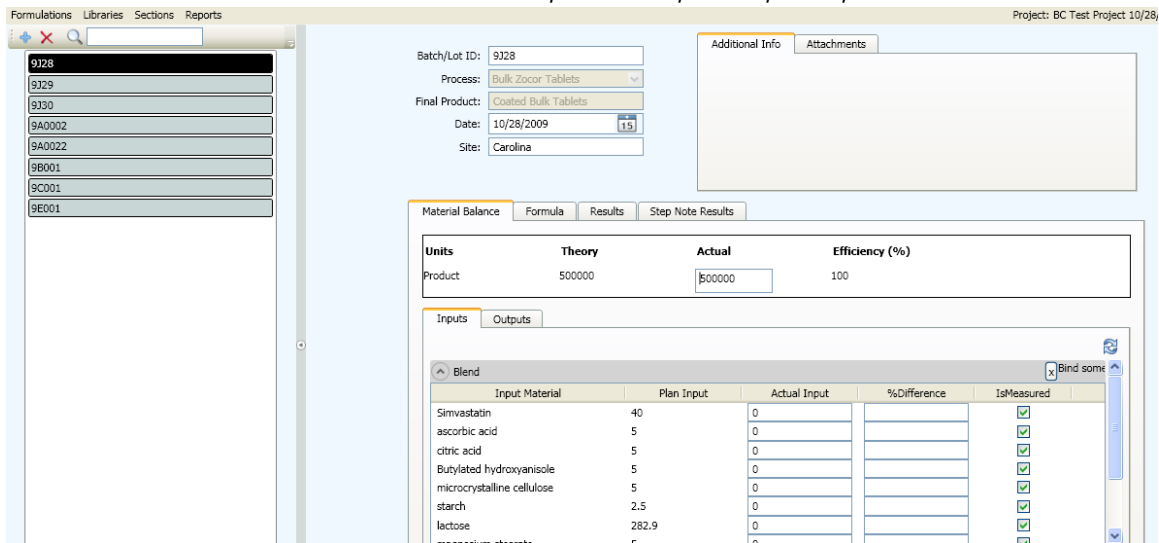


## Batches

Once a Process has set up in the application the user can record create batches. By using the Process information already in the system, the user can record results information on the batch, formula, analytical results, inputs, output, mass balance.




Enter Information such as Lot Number, Process, Date, Site, Quantities etc.



Results can be saved for a particular lot. Select the Specification that the lot was tested against, enter results and Save. Out of Spec results can be flagged.



Batch Information    Result

Specification Name :  

Assay	Specification	Method ID	Method Descripti	Attach Method	Results	Out Of Specification
Water by KF	Test for water				<input type="text" value="BLUE"/>	<input type="radio"/>



## Reports

The Application comes with the following reports.

Project Summary Report - Summary of Milestones information for a project.

Process Step Report - Summary of all Process Steps for a project.

The screenshot shows the 'Formulations' application interface. The 'Reports' menu is open, showing options for 'Project Summary Report', 'Process Step Report' (which is selected), and 'Batch Formula Report'. Below the menu, the 'Process Step Report' is displayed for the 'NewAPI Project' as of '11-03-2009'. The report contains two tables of process steps.

Step Type		Dry Milling	
Step	Material	Route Of Administration	Comments
Granule Milling	Milled Granulated NewAPI	Oral	
Step Type		Blending, Powder	
Step	Material	Route Of Administration	Comments
NewAPI Granule	Blended	Oral	

Batch Formula Report - Provide a Summary of the Formula Content By Batch for a particular project.