



## Summary of New Features and Functionality in *ASAPprime*® v5:

- Ability to import multiple data sets from single Excel file (LOAD SPECIAL)
- Custom excipients/blends can be added by users to subsequent session use
- Warnings when *ASAPdesign*™ involve significant extrapolation
- Ordering of analyses to reduce systematic errors
- More options for outputting tables and graphs
- Fully validated for Windows™ 7/8/10
- 21 CFR Part 11 compliant
- Customizable default file locations for sessions, data, parameters & reports (CUSTOM DIRECTORY)
- Ability to display all isoconversion plots simultaneously
- Calculation of critical RH by solubility
- New excipient and packaging options added to default database
- Ability to use PPM when entering degradation data
- Added the cross-validated  $R^2$  ( $Q^2$ ) to the Arrhenius model factors

# Additional Support For Selected New Features in ASAPprime® v5

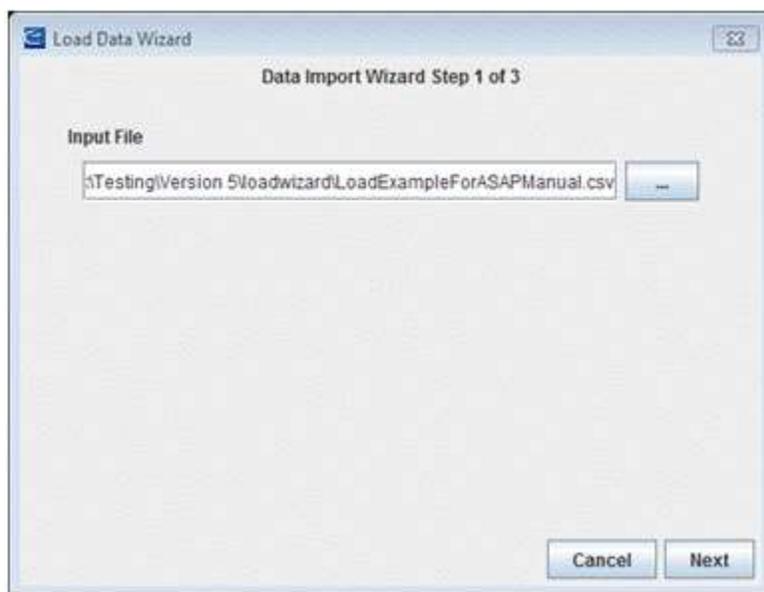
## Enhanced Data Handling Features:

**LOAD SPECIAL** – ASAPprime® can now conveniently add multiple data sets from a single Excel file.

When this option is used, the program first clears any data currently in the data table. The program then starts a Wizard that allows loading a file containing data (including multiple degradant or potency columns) for populating the table.

The Load Special Wizard consists of three panels to load the file, assign the data columns and read the data into the table.

### *Step 1 of 3: File input*

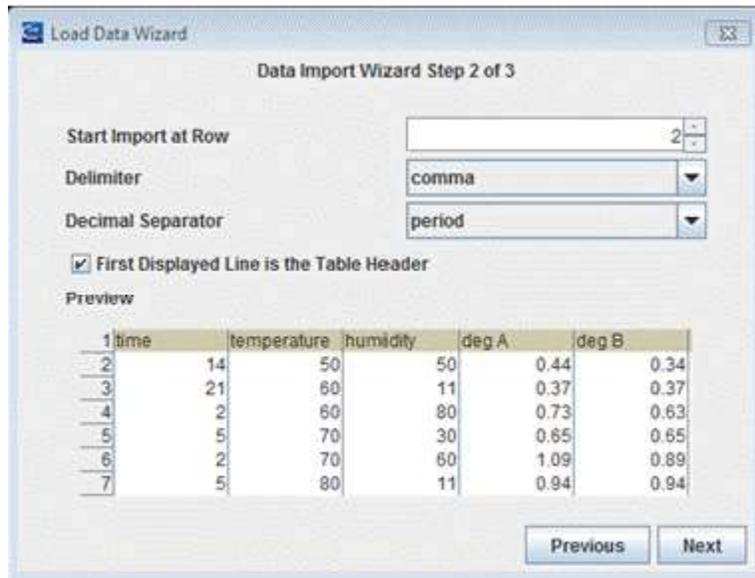


The Load Special Wizard needs to know the name of the file containing the data and some information about the data. The Load Special Wizard assumes that the data in the file is in the units currently in use by the program; therefore, the appropriate options (%degradant, ppm degradant or potency, whether humidity is considered and the units for the time) should be set in the main program before starting the Load Special Wizard. To cancel the Load Special Wizard at any point in the process, click on the “x” in the upper right hand corner of the panel.

Input File: The file containing the data.

Once the file name is specified, press “Next” to continue to the next step or “Cancel” to quit the Wizard.

### **Step 2 of 3: File type**



The Load Special Wizard needs to know some information in order to correctly parse the input file. The top portion of the panel is for gathering that information and the bottom portion of the panel (Preview) shows how the Load Special Wizard is currently interpreting the file.

*Start Import at Row:* The Load Special Wizard allows skipping any number of lines at the top of the file. The Preview table will update to show only the start of the rows that will be saved in the new file (and the header line, if appropriate).

*Delimiter:* This is the character that separates columns of data. By default the Load Special Wizard assumes the file is comma-delimited, but a tab, semi-colon or space can also be used to separate data columns.

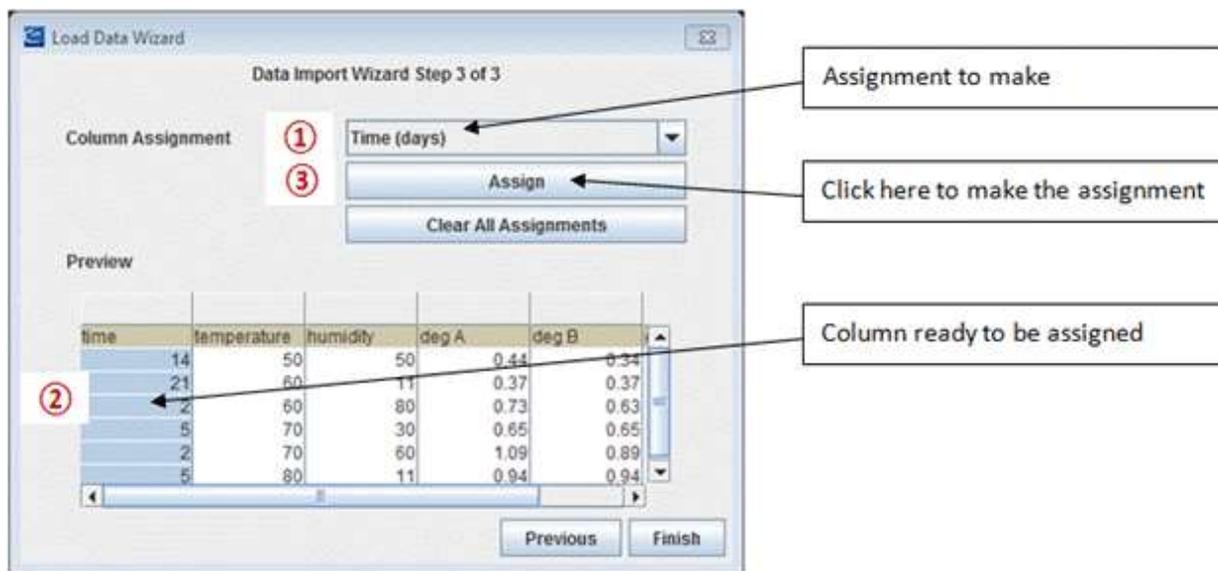
*Decimal Separator:* ASAPprime® expects numbers to use a period (“.”) as the decimal point. If the input data uses a comma (“,”) as the decimal point, the Load Special Wizard can make this conversion.

*First Displayed Line is the Table Header:* The Load Special Wizard allows one line to be retained in the display, which is not stored in the output files, but which can be useful for reference when selecting columns. This line must be the last line in the file prior to the first line of data. It must be delimited in the same way as the data lines and should contain the same number of fields as there are data fields.

*Preview:* This table shows how the Load Special Wizard is interpreting the options discussed above. If a header line was requested, it will appear highlighted in gray. A vertical line will be

drawn between the data values to indicate how the data is parsed using the current delimiter. Columns of numbers should appear right-justified. If they are left-justified, the Load Special Wizard is unable to parse the numbers and will treat them as strings.

### Step 3 of 3: Column Assignment



To unassign a column, choose the assignment option that is blank. The Assign button will switch to Unassign. Select the column to unassign and then click the unassign button. The assignment will be returned to the list and can then be used for a different column.

**CUSTOM DIRECTORY** -- Users can customize file locations for ASAPprime® sessions, data, parameters and reports.

ASAPprime® has many cases where the user is asked to provide the name of a file or directory. To handle this task, there are several distinct types of file and directory browsers:

Sessions: For storing ASAPprime® sessions.

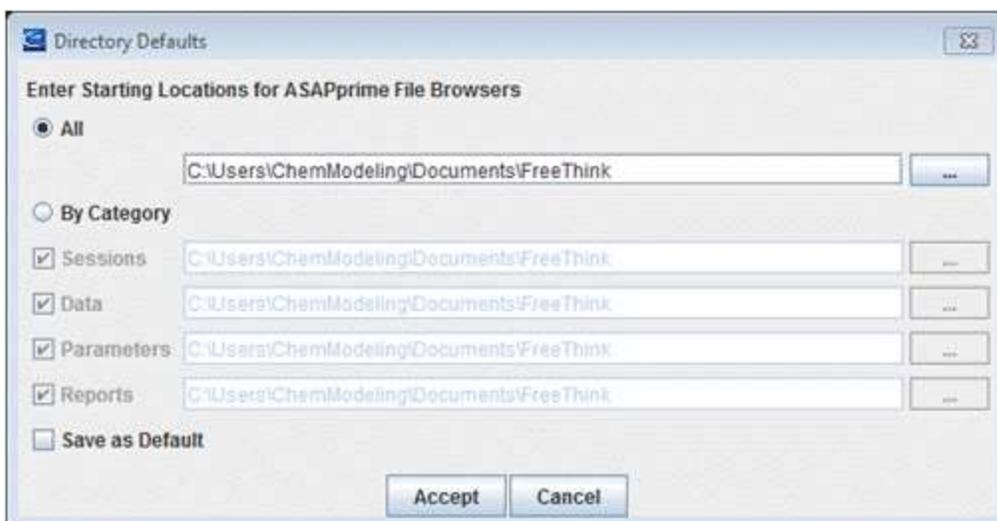
Data: For storing experimental data, such as degradation data.

Parameters: For storing parameters, such as excipient GAB values.

Reports: For storing reports generated by ASAPprime®.

When a browser of a particular type is first invoked in a program session, it opens with a pre-defined default location. The Custom Directories sub-dialog allows the user to set these default locations. (Note: the program tracks the user's last opened location for each browser type- so during a program session, the browser may open to a location other than the default).

The Directory Defaults sub-dialog is shown below.



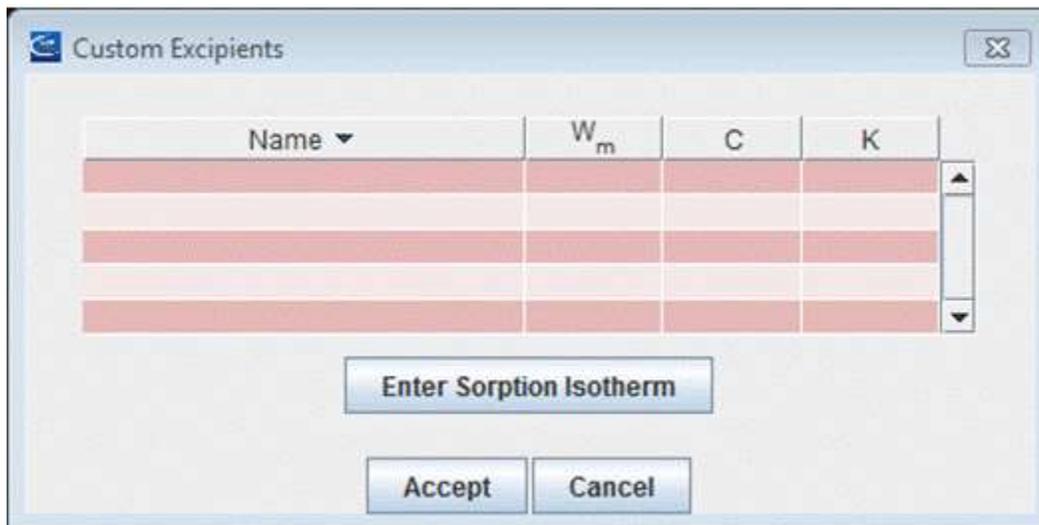
The radio buttons “All” and “By Category” allows one to toggle between setting the default for every browser type to the same location and setting default location of each browser type individually.

If “Save as Default” is checked and “Accept” is clicked, the program will save the locations in ASAPprime®’s program data directory. Each custom defaults file will be specific to a user.

Clicking “Cancel” will close the dialog without changing the custom defaults file.

## **Custom Excipients and Blends:**

ASAPprime® allows excipients (can include actives and/or formulations as well) to be added in addition to those supplied by the program. These additional excipients are stored in ASAPprime®'s program data directory with a separate custom file for each user. The dialog for adding custom excipients is shown below.



If the user has not defined any custom excipients, the custom excipients table will be empty. Once custom excipients have been defined, they will appear in the table. This dialog can thus be used for adding, modifying or removing custom excipients.

There are two methods for entering custom excipients:

- Directly, by supplying a name and appropriate GAB parameters for the excipient
- By supplying isotherm data for the excipient

The latter method is invoked by clicking “Enter Sorption Isotherm.” This brings up a sub-dialog almost identical to the dialog used to enter the GAB parameters for a dosage (Sorption Isotherm tab of the Dosage panel). A key difference is that in this case, GAB parameters for an “excipient” (or active or blend) are being entered as a component to the final blend rather than representing that final blend itself.

## Enter Sorption Isotherm

%RH	%water (exptl)	%water (calcd)

$W_m$      $C$      $K$

allow non-zero intercept

Compute

Accept    Cancel

GAB Predictions

wt% water

%RH

### Name of Excipient

Every excipient (or active or blend) needs a name by which it will be identified in the Material pulldown of the excipient table on the Excipients tab of the Dosage panel. Custom excipients will appear on the pulldown at the beginning of the list with an asterisk prepended to the name to indicate the excipient is not one of the program-supplied excipients (do not include the asterisk here). The name of each “excipient” must be unique.

### %RH vs %water Table

The table in the upper left of the dialog is where the %RH and % water data should be entered. Humidity measured as water activity ( $a_w$ ) should be converted before it is entered ( $RH = 100 * a_w$ ). The “%water (calcd)” column will be filled once the program has determined a set of GAB parameters for the data (Compute).

### Right Click Options %RH versus %water Table

- Add row: The user can enter values for weight percent water vs. RH one at a time. When more values need to be entered than the initial space allows, the user can add rows as needed by right clicking and hitting “add row”.
- Delete row: This option allows the user to delete the selected row.
- Save: This option allows the user to save the sorption isotherm data in an Excel CSV file. This file can be reloaded.
- Load: The user can load a previously stored sorption isotherm file (stored in Excel as a CSV file with the columns %RH, % water) with this option.
- Clear: The user can completely clear this table.

- Print: The user can print the sorption isotherm table with this option.

### **GAB predictions**

The table in the lower left of the dialog will contain the GAB parameters as determined by the program.

### **Allow non-zero intercept**

This should normally not be needed. *ASAPprime*® assumes that the %water in the dosage when the relative humidity is zero is also zero. If you do not believe this assumption is accurate for your data, you can allow the program to “float” the %water at zero %RH.

### **Compute**

This bar is clicked once the sorption isotherm data are entered. The program will try to fit the entered data to the GAB equation and show the best fit in the display. The program tries a number of initial guesses, so the calculation may take a few seconds. To best fit the data in the region of 10% - 70% relative humidity, the fitting function that was chosen minimizes the absolute value of the difference between the actual and computed relative humidity and biases against regions where the slope is high.

### **Accept**

Once the fitting is complete, choosing “Accept” will exit this dialog and add the new excipient to the table of custom excipients. For this action to be successful, a name must have been supplied and GAB parameters computed for the new excipient.

### **Cancel**

Close the dialog without using the sorption isotherm entered.

### **Completing the Sorption Isotherm Entry**

If the computed GAB parameters are accepted. The values will be transferred to the table of custom excipients. To save the new list of excipients choose “Accept” in the Custom Excipients dialog. To quit without saving the new excipients choose “Cancel.”

### **Accept**

Close the Custom Excipients dialog and update the custom excipients file.

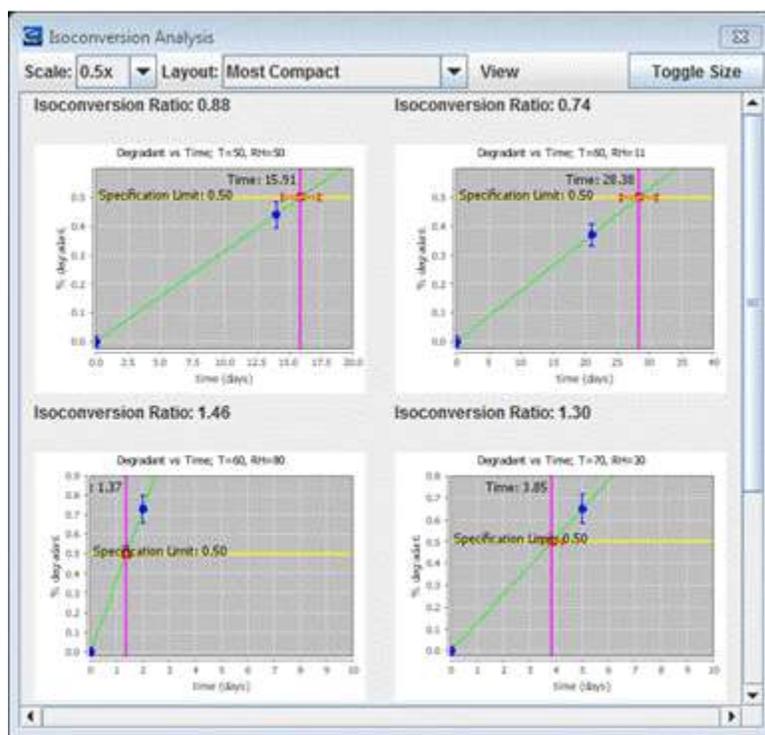
### **Cancel**

Close the Custom Excipients dialog without updating the custom excipients file.

## Expanded Data Analysis Options:

**ISOCONVERSION ANALYSIS** -- Users now have the option to view all isoconversion plots simultaneously. Users will also receive automatically generated warnings if the wizard-supplied DOE may impact the quality of predictions

This option produces a single dialog containing Degradant (Potency)/Time plots for all of the rows in the isoconversion table. Graphs are shown of the %degradant, ppm or %potency points at each of the conditions with the fit to the points at each condition. The fits will change with the different fitting options selected. These plots will remain displayed (without updating), so that multiple fit views can be displayed at once. The display will also show the error bars (one standard deviation) determined for each isoconversion condition. As designed, when isoconversion is extrapolated significantly from the data entries, the error bars for isoconversion will be large.



**Scale:** Sets the scale of the displayed plots relative to the size displayed with the “Plot” option. The available scaling factors are 2.0, 1.5, 1.0, 0.75, 0.67, 0.50 (default), 0.33 and 0.25.

**Layout:** Three layout options are provided for viewing the plots:

- **Most Compact:** Plots are sorted by temperatures and humidity then laid out in a rectangular grid.
- **One Temperature per Row:** Plots are sorted by temperatures and humidity then laid out such that all the plots in a given row contain conditions with the same temperature.
- **Temperature/RH Grid:** Plots are laid out so that each row represents unique temperature and each column represents a unique humidity (humidity values are rounded when assigned to columns, since saturated salt solutions produce slightly different humidity values at different temperatures).
- **View:** Allows viewing or hiding individual Degradant/Time plots. Each plot is listed by the condition (T/RH) for which the data were obtained.

- **Toggle Size:** Toggles the display of the Isoconversion Analysis dialog between full screen and its current dimension.

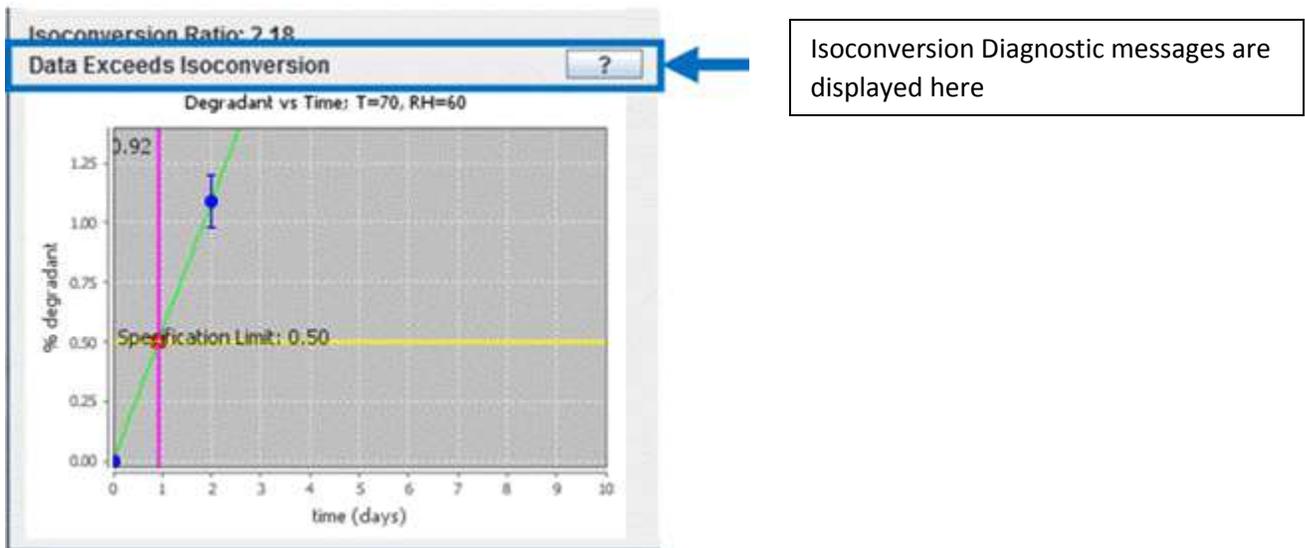
The Isoconversion Analysis dialog also supplies two lines of information for each plot.

### Isoconversion Ratio

The isoconversion ratio is the ratio between the time of the last measured data point and the calculated isoconversion time. Ideally, data points will straddle the isoconversion time. When the last measured point is either significantly earlier or significantly later than the isoconversion time, ASAP<sup>prime</sup>® will have more difficulty building a reliable model.

### Isoconversion Diagnostics

If the condition represents a case where building a reliable model may be more difficult, a second line of information will be provided identifying the problem.



Clicking on the “?” button will bring up more information as to the source of the problem and suggestions on how to resolve the issue.

### Save

This option stores the data in the calculated table as an Excel CSV file in a user-determined file location.

### Print

This option prints the table as shown.

### Copy to Clipboard

This option puts a copy of the table (formatted as in ASAP<sup>prime</sup>®) in the Windows clipboard. Once copied, the table can be pasted into applications that support the clip board, such as Microsoft Word and Excel. The table is copied in HTML format. In order for the paste to work properly, the program pasting the table must be able to understand HTML table format.

**For more information about the new features of *ASAPprime*® v5,  
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