PMI-LCA Tool Quick-Start Guide

For File Versions:

- ACSGCI_PR_PMI-LCA_V07.2P.xlsx

Contents

Introduction

Disclaimer

The PMI-LCA Tool is provided as-is without any warranty or guarantee of completeness, correctness, or accuracy.

Purpose

PMI-LCA Tool

The PMI-LCA Tool is a high-level estimator of Process Mass Intensity (PMI) and environmental life cycle information that can be customized to fit a wide variety of linear and convergent processes for synthesis of small molecule active pharmaceutical ingredients (APIs). An ecoinvent dataset is utilized as the source of the life cycle impact assessment (LCIA) data. By agreement with ecoinvent, no licensing fee is required for the use of the PMI-LCA Tool if the display is limited to six life cycle assessment (LCA) indicators. The indicators displayed are: Mass Net, Energy, Global Warming Potential (GWP), Acidification, Eutrophication, and Water. Collectively PMI and the six LCA indicators will be referred to as Metrics. Definitions for each of the metrics are below. By default, the PMI-LCA Tool will normalize steps to produce 1kg of API and display the contributions of steps and raw materials to each of the metrics in both tabular and graphical formats.

Metrics

The metrics described below are either directly calculated from the processing steps entered into the PMI-LCA Tool by the user (e.g., PMI and COG) or calculated by using that process information to produce a weighted sum of the LCIA values from ecoinvent (e.g., Mass Net, Energy, GWP, Acidification, Eutrophication, and Water). The metrics do not capture or describe utilities, waste products, or emissions from the process or from treatment of process waste streams.

Process Mass Intensity (PMI)

The total mass (in kg) of raw materials required to produce one kg of the API.

Mass Net

The total mass (in kg) of resources required for production of the raw materials needed to make one kg of the API. This excludes the mass of water consumed, which is calculated separately in the Water metric. This is a weighted sum of the LCIA data for each raw material.

Energy

The total energy (in MJ) required to produce the raw materials needed to make one kg of the API. This is a weighted sum of the LCIA data for each raw material and does not include energy expended in the processing steps entered in the PMI-LCA Tool.

Global Warming Potential (GWP)

The total carbon emissions (in kg CO_2 equivalents) associated with the production of the raw materials needed to make one kg of the API. This is a weighted sum of the LCIA data for each raw material and does not include any emissions from the processing steps entered in the PMI-LCA Tool.

Acidification

A measure of the propensity for raw material production to release protons into the environment (in kg SO_2 equivalents). This is a weighted sum of the LCIA data for each raw material and does not include any emissions from the processing steps entered in the PMI-LCA Tool.

Eutrophication

A measure of the propensity for raw material production to release nutrients (nitrates, phosphates) into the environment (in kg phosphate equivalents). Eutrophication can cause hypoxia, algal blooms, and other negative environmental shifts. This is a weighted sum of the LCIA data for each raw material and does not include any emissions from the processing steps entered in the PMI-LCA Tool.

Water

The total mass (in kg) of water required for production of the raw materials needed to make one kg of the API. This is a weighted sum of the LCIA data for each raw material.

Tutorials

Follow these tutorials in the sequence they are presented to use the PMI-LCA Tool without knowing how it works. The tutorials assume basic familiarity with Microsoft Excel, although some procedures are reviewed as necessary.

Tutorial 00: Familiarization and Navigation

Topics Covered

- General tool overview and navigation
- Enabling iterative calculations
- Use of in-cell dropdown menus
- Common Excel warnings

Instructions

1) Make a copy of the PMI-LCA Tool template and save it to a local directory on your computer (i.e., not OneDrive or other Cloud server or networked drive).

2) Open the file.

   If the following alert message appears, click 'OK' to dismiss the notification.
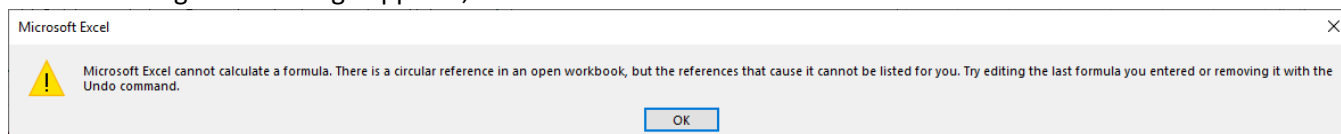
   (The text reads:

   > Microsoft Excel cannot calculate a formula. There is a circular reference in an open workbook, but the references that cause it cannot be listed for you. Try editing the last formula you entered or removing it with the Undo command.

   The tool relies on circular references to perform iterative calculations, but iteration is disabled in Excel by default. Iterative calculations will be enabled for this file in Step 5 below.)

3) Find the Sheet tabs at lower left of the Excel window. The file should open in Sheet **Introduction**.
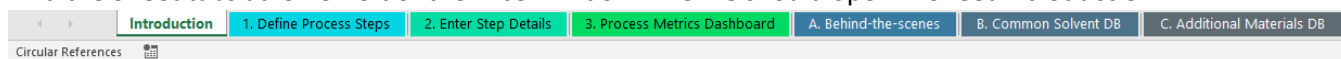
   Note that the text 'Circular References' may appear in the status bar beneath the Introduction Sheet Tab, as a reminder that iterative calculations have not been enabled.
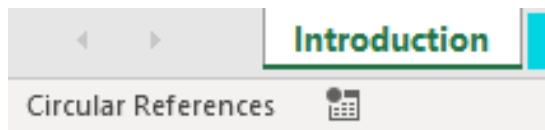
4) If AutoSave is enabled by default, **disable it** for this file. It is important to save work regularly, but the AutoSave feature may interfere with iterative calculations.

5) Follow the on-screen instructions to enable iterative calculations. (This graphic is included in the tool as a reminder that iterative calculations may need to be enabled each time a new tool file is opened.)

BEFORE YOU BEGIN:

1. Save all open documents and files and (if possible) close other work or software programs that may interfere with Microsoft Excel.

2. Save a copy of this tool so that you always have a 'Fresh' version from which to start your work.

3. Under "File" ⇨ "Options" ⇨ "Formulas" ensure that the box titled "Enable iterative calculation" is checked with the settings as shown.

4. Delete this image and proceed. Remember to save your work often!

☑ Enable iterative calculation

Maximum Iterations: 100

Maximum Change: 0.001

Iterative calculations menu in Excel Version 2202
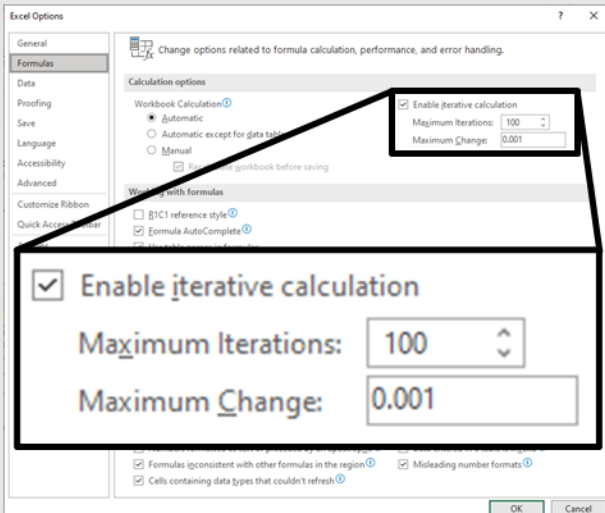
6) To verify that iterative calculations have been enabled, confirm that the 'Circular References' notification in the status bar has changed to read 'Calculate'.

Introduction

Calculate
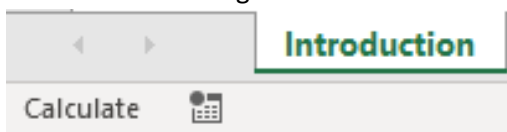
7) Review the remaining information on Sheet **Introduction**.

8) Navigate to Sheet **1. Define Process Steps**.
As the name suggests, this sheet is where the user defines the steps that make up the process to be evaluated. A step can be an individual unit operation such as a chemical reaction, preparation of a solution or mixture, a physical transformation like crystallization or drying, or other actions like packaging. A step can also be any convenient *sequence* of unit operations. The only restriction placed on what can be defined as a step is that it must have one or more specific defined input(s) with known mass(es), and one product stream, also with a known mass.

Note: under certain circumstances, a step can also be used to define a raw material. This is explored in more detail in Tutorial 01: Recrystallization of NaBr.

9) Review the yellow table headings: **Name**, **Real or Virtual?**, **Product Display Name**, and **Reference**. In general, only cells identified with a heading highlighted in yellow and emphasized with an arrow require data input. Images of chemical reaction schema may be pasted into the Scheme column if desired.

	A	B	C	D	E
5	↓	↓	↓	↓	→
6	Name	Real or Virtual?	Product Display Name	Reference	Scheme
7	Placeholder Step	Real	Placeholder Product	Placeholder Process Description § 1	
8	PACKAGE	Real	Packaged Placeholder Product	PACKAGE	

10) Click on each of the first five grey cells and read the popup instructions associated with each.

	A	B	C
5	↓	↓	↓
6	Name	Real or Virtual?	Product Display Name
7	Placeholder Step	Real	Placeholder Product
8	PACKAGE		Packaged Placeholder Product
9			
10	NOTE: Do		v, in this version of the tool it is nece:
11	freedom		ator, and the name "PACKAGE" is a re
12			
13			

Instructions:
Enter the step name.
Step name must be a unique identifier.

Tap 'Esc' to close this popup.

As the column headings and popup instructions indicate, each row in this Table is a representation of a unique step, and steps have associated information such as the **Name**, the **Real or Virtual?** parameter (discussed below), the name of the step's product, and any links to reference documents. Use of the PMI-LCA Tool to analyze a process involves inserting rows to this Table, with each row defining a new step**,** and the sequence of steps building up to a complete description of the chemical process. By default, the Table is populated with two rows: the Placeholder Step row (which will be modified), and the PACKAGE row (which should not be modified).

The *row* for the Placeholder Step therefore represents a unit operation (or sequence of unit operations) *called* the Placeholder Step. This row is provided as a template for the user to modify and follow when entering additional steps (additional rows) into the Tool, and the name 'Placeholder' is intended to convey that this is the space where the user will fill in the details of their specific process. The user can overwrite the Placeholder Step row, as well as insert as many new rows as required to define each of the steps in the process to be evaluated.

The PACKAGE row is required by the tool to fix the *basis* of calculation (i.e., 1 kilogram of API). It can be helpful to think of the PACKAGE row as describing the final unit operation, in which 1kg of final product is packaged into a drum (regardless of whether or not this is actually performed in processing). Unlike typical processing steps that follow the template of the Placeholder Step, there can be only one PACKAGE step, and it is limited to just one material input which is intended to be the final product or API.

Note that the tool automatically identifies Packaged Placeholder Product as the final product or API.

	A	B
2	**Name of Final Product Selected From Current Process Information:**	Packaged Placeholder Product

This works because the Tool 'knows' the **Name** of the material input to the PACKAGE step. By default, the product of the Placeholder Step is the input to the PACKAGE step. Note that relationships between steps (including defining

which material is being packaged) are defined by the user in Sheet **2. Enter Step Details**, which is discussed below.

11) Navigate to the Sheet titled **2. Enter Step Details**
    As the name suggests, this sheet is where the Tool captures the *details* of each step defined on Sheet **1. Define Process Steps.** The details pertain to the identity, classification, and masses of the inputs to each step, as well as the mass of the product of each step. By indicating that the product of one step is an input to another, a directional (or *directed*) relationship between those steps is established.

12) Examine the headings and popup instructions. Note that the first few yellow headings have additional, more detailed instructions than the cells below them. Again, note the yellow highlighting and emphasis arrows indicating which columns require data. Do not directly modify the contents of cells in blue-highlighted columns or the blue cells corresponding to the `PACKAGE` step.

	A	B	C	D	E	F	G	H	I
3	↓	↓	↓	↓	↓	↓	↓	↓	→
4	Step Name	Input or Output	LCA Data Source Class	LCA Data Source Subclass	Display Name	Physical	Step Instructions	Notes	Reviewer Comments
5	Placeholder Step	Input	iGAL_Aligned_Organic	Default iGal Aligned Organic Reagent	Placeholder RM	1.00	1) Charge 1X (basis) Placeholder RM	1kg = 1X basis	
6	Placeholder Step	Output	None	None	Placeholder Product	1.00	2) Isolate 1kg Placeholder Product	This gets packaged	
7	PACKAGE	Input	Process_Steps	Placeholder Step	Placeholder Product	1.00			
8	PACKAGE	Output	None	None	Packaged Placeholder Product	1.00			

In this Table, there are four rows. The first two are associated with the `Placeholder Step` that was defined in Sheet **1. Define Process Steps**. The first row specifies that the `Placeholder Step` takes a `1.00 kg` charge of `Placeholder RM` as an input, and that the `Placeholder RM` borrows LCA metric values from the default iGAL aligned organic reagent. The second row specifies that `Placeholder Step` yields `1.00 kg` of `Placeholder Product`. The product is identified as such by the `Output` label in the **Input or Output** column. Note also that the **Display Name** is identical to the value in the **Product Display Name** column and `Placeholder Step` row in Sheet **1. Define Process Steps**. This is how a typical step will be defined with one or more inputs of a specified mass and LCA classification, and a single output also with a defined mass. Any pertinent information on stoichiometry, yield, or purity or an input or output must be reflected in the mass for that material.

The second two rows of the table (in blue) are unique to the `PACKAGE` step, and should not be modified except by experienced users. Generally, the format of the `PACKAGE` step is the same as any other, except that it is pre-defined to have an output of `1.00 kg` which is necessary to correctly constrain the iterative calculation that is performed to re-scale the process steps. The value `Process_Steps` in the **LCA Data Source Class** column indicates that the input to the `PACKAGE` is the product of a previous processing step. The specific step is selected according to the entry in the **LCA Data Source Subclass** column. In this case, it is the product of `Placeholder Step` that is being packaged, and the **Display Name** `Placeholder Product` is filled in automatically.

13) At the bottom of the sheet, a graphic with some examples of in-cell calculations is provided:

Examples of Common Calculations

Charging a complex reagent with a special metal:

Template:

$$Metals\ Mass\ [kg] = \frac{(Overall\ Mass\ [kg])}{(Overall\ MW)} \times \sum(Metals\ MW)$$

$$Nonmetals\ Mass\ [kg] = \frac{(Overall\ Mass\ [kg])}{(Overall\ MW)} \times \sum(Nonmetals\ MW)$$

Example: Charge 1.5kg of lithium bis(trimethylsilyl)amide.

LCA Data Source Class	LCA Data Source Subclass	Display Name	Physical Mass (kg)
Non_iGAL_Aligned_Organic	Default Non-iGAL Aligned Organic Reagent	bis(trimethylsilyl)amide	=1.5/167.33*160.39
Special_Metal	Lithium	Li+	=1.5/167.33*6.94

Define a solution by weight percent or mass fraction

Template:

$$Solute\ A\ Mass\ [kg] = (Solute\ A\ weight\ \%)$$
$$Solute\ B\ Mass\ [kg] = (Solute\ B\ weight\ \%)$$
$$Solvent\ Mass\ [kg] = (100 - \sum Solute\ wt\ \%)$$
$$Output\ Mass\ [kg] = 100\ (or\ \sum Solvent + Solute)$$

Example: Aqueous solution with 10 wt% NaCl and 5 wt% $MgCl_2$

	Input or Output	LCA Data Source Class	LCA Data Source Subclass	Display Name	Physical Mass (kg)
4					
5	Input	Common_Inorganic	Default Inorganic Material	Sodium Chloride	10
6	Input	Common_Inorganic	Default Inorganic Material	Magnesium Chloride	5
7	Input	Common_Solvent	water, deionized	Water	=100-(F5+F6)
8	Output	None	None	Example Solution	=SUM(F5:F7)

Define a solution by molarity

Template:

$$Solute\ Mass\ [kg] = (Molarity\ of\ Solution) \times \left(Solute\ MW\ \left[\frac{g}{mol}\right]\right) \times \left(\frac{1\ [kg]}{1000\ [g]}\right)$$

$$Solvent\ Mass\ [kg] = (1\ [L]) \left(solution\ density\ \left[\frac{kg}{L}\right]\right)$$

$$Output\ Mass\ [kg] = (\sum solvent + solute)$$
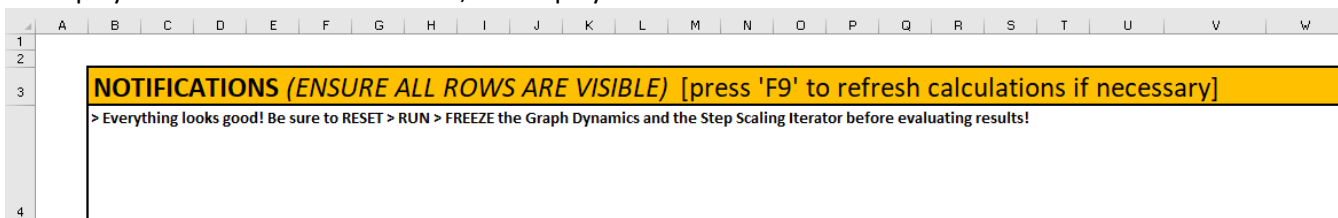
Example: 2M KOH in water (neglecting solvent density change)

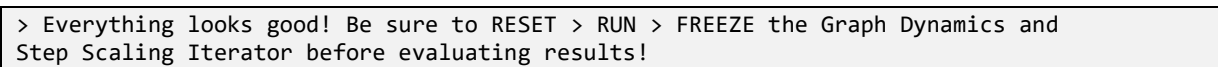|	Step Name	Input or Output	LCA Data Source Class	LCA Data Source Subclass	Display Name	Physical Mass (kg)
4						
5	Placeholder Step	Input	Common_Inorganic	Default Inorganic Material	Potassium Hydroxide	=2*56.105/1000
6	Placeholder Step	Input	Common_Solvent	water, deionized	Water	=1*1
7	Placeholder Step	Output	None	None	Placeholder Product	=F6+F5

The use of these calculations will be explained in more detail later.

14) Navigate to the third Sheet titled **3. Process Metrics Dashboard** and note the various headings.

15) First review the **NOTIFICATIONS** area, where any warnings or errors identified by the tool's self-error-checking will be displayed. If no errors are detected, the display should look like this:


If no errors are detected, the **NOTIFICATIONS** area should read:

```
> Everything looks good! Be sure to RESET > RUN > FREEZE the Graph Dynamics and
Step Scaling Iterator before evaluating results!
```

16) The next section, down the page from NOTIFICATIONS, is the **Process Network Graph**, which has additional inputs and troubleshooting instructions. This area will display the process topology as a directed graph. This graph may be useful for identifying errors in data entry or previewing an entire process. Note that the heading title **Process Network Graph for the Synthesis of Packaged Placeholder Product** refers automatically to the final product that the tool has identified from Sheet **1. Define Process Steps**.
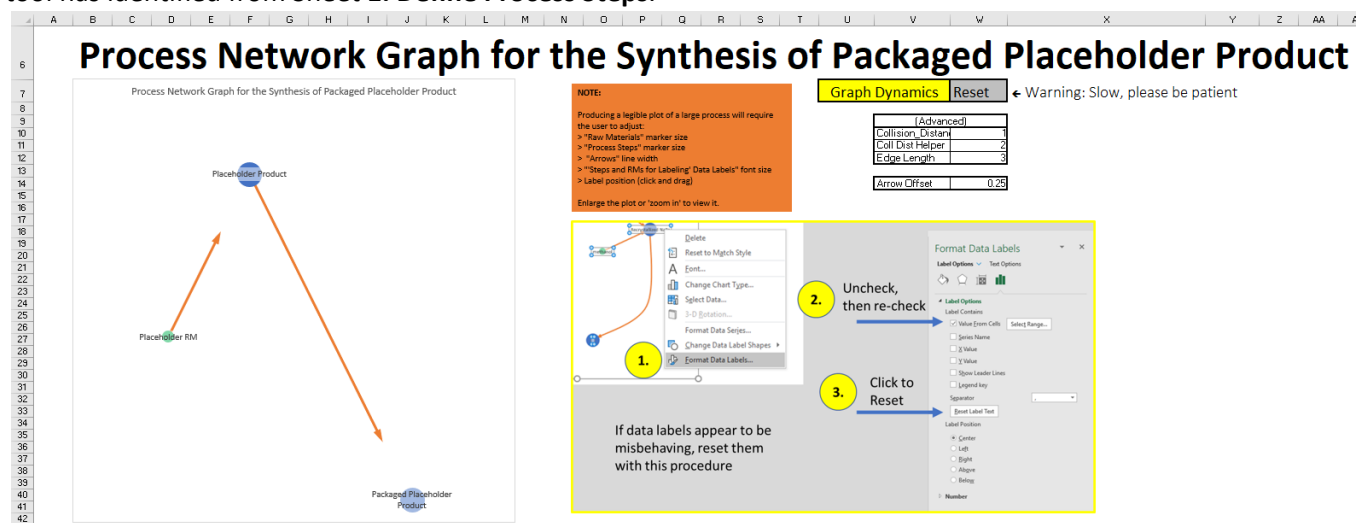

The process network graph should currently consist of three nodes connected by arrows. Each node is automatically labeled according to the information entered in the previous Sheets:
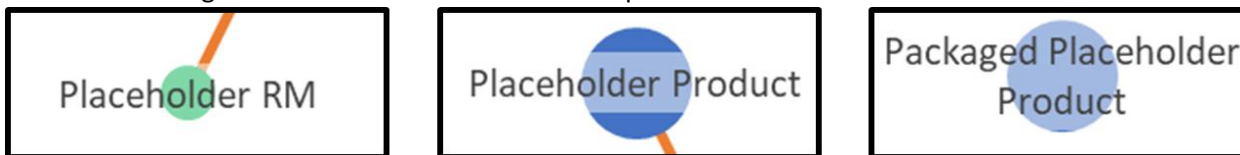
The arrows between the nodes are drawn automatically based on the inter-step relationships generated in Sheet **2. Enter Step Details**. This **Process Network Graph** illustrates that `Placeholder RM` is an input to the step producing `Placeholder Product`, which in turn is used to produce `Packaged Placeholder Product`. The plot layout (i.e., the positions of the drawing elements) is determined automatically. The layout is a Force-Directed Graph.

17) The Graph Dynamics dropdown is used to **Reset**, **Run**, and **Freeze** the iterative calculation that is required to achieve a plot layout.
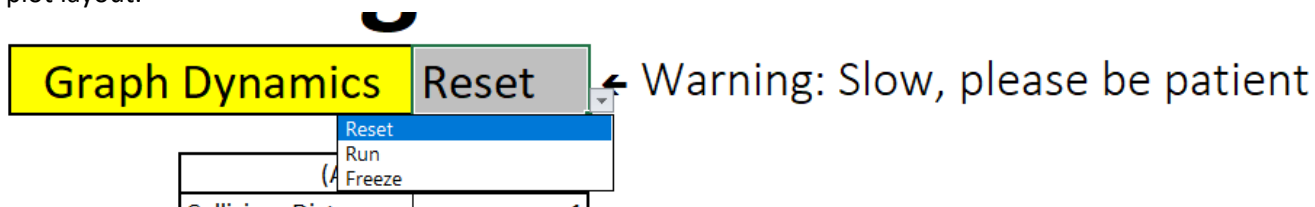

It is necessary to regenerate the layout anytime steps are added or removed, or when the relationship between steps has been modified.

NOTE: Do not set the Graph Dynamics iterator to 'Run' mode while modifying inputs as this may cause Excel to become slow and unresponsive. When the iterator is in 'Run' mode avoid clicking anywhere within Excel until the calculation is complete.

18) Scroll further down the page to the **Overall Process Metrics** section which will concisely summarize the PMI and LCA metrics for your entire process.

If this warning appears while scrolling down click 'OK' to dismiss:
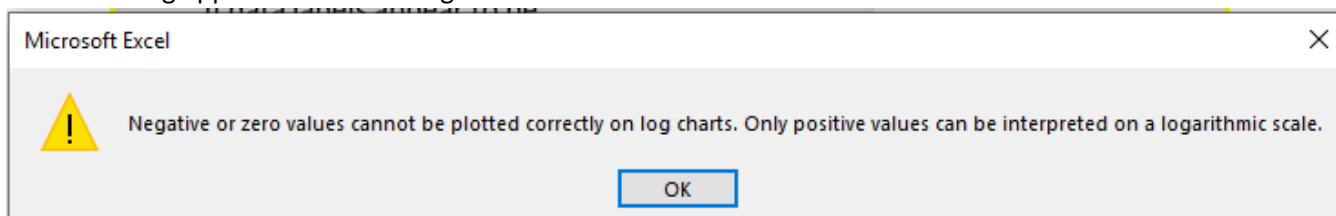
(The text reads:

Negative or zero values cannot be plotted correctly on log charts. Only positive values can be interpreted on a logarithmic scale.

This warning appears because the two plots immediately below have logarithmic Y-axes and are expecting non-zero values. However, one of the data series, **COG (USD)**, has no data, and only zero values are available.).
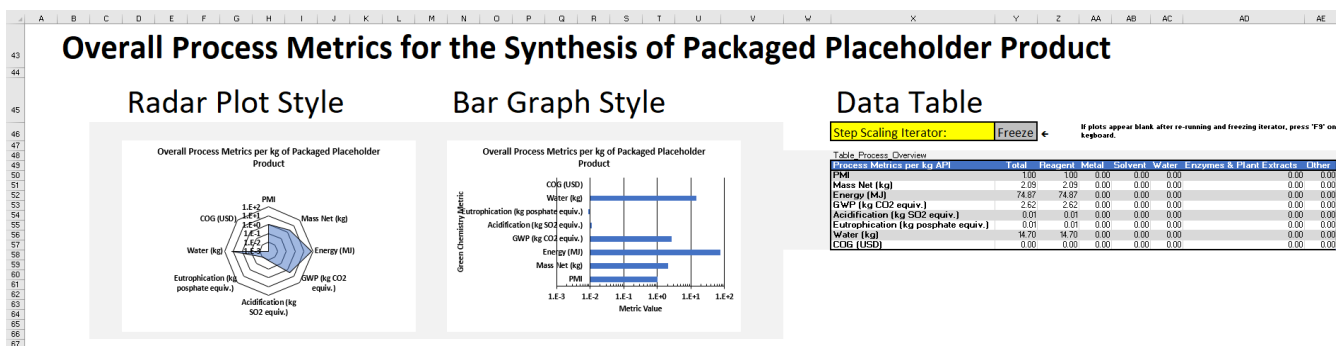
19) Take note of the **Data Table** on the right. At this point, it should display only the LCA metric values for the default iGAL aligned organic reagent (which was selected as the only process input in Sheet **2. Enter Step Details**).

The two plots in this section display the same data, but in different styles. The source of the data for the two plots is the **Total** column in the **Data Table**. Associated with the **Data Table** is another iteration control box:
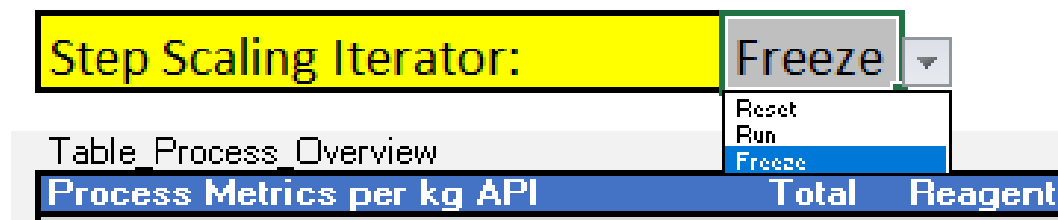

This dropdown controller is used to **Reset**, **Run**, and **Freeze** the iterative calculation that rescales all steps to the basis provided in the PACKAGE step (typically 1kg of API). Iteration is necessary for this calculation because the tool is setup to handle recycle loops, in particular to capture significant seed charges in crystallization steps. The Step Scaling Iterator should be reset and re-run any time changes are made to the process. The iterator will only converge correctly for processes that are input correctly and adequately constrained. Results should always be double-checked and validated independently.

NOTE: Do not set Scaling Iterator to 'Run' mode while modifying inputs as this may cause Excel to become slow and unresponsive. While the iterator is in 'Run' mode avoid clicking anywhere within Excel until the calculation is complete.

20) The next section down the page provides a pie chart for each PMI-LCA metric showing the contribution of each material class to that metric. The Placeholder Step has only one material input, so these plots are not very interesting at this stage of the tutorial.
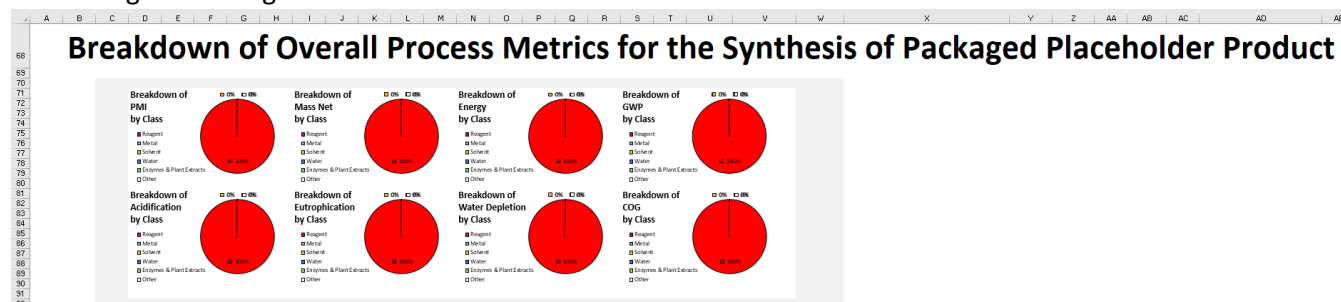
21) Finally, there should be a section with 16 additional plots, which will display a more detailed breakdown of each green chemistry metric (or cost of goods) by material input and by processing step. This section is useful for identifying potential areas for improvement within a process. The Synthesis of Placeholder Product has only one step and one raw material, so these plots are also not very interesting at this stage.
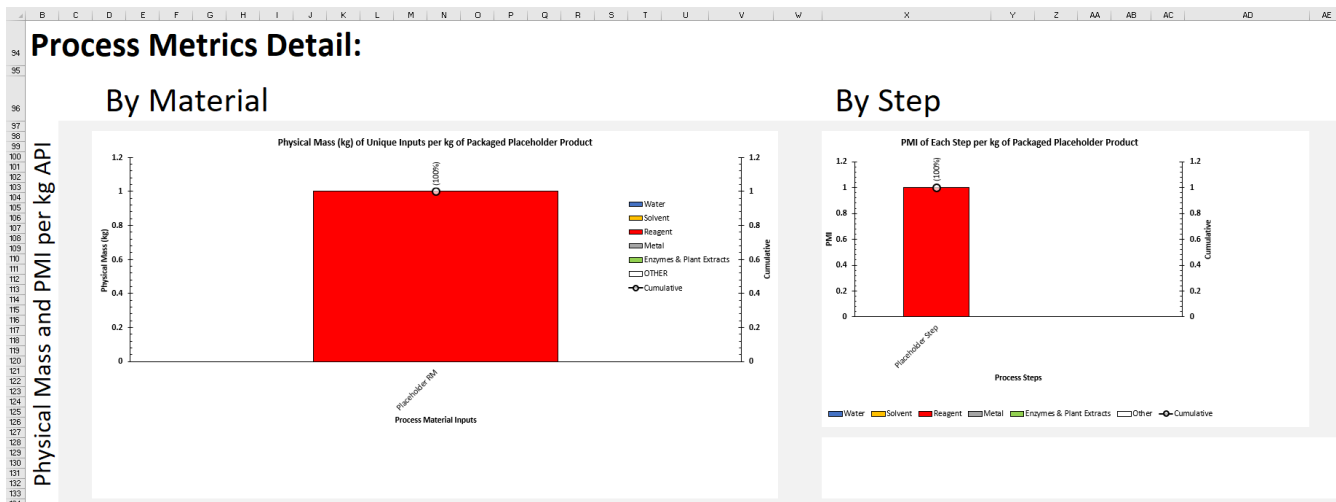
Note that the two COG plots at the bottom will appear blank because no raw material costs are included with this tool.
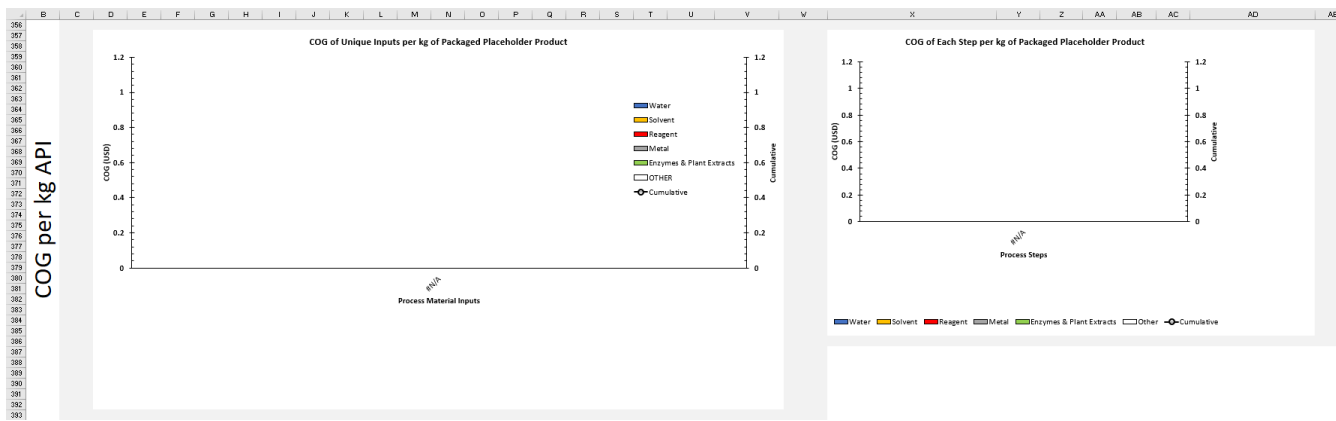
22) Navigate through the remaining sheets.

Sheet **A. Behind-the-scenes** contains helper Tables that define dropdown list options, as well as the **Messages** table that evaluates which alerts to display in the **Notifications** area on Sheet **3. Process Metrics Dashboard**. Sheet **A. Behind-the-scenes** also contains **Table_Arrow_Cords** which supports the functionality of the **Process Network Graph** that is displayed on Sheet **3. Process Metrics Dashboard**. If you are working on a very long process, you may see a warning in the **Notifications** area asking you to add a certain number of additional rows to Table_Arrow_Cords.

Sheet **B. Common Solvent DB** has one long Table that contains all of the solvents that are available for use as raw materials when entering the details of processing steps. Each solvent in the Table also has LCIA metrics provided from ecoinvent, and a column to add pricing information.

Sheet **C. Additional Materials DB** contains tables with LCIA metrics for iGAL aligned organic reagents, non-iGAL aligned organic reagents, common inorganic reagents, enzymes and plant extracts, and a selection of metals (with

some literature recycling values). Additionally, there is a **Custom_Material** Table where the user can organize additional custom materials.

Tutorial 01: Recrystallization of NaBr

Topics Covered

- Process data entry
- Evaluating common errors in the **NOTIFICATIONS** area
- How to handle common plotting bugs
- **Real** and **Virtual** processing steps
- Seeded crystallization (with a recycle loop)
- Double-checking results with manual calculation
- Cost of Goods (COG) analysis
- Adding custom materials and reagents

Process Description

According to solubility data presented in *J. Chem. Eng. Data* 2005, 50, 1, 29-32, the solubility of NaBr in water is 48.620 wt% and in a mixed solvent of ≈1:1 water:methanol (salt-free mass basis) it is 35.862. Let's assume we have developed a process to recrystallize NaBr from water beginning with a 45 wt% solution, to which we add enough methanol to bring the salt-free-basis water content down to 50%. By filtration, we will recover 98% of the NaBr that precipitates.

Instructions:

NOTE: Be sure to save and close any open files before you start, and to save your work as you go!

1) Return to Sheet **1. Define Process Steps** and overwrite the text `Placeholder Step` in the **Name** column with the text `Dissolve NaBr`. Under **Product Display Name**, type `45 wt% NaBr (aqueous)`. Under **Reference**, type `Tutorials Section 01 Step 1` or `Tutorials § 01 Step 1`. The Section Sign glyph (**§**) is not required, but it is more concise.

	A	B	C	D
5	↓	↓	↓	↓
6	**Name**	**Real or Virtual?**	**Product Display Name**	**Reference**
7	Dissolve NaBr	Real	45 wt% NaBr (aqueous)	Tutorials § 01 Step 1
8	PACKAGE	Real	#N/A	PACKAGE

NOTE - the Section Sign glyph is under **Insert ⇨ Symbol ⇨ Latin-1 Supplement**:
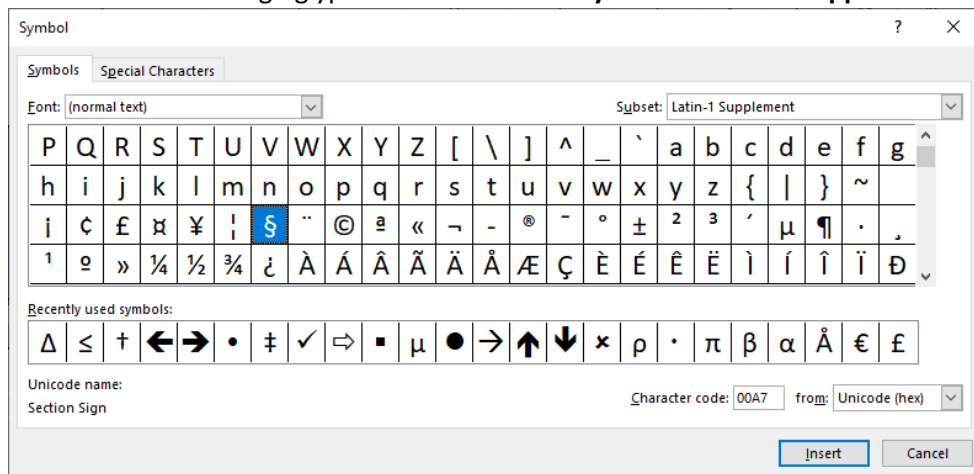
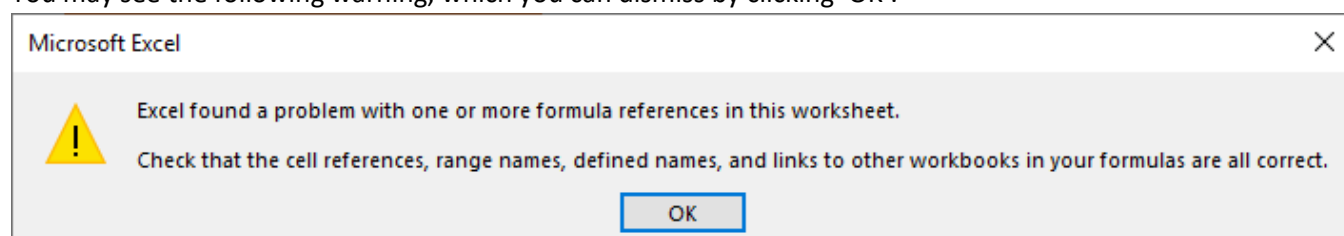2) Navigate to Sheet **2. Enter Step Details**. Notice that the first two rows in the Table are both still associated with `Placeholder Step,` which no longer exists. It is important to remember that editing a step name in Sheet **1. Define Process Steps** will not automatically update the name in Sheet **2. Enter Step Details**. This is also broadly true for any change made to an item that supplies a dropdown list after that item has already been selected in a dropdown.

Don't fix it yet! We'll update the name in a moment, but first we'll demonstrate the issues a mismatched Step Name can cause, so that the error can be more easily recognized during troubleshooting if it recurs in the future.

	A	B	C	D	E
3	↓	↓	↓	↓	↓
4	Step Name	Input or Output	LCA Data Source Class	LCA Data Source Subclass	Display Name
5	Placeholder Step	Input	iGAL_Aligned_Organic	Default iGal Aligned Organic Reagent	Placeholder RM
6	Placeholder Step	Output	None	None	Placeholder Product
7	PACKAGE	Input	Process_Steps	Placeholder Step	#N/A
8	PACKAGE	Output	None	None	#N/A

You may see the following warning, which you can dismiss by clicking 'OK'.

> **Microsoft Excel** ✕
>
> ⚠ Excel found a problem with one or more formula references in this worksheet.
>
> Check that the cell references, range names, defined names, and links to other workbooks in your formulas are all correct.
>
> [OK]

The text reads:

```
Excel found a problem with one or more formula references in this worksheet.

Check that cell references, range names, defined names, and links to other workbooks in your
formulas are all correct.
```

3) Navigate back to Sheet **3. Process Metrics Dashboard**. Depending on the tool version you may also see this warning:
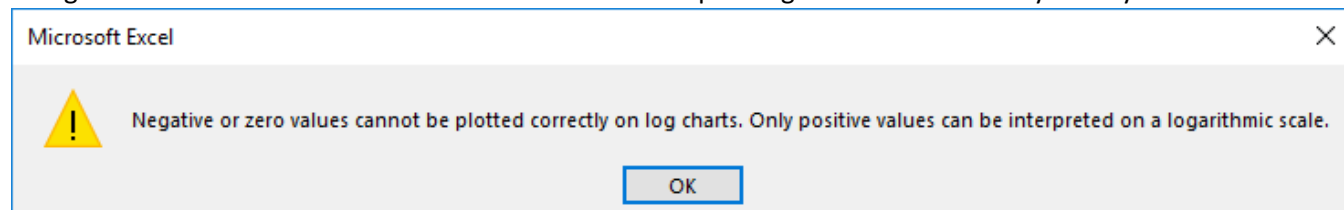
> **Microsoft Excel** ✕
>
> ⚠ Negative or zero values cannot be plotted correctly on log charts. Only positive values can be interpreted on a logarithmic scale.
>
> [OK]

The text reads:

```
Negative or zero values cannot be plotted correctly on log charts. Only positive values can be
interpreted on a logarithmic scale.
```

Click 'OK' on the alerts above and the **Overall Process Metrics** plots will go blank:
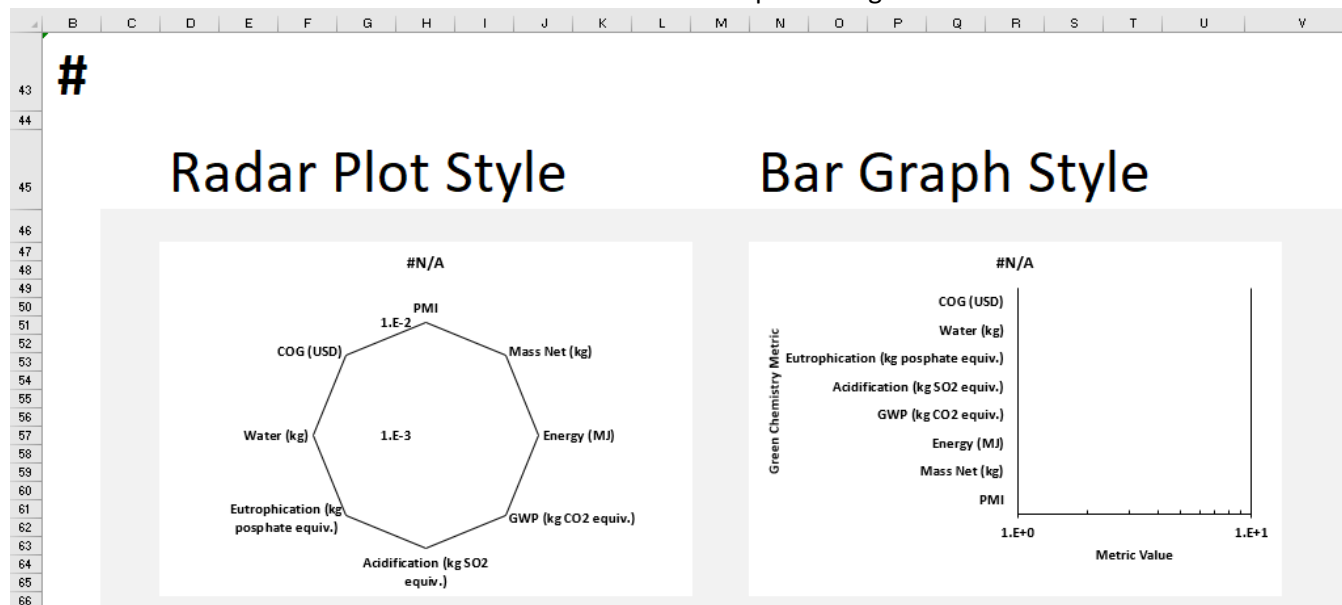
The Tool identifies the issue by displaying new messages in the **NOTIFICATIONS** area:
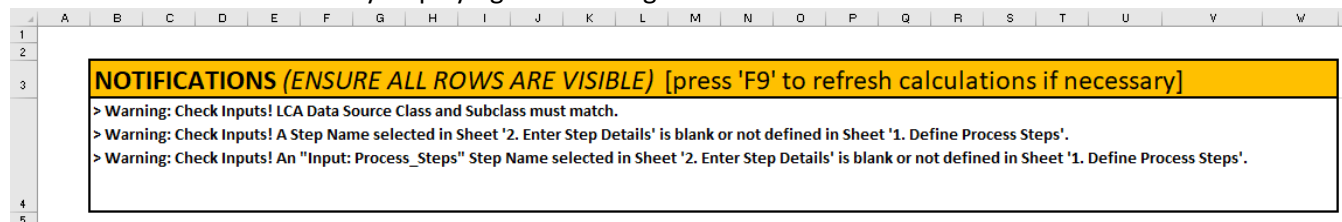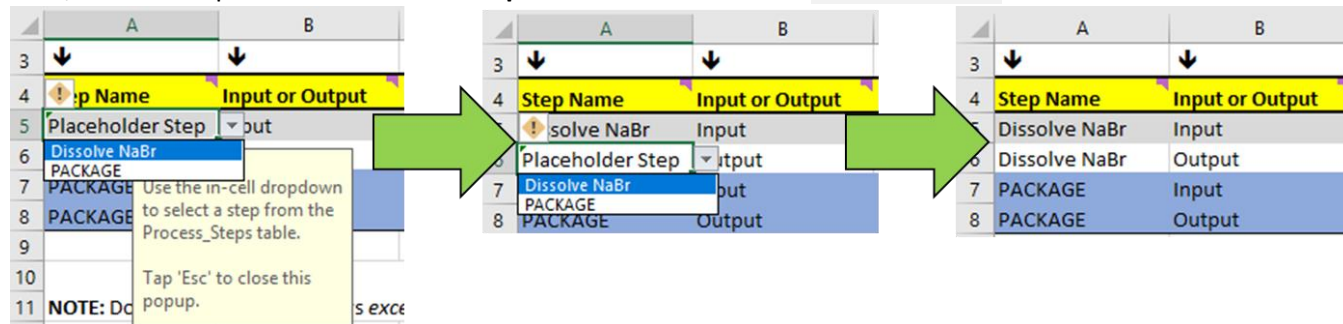

The notifications read:

> ➢ Warning: Check Inputs! LCA Data Source Class and Subclass must match.
> ➢ Warning: Check Inputs! A Step Name selected in Sheet '2. Enter Step Details' is blank or not defined in Sheet '1. Define Process Steps'.
> ➢ Warning: Check Inputs! An "Input: Process_Steps" Step Name selected in Sheet '2. Enter Step Details' is blank or not defined in Sheet '1. Define Process Steps'.

In this case, all of these notifications are related to the same root cause, as we'll see below.

4) Return to Sheet **2. Enter Step Details.**
The first notification we saw was because the entry in Sheet **2. cell D7**, `Placeholder Step`, is no longer a valid subset of the entry in **C7**: `Process_Steps`. The second notification was because the `Placeholder Step` entries in the **Step Name** column (cells **A5** and **A6**) no longer appear in the **Name** column in Sheet **1. Define Process Steps**, since we changed the name to `Dissolve NaBr`. The third notification is because the `Placeholder Step` entry in **D7** no longer appears in the **Name** column in Sheet **1. Define Process Steps**. So while these errors are all subtly different, they are all caused by our having changed the step name, cell A7(?) in Sheet **1. Define Process Steps,** without updating Sheet **2. Enter Step Details.**

Now, use the dropdown menus in the **Step Name** column to select `Dissolve NaBr` in the first two rows.

Navigate back to Sheet **3. Process Metrics Dashboard** and confirm that this has resolved one of the three error messages in the **NOTIFICATIONS** area.

5) Return to Sheet **1. Define Process Steps**.
Our process has two steps in addition to packaging, (dissolve NaBr, and precipitate NaBr), but the table currently has only one row for processing. Because the table is actually a **T**able (with a capital "T"), we can easily add rows while preserving existing equations and relationships. Right click in cell **A8** (or anywhere in the `PACKAGE` row) and select 'Insert' and then 'Table Row <u>A</u>bove'.
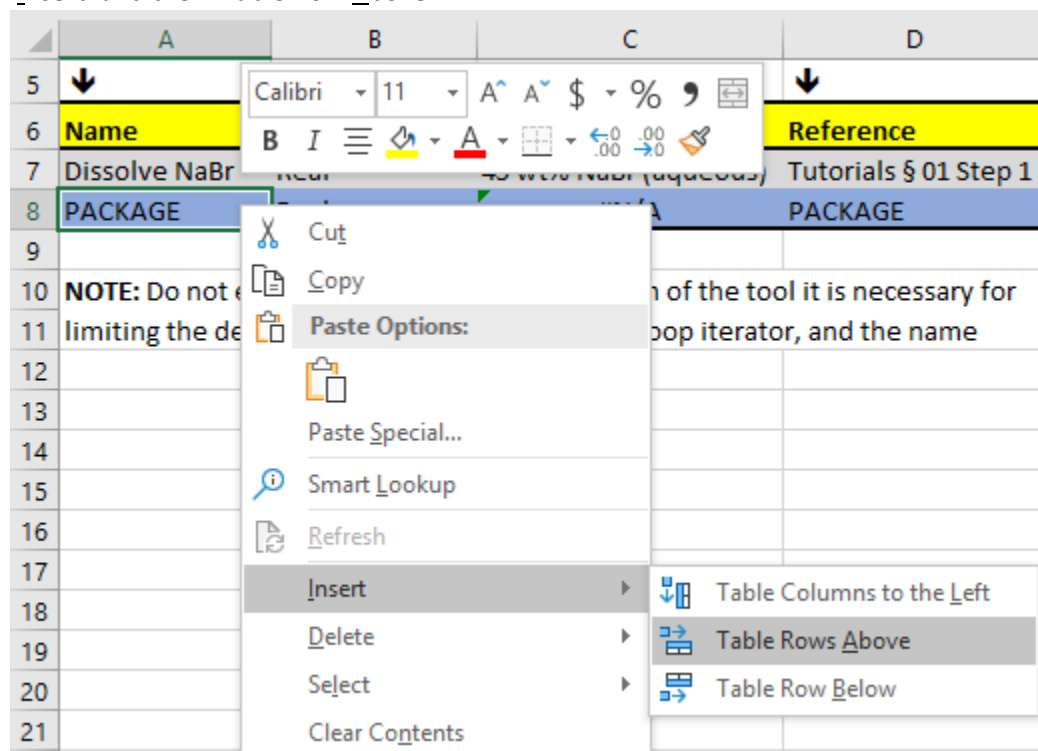
Because this is a Table, the context menu should appear slightly different than the normal right click context menu that would appear elsewhere in the Sheet. The typical method of inserting a row in Excel would also work here but would not have illustrated the unique context menu available for Tables.

The result should look like this:

	A	B	C	D	E	F
5	↓	↓	↓	↓	→ ←	
6	**Name**	**Real or Virtual?**	**Product Display Name**	**Reference**	**Scheme**	**Unscaled Step Product Mass**
7	Dissolve NaBr	Real	45 wt% NaBr (aqueous)	Tutorials § 01 Step 1		1.000
8						#N/A
9	PACKAGE	Real	#N/A	PACKAGE		1.000

The #N/A value in the second row of the **Unscaled Step Product Mass** column indicates that the equations of the first row have propagated successfully down to the second.

Type `Precipitate NaBr` into cell A8 in the **Name** column. In the next column, select `Real` from the in-cell dropdown. Under **Product Display Name**, type `Recrystallized NaBr`, and under **Reference**, type `Tutorials § 01 Steps 5-8`:

	A	B	C	D
5	↓	↓	↓	↓
6	**Name**	**Real or Virtual?**	**Product Display Name**	**Reference**
7	Dissolve NaBr	Real	45 wt% NaBr (aqueous)	Tutorials § 01 Step 1
8	Precipitate NaBr	Real	Recrystallized NaBr	Tutorials § 01 Steps 5-8
9	PACKAGE	Real	Packaged Recrystallized	PACKAGE

6) Now return to Sheet **2. Enter Step Details** and we will enter the details for our processing steps.

In the **LCA Data Source Class** column of the first row in the Table, select `Common_Inorganic` from the in-cell dropdown. In the next column, **LCA Data Source Subclass**, select `Default Inorganic Material`. This will tell Excel to pull LCIA metric values from the Default Inorganic Material in the `Common_Inorganic` database in Sheet **C. Additional Materials DB**. Under Display Name type `NaBr`, and enter 45 under **Physical Mass (kg)**.

	A	B	C	D	E	F
3	↓	↓	↓	↓	↓	↓
4	**Step Name**	**Input or Output**	**LCA Data Source Class**	**LCA Data Source Subclass**	**Display Name**	**Physical Mass (kg)**
5	Dissolve NaBr	Input	Common_Inorganic	Default Inorganic Material	NaBr	45.00
6	Dissolve NaBr	Output	None	None	Placeholder Product	1.00
7	PACKAGE	Input	Process_Steps	Placeholder Step	#N/A	1.00
8	PACKAGE	Output	None	None	#N/A	1.00

Insert a new row below the first row and enter the following:

Step Name	`Dissolve NaBr`
Input or Output	`Input`
LCA Data Source Class	`Common_Solvent`
LCA Data Source Subclass	`water, deionized`
Display Name	`Water`

In the last column, **Physical Mass (kg)**, type `=100-`, then hit the up arrow (↑) on the keyboard, and then hit 'Enter'. Double click on the cell F6(?) again to confirm that you have entered the following formula:

	F
3	↓
4	**Physical Mass (kg)**
5	45.00
6	=100-F5

In the next row, which should still be listed as an `Output`, notice that `None` is the only option available for either LCA Data Source Class or LCA Data Source Subclass. Under **Display Name**, type `45 wt% NaBr (aqueous)`. It is important that this text exactly matches the **Product Display Name** listed in Sheet **1. Define Process Steps**.

In the last column, **Physical Mass (kg)**, cell F7, type `=` then hit the up arrow (↑) on the keyboard, then type `+`, then hit the up arrow twice (↑↑) and then hit 'Enter'. Double-click on the F7 to confirm that you have entered the following formula:

	F
3	↓
4	**Physical Mass (kg)**
5	45.00
6	55.00
7	=F6+F5
8	1.00
9	1.00

Numerical values can be hard-coded into the **Physical Mass (kg)** column, but this example is designed to show how typical Excel features can still be leveraged within the scope of PMI-LCA tool data entry.

Now enter something reasonable into the **Step Instructions** and **Notes** columns and confirm that your Sheet now looks like this:

	A	B	C	D	E	F	G	H
3	↓	↓	↓	↓	↓	↓	↓	↓
4	**Step Name**	**Input or Output**	**LCA Data Source Class**	**LCA Data Source Subclass**	**Display Name**	**Physical Mass (kg)**	**Step Instructions**	**Notes**
5	Dissolve NaBr	Input	Common_Inorganic	Default Inorganic Material	NaBr	45.00	Charge Solute	45 wt%
6	Dissolve NaBr	Input	Common_Solvent	water, deionized	Water	55.00	Charge Solvent	55 wt%
7	Dissolve NaBr	Output	None	None	45 wt% NaBr (aqueous)	100.00	Discharge NaBr Soln	100% (total)
8	PACKAGE	Input	Process_Steps	Placeholder Step	#N/A	1.00		
9	PACKAGE	Output	None	None	#N/A	1.00		

7) Now, we will complete the data entry for the second processing step.
   Insert three new rows to the table by highlighting **Row 8 – Row 10**, right-clicking, and selecting "Insert"

Select `Precipitate NaBr` as the **Step Name** for all three new rows. Define the first two rows (B5,6) as `Inputs` and the last row (B7) as `Output` using the in-cell dropdown menus.

One of the inputs for this step is the product of the first step. In the first Input row, under **LCA Data Source Class**, cell C5, use the in-cell dropdown menu to select `Process_Steps`. In the next column, **LCA Data Source Subclass**, note that the in-cell dropdown now lists the step names. Select `Dissolve NaBr` to indicate that this input is the product of the previous step. Under **Display Name**, type `45 wt% NaBr (aqueous)` and ensure that the **Display Name** text exactly matches the previous instance of that material stream.

8) Complete the Table as shown:

Step Name	Input or Output	LCA Data Source Class	LCA Data Source Subclass	Display Name	Physical Mass (kg)	Step Instructions	Notes
Dissolve NaBr	Input	Common_Inorganic	Default Inorganic Material	NaBr	45.00	Charge Solute	45 wt%
Dissolve NaBr	Input	Common_Solvent	water, deionized	Water	55.00	Charge Solvent	55 wt%
Dissolve NaBr	Output	None	None	45 wt% NaBr (aqueous)	100.00	Discharge NaBr Soln	100% (total)
Precipitate NaBr	Input	Process_Steps	Dissolve NaBr	45 wt% NaBr (aqueous)	100.00	Charge NaBr Solution	Charge all
Precipitate NaBr	Input	Common_Solvent	methanol	Methanol	55.00	Charge MeOH	Equal to Water Mass
Precipitate NaBr	Output	None	None	Recrystallized NaBr	8.96	Filter Product	Solub. is 35.862 wt%
PACKAGE	Input	Process_Steps	Precipitate NaBr	Recrystallized NaBr	1.00		
PACKAGE	Output	None	None	Packaged Recrystallized	1.00		

The physical mass yield of Recrystallized NaBr (recall from the Process Description: 98% of the precipitate is recovered) is `=0.98*(F5-35.862)` (don't forget the parentheses!). Once you select `Precipitate NaBr` as the **LCA Data Source Subclass** for the **Input** to the `PACKAGE` step, the **Display Name** should automatically update. (Note: this is only true for the `PACKAGE` step).

Before we move on, note that as you selected the steps in the **Step Name** column dropdowns, the Reference column updated automatically with the document references we provided for those steps in Sheet **1. Define Process Steps**. In this example it may seem superfluous, but if you find yourself referring to procedures spanning multiple documents it could prove a useful feature.

9) Navigate to Sheet **3. Process Metrics Dashboard**. If all of the previous steps were completed successfully, then the notification area should appear as follows:
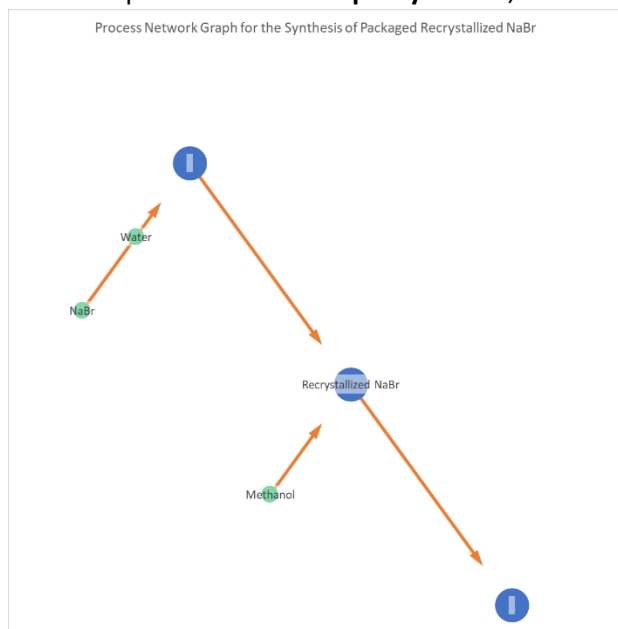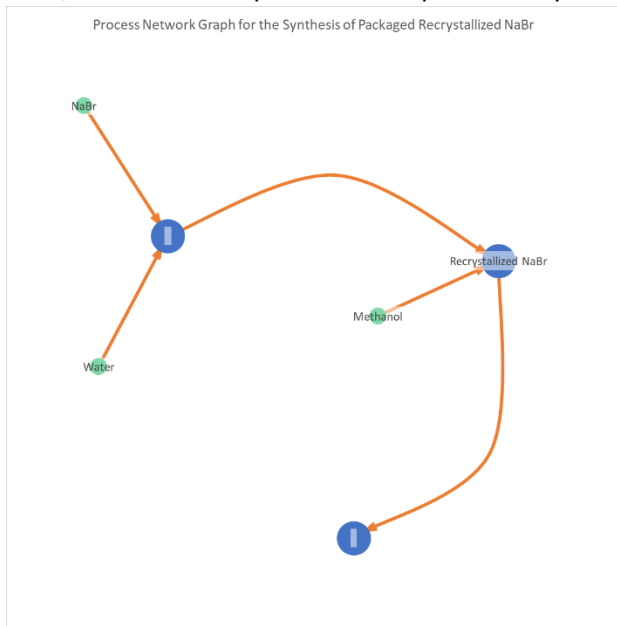

The notification reads:

> ➢ Everything looks good! Be sure to RESET > RUN > FREEZE the Graph Dynamics and the Step Scaling Iterator before evaluating results!

As indicated in the notification, we must remember to Reset, Run, and Freeze the iterators for the Process Network Graph and for the Recycle Loop Iterator.
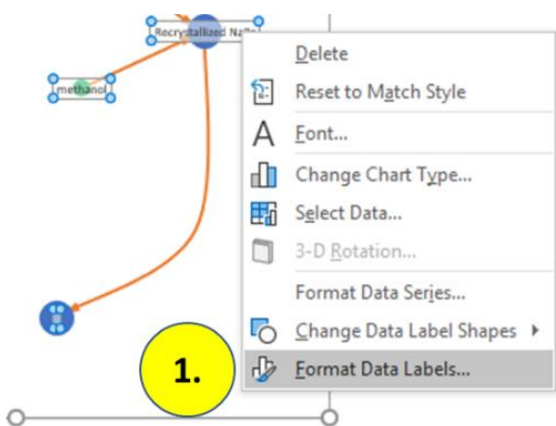
In the dropdown labeled **Graph Dynamics**, select '**Reset**' to produce the following initialized plot:

Process Network Graph for the Synthesis of Packaged Recrystallized NaBr

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Next, select '**Run**' to produce the optimized layout:

This layout may not look optimal for this particular process, but it is a great way to plot more complex processes. To prevent Excel from changing the plot, now select '**Freeze**' in the **Graph Dynamics** dropdown menu. Finally, let's fix labels, if any are broken (as is the case for 2 of the 3 blue circles in the example above). Right click on any label and select 'Format Data Labels...' then uncheck and re-check the 'Value From Cells' checkbox and then click 'Reset Label Text'.
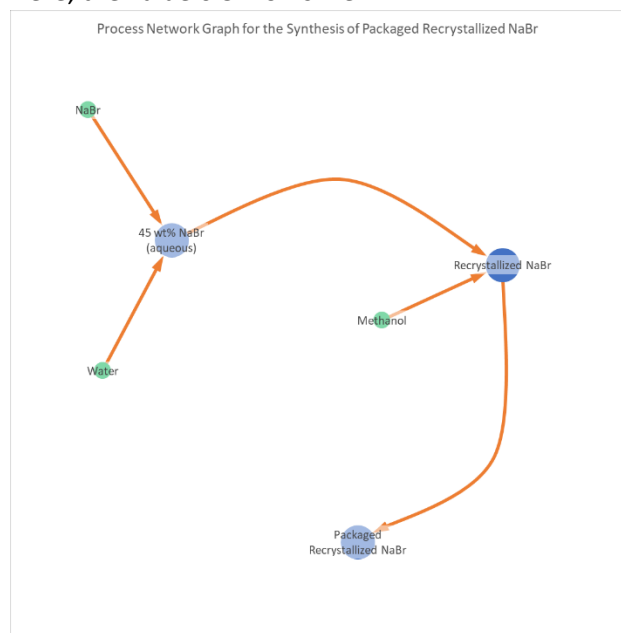
If necessary for aesthetics, change the value in **Arrow Offset** until the arrow heads are just touching the blue nodes. Here, the value 0.5 works well.


10) Reset, Run, and Freeze the **Recycle Loop Iterator**. The data table and plots should update, and **Table_Process_Overview** should show a **Total PMI** of 18.82.

Process Metrics per kg API	Total	Reagent	Metal	Solvent	Water	Enzymes & Plant Extracts	Other
PMI	17.31	5.02	0.00	6.14	6.14		0.00	0.00
Mass Net (kg)	11.04	6.73	0.00	4.30	0.01		0.00	0.00
Energy (MJ)	284.17	53.42	0.00	230.63	0.12		0.00	0.00
GWP (kg CO2 equiv.)	11.54	6.96	0.00	4.57	0.01		0.00	0.00
Acidification (kg SO2 equiv.)	0.08	0.07	0.00	0.01	0.00		0.00	0.00
Eutrophication (kg posphate equiv.)	0.01	0.00	0.00	0.00	0.00		0.00	0.00
Water (kg)	22.57	3.47	0.00	11.33	7.76		0.00	0.00
COG (USD)	0.00	0.00	0.00	0.00	0.00		0.00	0.00

Examine the breakdown plots:
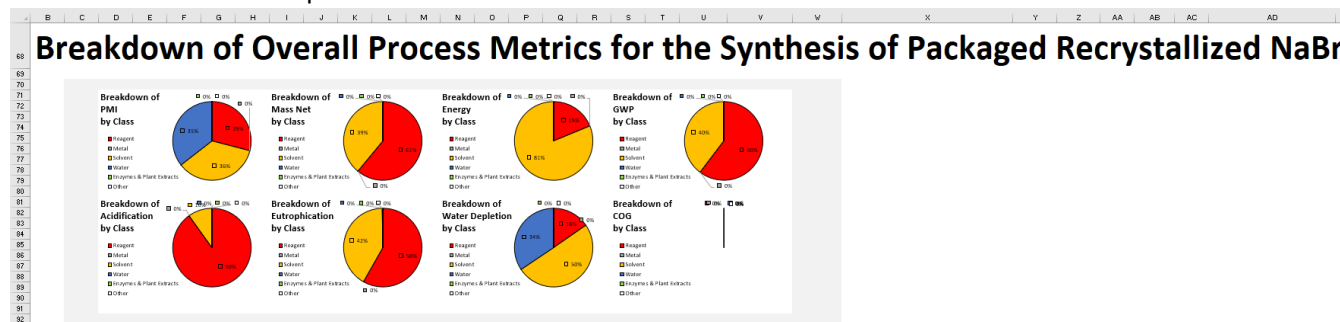
Immediately we see how much each of the material classes contributes to the final PMI. You should always feel free to edit the plot formatting as necessary to suit the needs of your report or presentation.
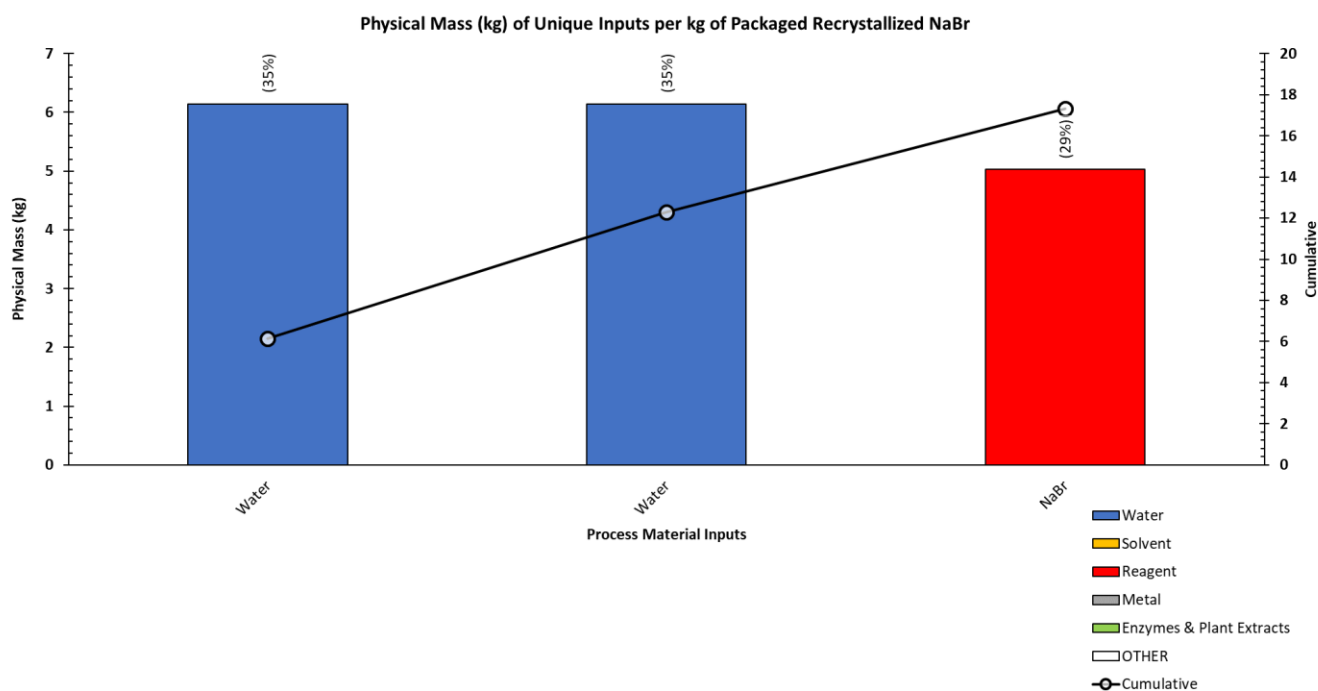
Breakdown of PMI by Class

☐ 0% ☐ 0%
☐ 35% ☐ 29%
☐ 0%
☐ 36%

■ Reagent
☐ Metal
■ Solvent
■ Water
■ Enzymes & Plant Extracts
☐ Other
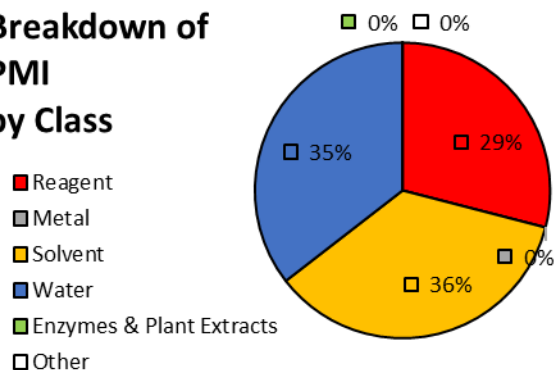
Scrolling down further, we see a breakdown of charged mass by material, with each material color-coded according to its general classification.

Physical Mass (kg) of Unique Inputs per kg of Packaged Recrystallized NaBr

■ Water
■ Solvent
■ Reagent
☐ Metal
■ Enzymes & Plant Extracts
☐ OTHER
–O– Cumulative

11) **<u>IMPORTANT</u>**: Note the plotting error here, that `Water` appears twice, when one instance of `Water` should actually be `Methanol`. This occurs because the mass input masses of `Water` and `Methanol` are *exactly* the same. This is uncommon in real processes, but if it occurs, here is how to fix it:

Return to Sheet **2. Enter Step Details** and change the mass of methanol from `55.00` to `55.001`, or some other negligibly but finitely different value from 55.00. Now navigate again to Sheet **3. Process Metrics Dashboard** and Reset, Run, and Freeze the Step Scaling iterator. The corrected chart is shown on the following page.

Physical Mass (kg) of Unique Inputs per kg of Packaged Recrystallized NaBr
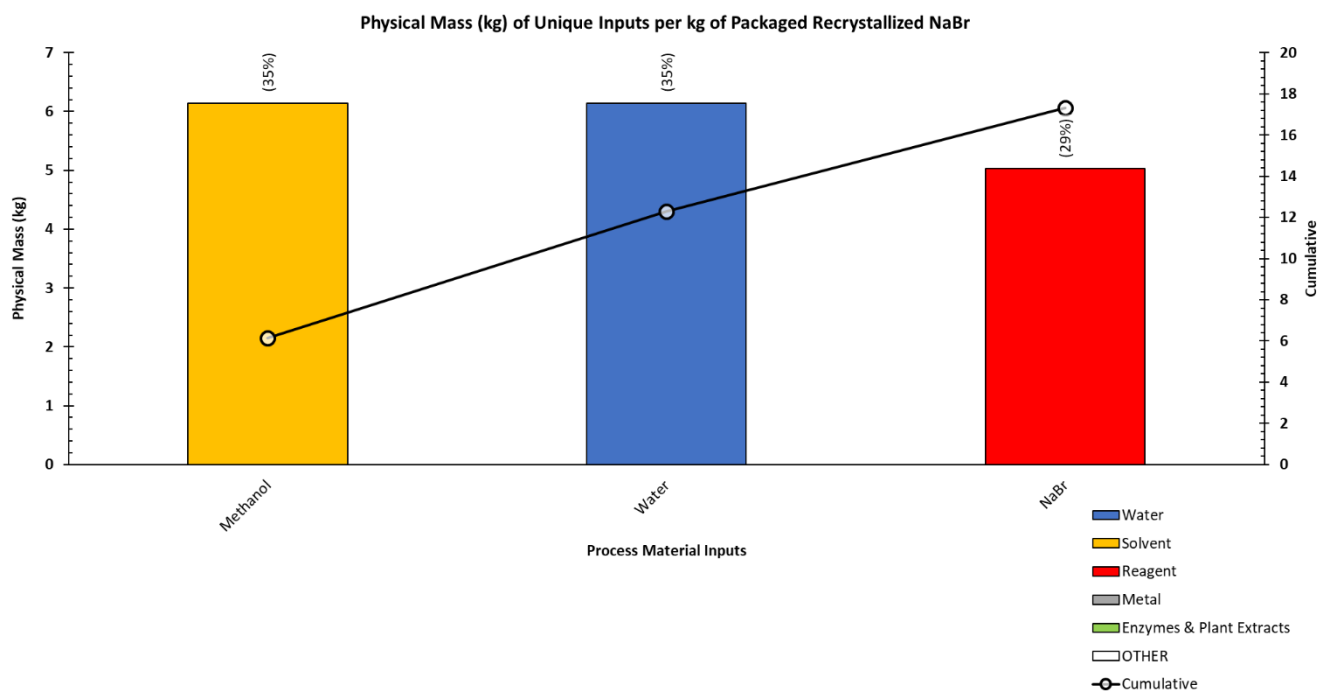
The chart styles are designed so that the color coding of the bar graphs is consistent with that of the pie charts. We charged three raw materials, so there are three columns. The label for each column is the name of the material. The height of each column represents the total mass of the material that was charged and corresponds to the left vertical axis. The rotated numbers in parentheses above each column (35%, 35%, and 29%) tell us the percentage each material contributes to the total PMI. In this example, we had only one material from each of these three classes, so these numbers should exactly match those displayed in the pie chart above.

The black trace in this plot shows the cumulative total mass. Looking at the right-most point and its corresponding value on the right vertical axis, we can see that it takes a total of about 17 kg of material to produce 1 kg of recrystallized sodium bromide using our process. To view the exact value, we can hover the mouse pointer over that point, or scroll up to the **Data Table** discussed previously.

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To the right of the breakdown of PMI by material, we can also see a breakdown of the PMI by process step. In the copy of Excel used for this example, a bug caused only one label to be visible. Use the same label reset instructions provided next to the Process Network Graph in Step 9 above to correct this bug if it occurs.
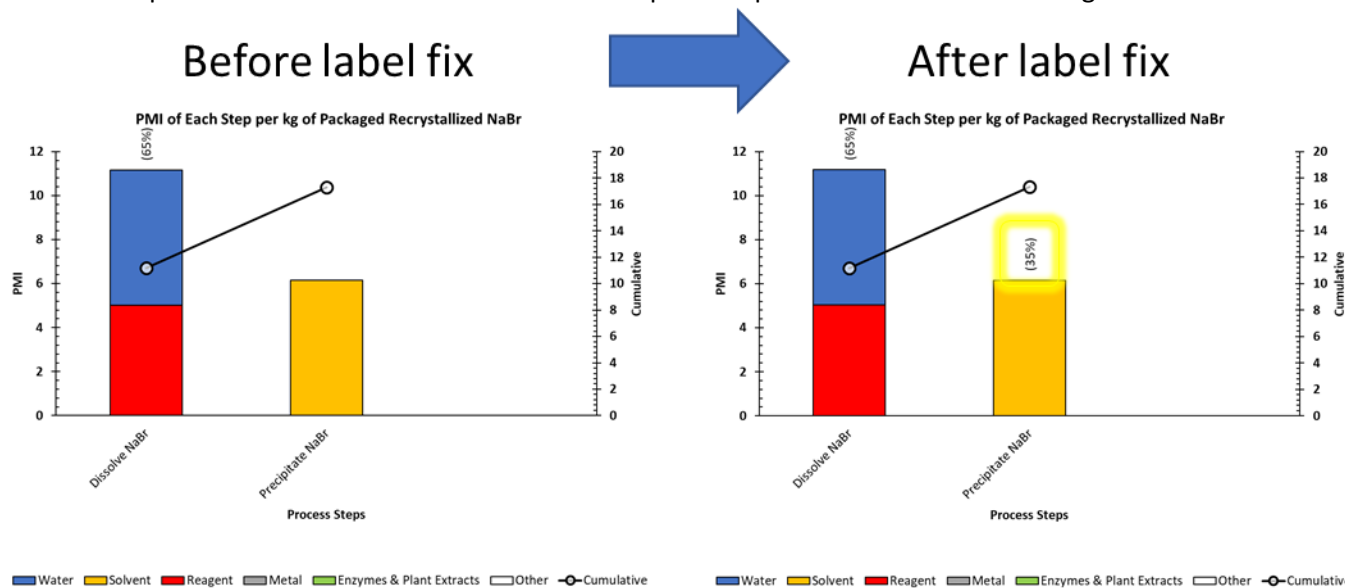

In this plot, we can see that the first step has material inputs in both the Water and Reagent classes, and accounts for about 11 kg of the total mass inputs per kg of product.

12) What would we do though, if the NaBr was already in a 45 wt% aqueous solution when we received it? In that case our process would only have one step – the precipitation step. This is where the **Real** and **Virtual** classification comes into play.

    Navigate to Sheet **1. Define Process Steps** and use the in-cell dropdown menu to change `Dissolve NaBr` from `Real` to `Virtual`. This change tells the PMI-LCA tool that the 45 wt% NaBr (aqueous) is a raw material, but it has multiple components, which may or may not span different LCA or material classification categories.

    Return to Sheet **3. Process Metrics Dashboard** and observe the changes to the plots. Here's a comparison:
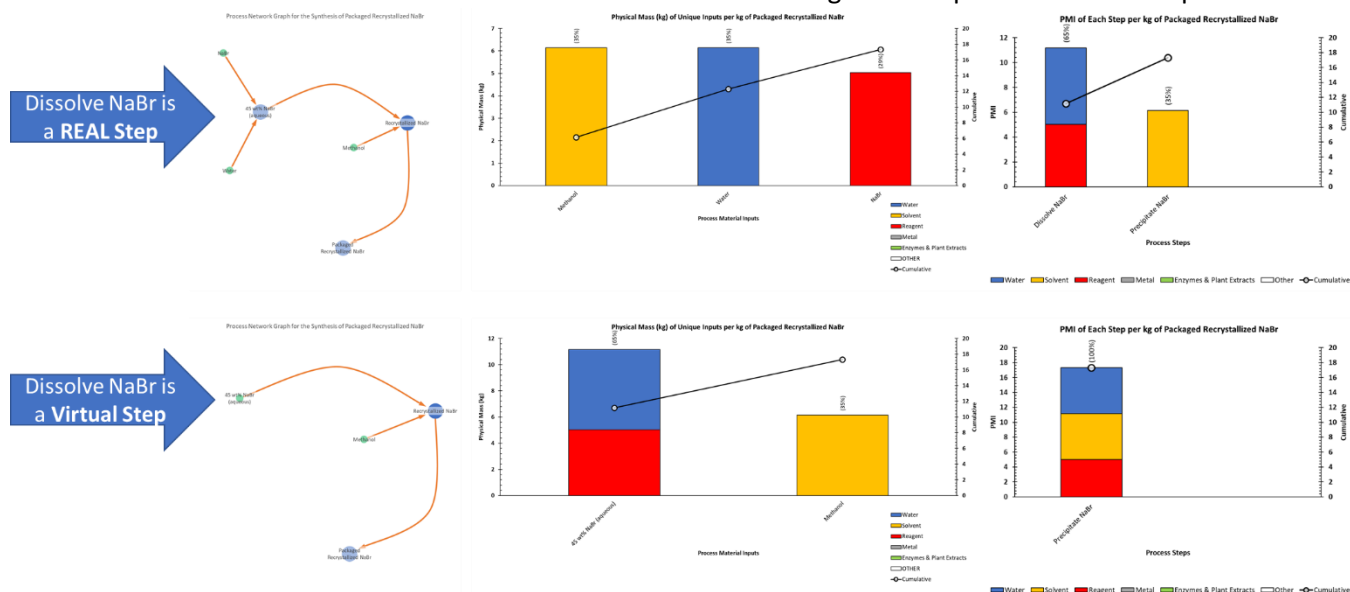
Now we can see that instead of showing water and NaBr as separate raw materials, we have combined them to a

single raw material called `45 wt% NaBr (aqueous)` that correctly weights the LCA metric contributions from each constituent part.
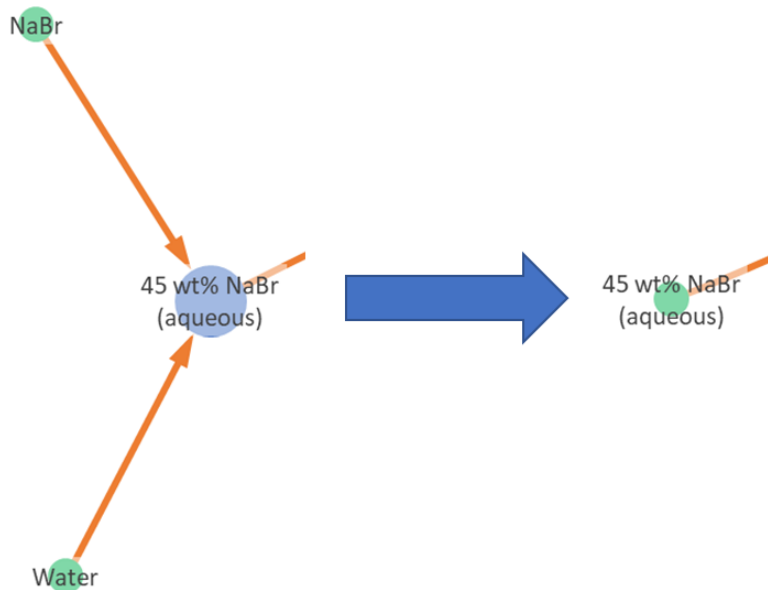
Note that this change does not require resetting and re-running the iterators, because it is only updating how the steps are displayed but does not change the scaling factors for each step.

Physical Mass (kg) of Unique Inputs per kg of Packaged Recrystallized NaBr
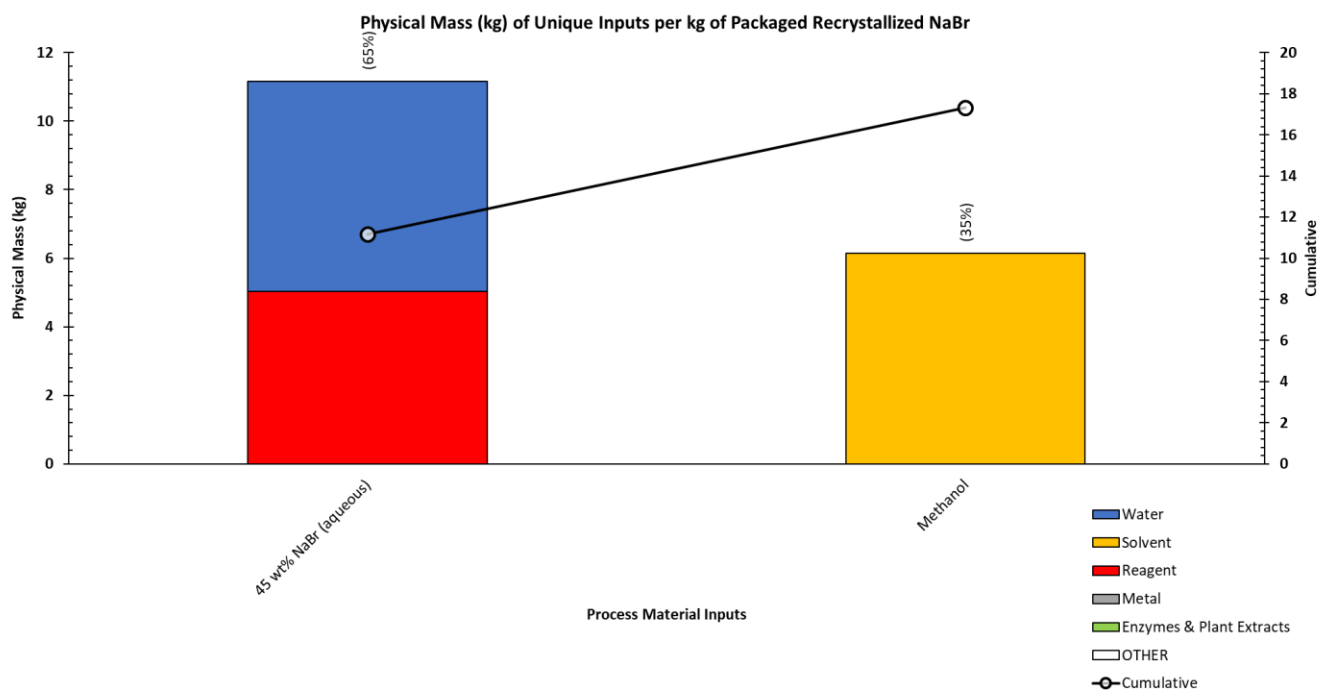
In the step breakdown, we can see that our process now has only the one step, but it has raw materials in all three categories of Water, Solvent, and Reagent.

PMI of Each Step per kg of Packaged Recrystallized NaBr

Legend: Water · Solvent · Reagent · Metal · Enzymes & Plant Extracts · Other · Cumulative
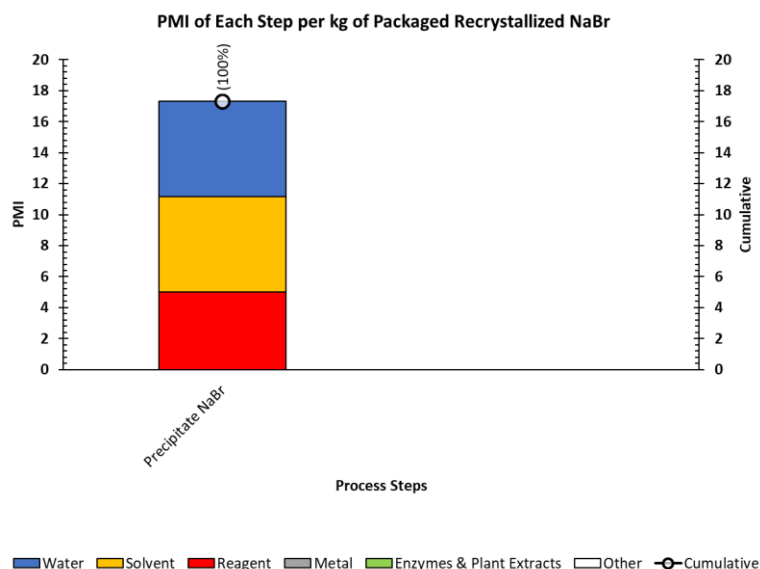
13) Let's assume now that we've determined we must add a crystalline seed of already-recrystallized NaBr into the precipitation step, and we need to know how it will impact the process metrics.
Return to Sheet **2. Enter Step Details** and add a row to the table for another input to the `Precipitate NaBr` processing step - you can add it anywhere, steps do not have to be entered in order, although it usually makes sense to keep things organized. To illustrate the flexibility of data entry, we've put the new row between the **input** and **output** of `Dissolve NaBr`, where it might actually make the *least* amount of sense. Select the new input to be the step's own output, `Recrystallized NaBr`, with a mass of 15% of the expected mass of `Recrystallized NaBr`.

	A	B	C	D	E	F	G	H
3	⬇	⬇	⬇	⬇	⬇	⬇	⬇	⬇
4	**Step Name**	**Input or Output**	**LCA Data Source Class**	**LCA Data Source Subclass**	**Display Name**	**Physical Mass (kg)**	**Step Instructions**	**Notes**
5	Dissolve NaBr	Input	Common_Inorganic	Default Inorganic Material	NaBr	45.00	Charge Solute	45 wt%
6	Precipitate NaBr	Input	Process_Steps	Precipitate NaBr	Recrystallized NaBr	1.34	Charge Seed	15% Seed Charge
7	Dissolve NaBr	Input	Common_Solvent	water, deionized	Water	55.00	Charge Solvent	55 wt%
8	Dissolve NaBr	Output	None	None	45 wt% NaBr (aqueous)	100.00	Discharge NaBr Soln	100% (total)
9	Precipitate NaBr	Input	Process_Steps	Dissolve NaBr	45 wt% NaBr (aqueous)	100.00	Charge NaBr Soln	Charge all
10	Precipitate NaBr	Input	Common_Solvent	methanol	Methanol	55.00	Charge MeOH	Equal to water mass
11	Precipitate NaBr	Output	None	None	Recrystallized NaBr	8.96	Filter Product	Solub. is 35.862 wt%
12	PACKAGE	Input	Process_Steps	Precipitate NaBr	Recrystallized NaBr	1.00		
13	PACKAGE	Output	None	None	Packaged Recrystallized	1.00		

New →

14) Now, return to Sheet **3. Process Metrics Dashboard** and **Reset**, **Run**, and **Freeze** the **Graph Dynamics**. Reset the data labels if necessary. Your Process Network Graph should look like this:

Process Network Graph for the Synthesis of Packaged Recrystallized NaBr
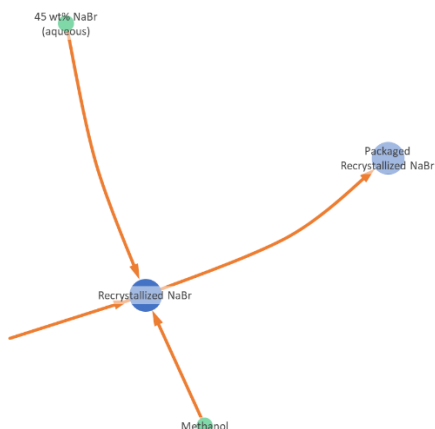
The inward pointing arrow with no apparent source indicates that the step recycles *into itself*. The arrow both originates and terminates with the `Recrystallized NaBr` node.

15) **Reset**, **Run**, and **Freeze** the **Recycle Loop Iterator**. The **Data Table** should show that the PMI has increased from `17.31` to `20.36`, nearly an 18% increase. If the plots appear blank, press '**F9**' on the keyboard to refresh them.

16) Navigate to Sheet 1. Define Process Steps, examine the values in the columns **Total Mass that must be produced** and **Step Scale Factor for 1kg Packaged API** and confirm that they make sense for the inputs that we have entered.

	A	B	C	D	E	F	G	H
5	↓	↓	↓	↓	→ ←		Recycle loop scaling iterators	
6	Name	Real or Virtual?	Product Display Name	Reference	Scheme	Unscaled Step Product Mass	Total Mass that must be produced	Step Scale Factor for 1kg Packaged API
7	Dissolve NaBr	Virtual	45 wt% NaBr (aqueous)	Tutorials § 01 Step 1		100.000	13.137	0.13137
8	Precipitate NaBr	Real	Recrystallized NaBr	Tutorials § 01 Steps 5-8		8.955	1.176	0.13137
9	PACKAGE	Real	Packaged Recrystallized	PACKAGE		1.000	1.000	1.00000

Starting from the end and working our way backwards:
   a. We want to package 1 kg of product to get the 1 kg packaged product calculation basis, so that checks out.

   b. The precipitation step is more complicated because it has to produce the material that is packaged *and* the material that is used for the seed, and the step must be re-scaled from the initial way the step was written, where it produces a total of `8.96` kg.

$$\text{Mass to be produced} = 1.00 \ (packaging) + 15\% \text{ of mass to be produced} \ (seed)$$
$$x = 1 + 0.15x$$
$$x - 0.15x = 1$$
$$0.85x = 1$$
$$x = \frac{1}{0.85}$$
$$\boxed{x = 1.176}$$

This represents a downscaling of the step by a factor of $1.176/8.96 = \boxed{0.131}$
So that checks out too.

   c. The precipitation step requires 100 kg of dissolved NaBr at the nominal scale, so at a scale factor of 0.131, it requires $\boxed{13.1 \text{ kg}}$ so that value appears to be correct as well.

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It is good practice to perform these types of checks to confirm (1) that data has been entered correctly, and (2) that the Tool is functioning as desired.

17) Save your work and close the file.