February 11, 2011

ACS GCI Pharmaceutical Roundtable Green Chemistry Reporting Requirements for an Electronic Laboratory Notebook (ELN)

Background. The ACS GCI Pharmaceutical Roundtable is a partnership between the American Chemical Society Green Chemistry Institute® and pharmaceutical and fine chemical companies dedicated to catalyzing the integration of green chemistry and green engineering into the pharmaceutical industry globally. A current list of members can be found at www.acs.org/gcipharmaroundtable.

Objective. In 2009/2010 the ACS GCI Pharmaceutical Roundtable indentified that a majority of member companies had at least one electronic laboratory notebook (ELN) in operation within their organization. It was recognized that adoption of this new technology provides a unique opportunity to operationalize the twelve principles of Green Chemistry. In addition, Roundtable member companies have expressed a strong desire for standardized Green Chemistry reporting independent of ELN supplier.

Process Mass Intensity (PMI) Calculation

1) Process Mass Intensity (PMI) = kg material / kg product. PMI should be calculated by the ELN in the following manner:

$$A + B \longrightarrow C \text{ (Intermediate)}$$

$$C + D \longrightarrow E \text{ (API)}$$

$$PMI = (A + B + D) / E$$

This calculation does not include the contribution of intermediary compounds in the overall reaction PMI calculation.

2) The ELN should calculate PMI for an individual step and for an entire process.
3) Step and total PMI should be displayed as kg/kg API units
4) % contribution of individual steps to overall PMI should be displayed.
5) PMI report should contain yield values per step
6) PMI should break steps into PMI contribution from aqueous and solvents. PMI should be reported accurately for mixed reagents (i.e. 10% sodium chloride (aqueous) = 10% NaCl + 90% water).
   Reporting requirements are displayed in Figure 1.

E-Factor

The E-Factor metric is similar, although not identical to PMI.

E-Factor = kg Waste / kg product.

Atom Economy

Atom economy = (MW Product / Sum of MW of Reactants) X 100.

Atom economy is a metric which takes into account how much reactant atoms are incorporated into product. Solvents, reagents and yield do not factor into this calculation.

TRI and PBT Reporting

The Toxics Release Inventory (TRI) is a publicly available database maintained by the Environmental Protection Agency (EPA) containing information on toxic chemical releases and other waste management activities in the United States. Persistent, Bioacumulative Toxic Chemicals (PBT) are resistant to environmental degradation through chemical or biological processes. A list of these chemicals is publically available through the US EPA. Within the ELN, a report should be generated that flags any TRI or PBT chemical used in a process (Figure 2).

REPORT DISPLAY

Figure 1. PMI/ e-Factor/ Atom Economy Report.

Single Experiment Report View:

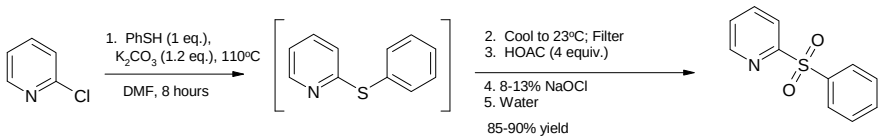
Step	Yield (%)	Theor. Step PMI (kg/kg product)	Actual Step PMI (kg/kg product)	Aqueous PMI	Solvent PMI	e-Factor	Atom Economy
1							

Linked Multiple Experiment Report:

Step	Yield (%)	Theor. PMI (kg/kg API)	Actual. PMI (kg/kg API)	Aqueous PMI	Solvent PMI	e-Factor	Atom Economy
1							
2							
3							
Total							

Figure 2. TRI and PBT Reporting.

Reaction
Step 1



Materials Step 1			***Actual***		PBT Listed Chemicals	TRI Listed Chemicals	**Planned**	
Class	**Name**	**Lot Number**	**g**	**moles**			**g**	**moles**
Reactants								
	Pyridine, 2-Chloro-	1420KB	14.2	0.13			14.4	0.13
	benzenethiol [LR]	16709AB	15.0	0.13			15.1	0.13
Chemicals								
	K2CO3	072K01381	22.1	0.16			22.0	0.16
	DMF	01946EC	179.6	2.46		X	151.2	2.08
	10.6 % NaOCl	A019794301	280	0.40			240	0.34
	Water		30	1.67			130	7.22
	Potassium Hydroxide		27.1	0.10			42.1	0.15
	Acetic Acid		7.9	0.13			10.5	0.17
Products								
	2-Benzene sulfonyl Pyridine	XXX	28.96	0.13			24.7	0.11
Step PMI			19.9				25.3	

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