Pharma and Suppliers: Collaborating on Green Chemistry. Launch of PMI tool

ACS Green Chemistry Institute® Pharmaceutical Roundtable

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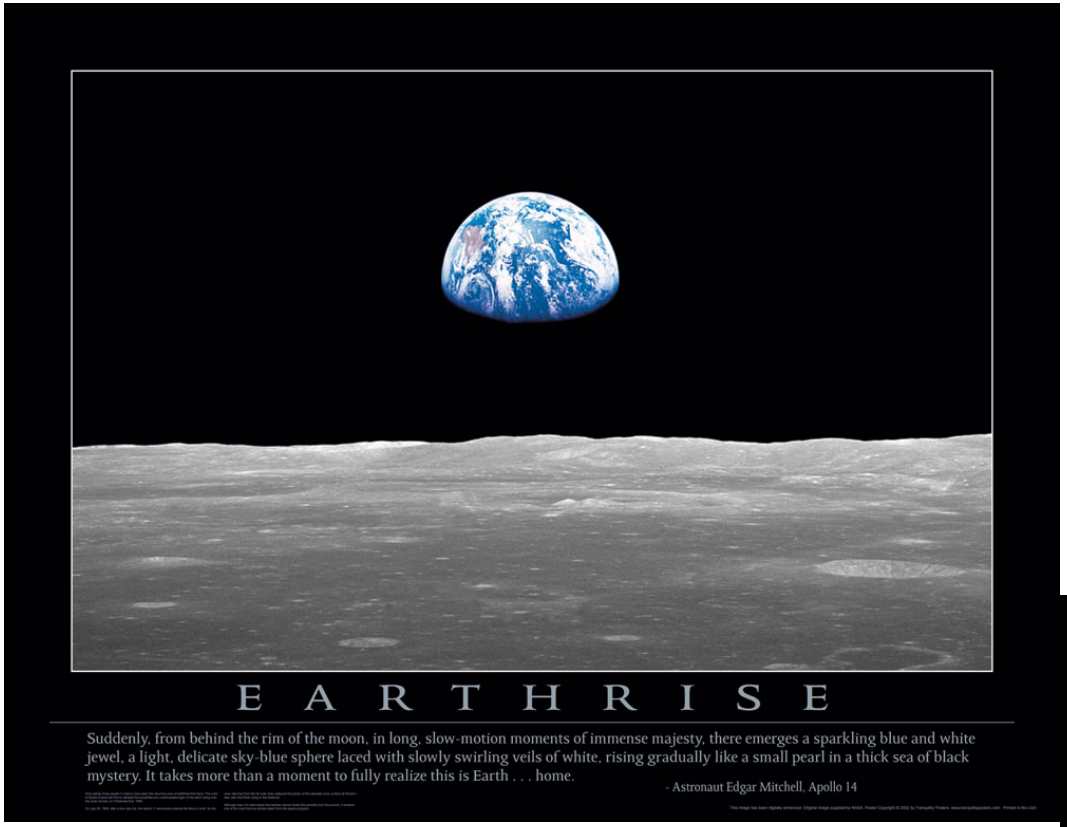
Pharma and Suppliers: Collaborating on Green Chemistry. Launch of PMI tool

- **Presentation Agenda**
  - **What is green chemistry and why is it important?**
  - **What is the Pharmaceutical Roundtable?**
  - **Introduce Process Mass Intensity as a Measure of Process Efficiency**
  - **Introduce PMI calculator tool**

- **Desired Outcome: Use of a single tool for calculating PMI across the industry, including suppliers**



Sustainability: Meeting the needs of today without compromising the ability of future generations to meet their needs.

Brundtland Commission report, *Our Common Future*, 1987

Green chemistry is not just a catchphrase. It is an indispensable principle of chemical research that will sustain our civilized society in the twenty-first century and further into the future.

R. Noyori
Nature Chemistry, **2009**, *1*, 5-6.

What is a Sustainable Future?

Social

Economic

Environmental

The pharmaceutical industry will be expected to meet the needs of patients around the world at a cost they can afford while minimizing our environmental footprint.

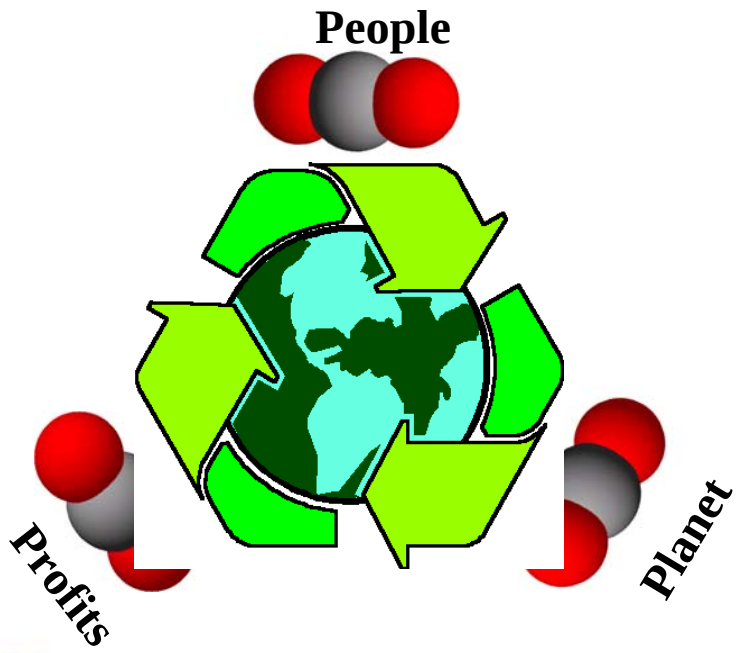
Balance Social, Environmental & Economic Needs
Globally and Across Generations

Triple Bottom Line

"Business is the only mechanism on the planet today powerful enough to produce the changes necessary to reverse global environmental and social degradation."

- Paul Hawken

The triple bottom line captures an expanded spectrum of values and criteria for measuring organizational success - economic, environmental and social.



What is Green Chemistry?

*The **highest efficiency** potential that exists for each chemical process.*

*Green Chemistry is a **privileged opportunity for innovation** and represents an emerging new frontier of exploration.*

*The achievement of superior synthetic efficiency will ultimately deliver a **competitive advantage**.*

J. Tucker, *Org. Proc. Res. Dev*. **2006**, *10*, 315-319

Green Chemistry provides a platform to align Corporate environmental, social, and economic goals.

Environmental and Economic Sustainability through Green Chemistry

	Environmentally Thinking	Economically Thinking
Atom Economy	Minimal by-product formation ***reduced environmental burden***	More from less – incorporate total value of materials
Solvent Reduction	Less solvent waste ***reduced environmental burden***	Less spend on solvent
Reagent Optimization	Catalytic, low stoichiometry, recyclable reagents minimize usage, ***reduced environmental burden***	Increased productivity
Convergency	***Reduced environmental burden*** due to increased process efficiency	Higher efficiency
Energy Reduction	***Reduced environmental burden*** from power generation, transport, and use	Reduced energy costs
In-situ Analysis	Reduced possibility for exposure or release to the environment	Increased throughput
Safety	Non-hazardous materials reduce risk of exposure, release, explosions and fires	***Worker safety*** and reduced down time

"In every case I know, the green option is the low cost option"

- David Constable, 2008

John Tucker, *Org. Proc. Res. Dev.*, **2006**, *10*, 315

ACS GCI Pharmaceutical Roundtable

ACS GCI Pharmaceutical Roundtable

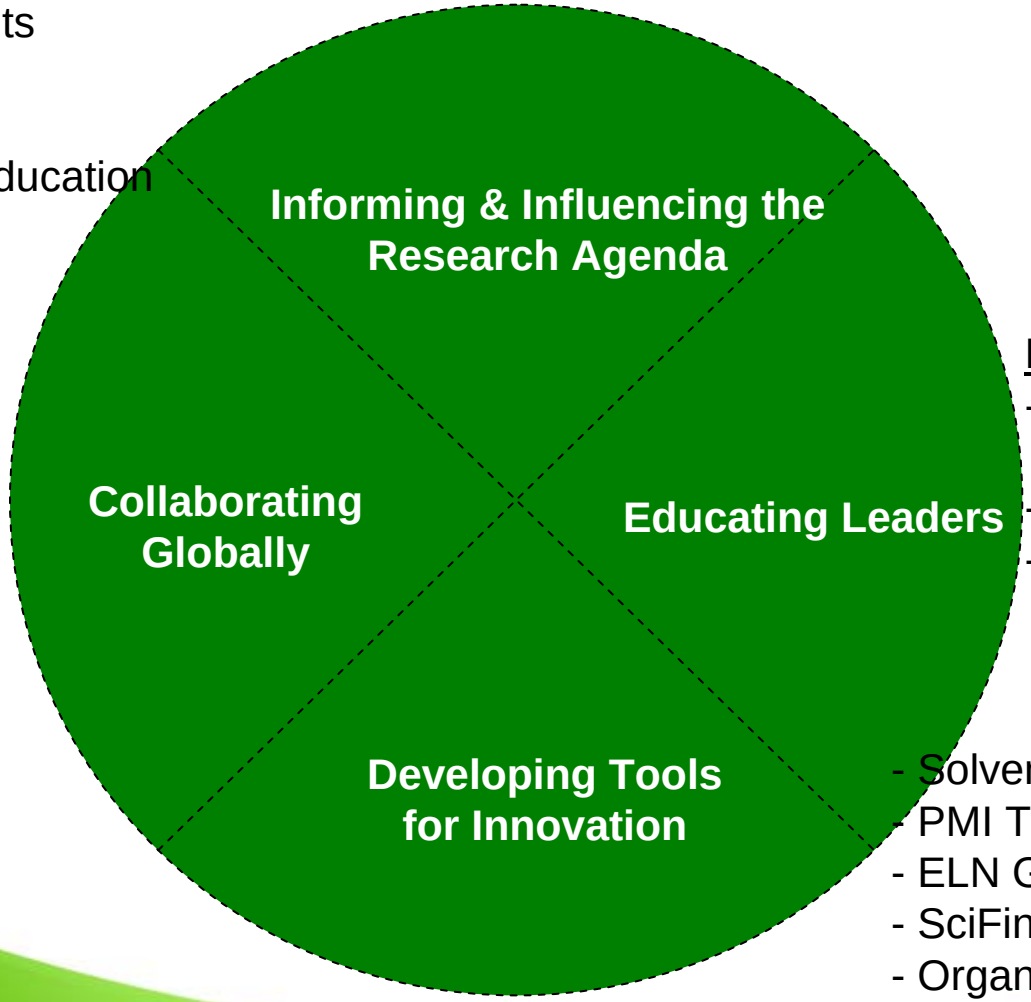
To catalyze the implementation of green chemistry and engineering in the pharmaceutical industry globally.

ACS GCI Pharmaceutical Roundtable:

Membership January 2011

Strategic Priorities of ACS GCI Pharmaceutical Roundtable

~$1 million in Grants
- GOALI Grant
- NIH collaboration
- Support Green Education



- Global membership
- Meetings in EU and US

<u>Publications</u>
- Green Chem Articles of Interest
-Aspirational Reactions
-Key Engineering Challenges

- Solvent Selection Guide
- PMI Tool
- ELN Green Tools
- SciFinder
- Organometallics in greener solvents

The Challenge

- Decreasing the amount of material used to make a drug is one of the major green chemistry challenges for the pharmaceutical industry

- ACS GCI Pharmaceutical Roundtable members have developed a common process mass intensity metric that allows data from each company to be compared on a **transparent** and **equitable** basis

Process Mass Intensity Metric

$$\textbf{Process mass intensity} = \frac{\textbf{quantity of raw materials input (kg)}}{\textbf{quantity of bulk API out (kg)}}$$

Where:

Process is all steps of a synthetic path from **commonly available materials** to the final bulk active pharmaceutical ingredient ("API")

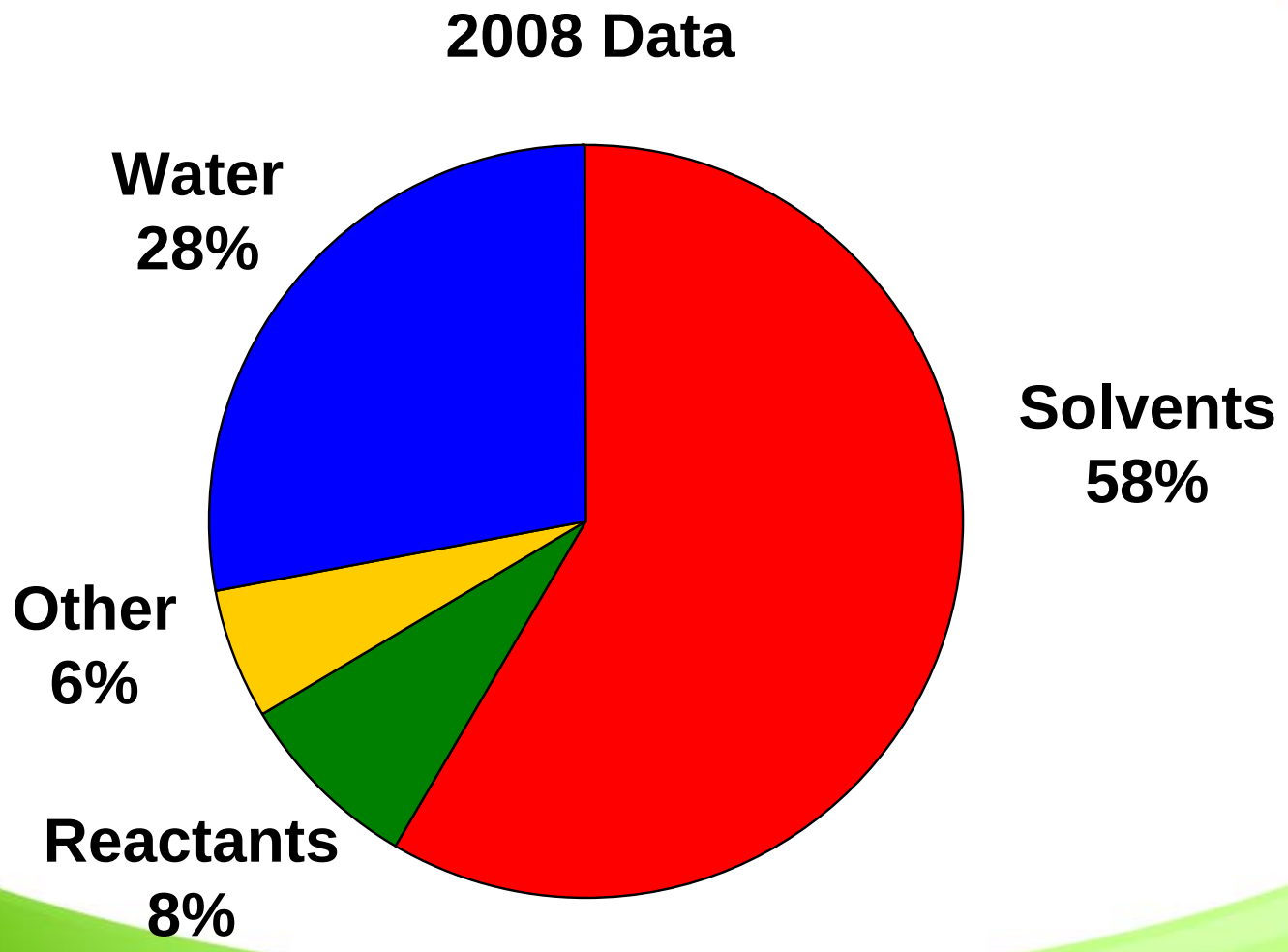
Raw Materials are all materials including water that are used directly in the process of synthesizing, isolating, and purifying the API final form

Bulk API out is the final form of the active ingredient that was produced in the synthesis, dried to the expected specification

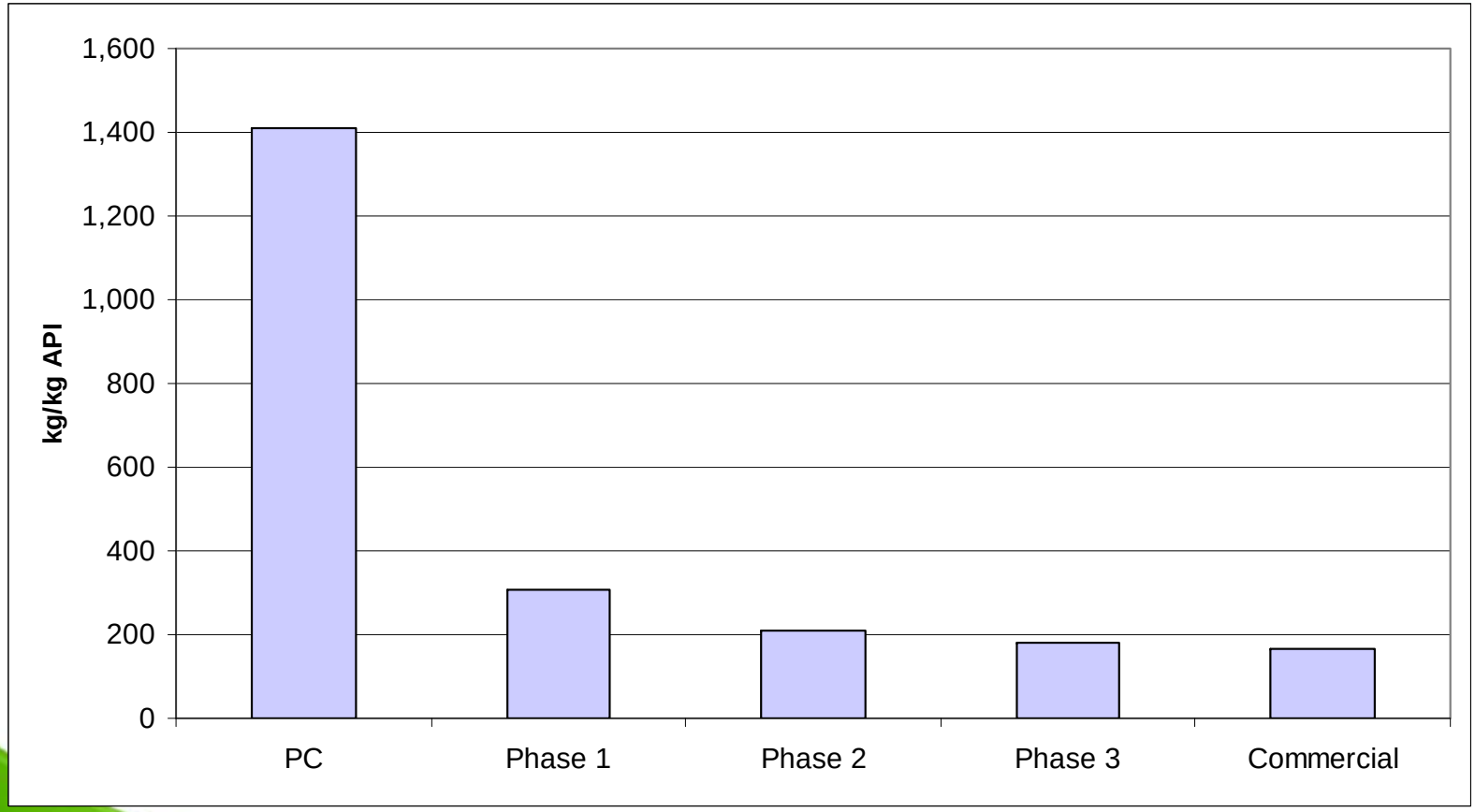
Why measure PMI?

- Drive change towards more sustainable/green manufacturing processes
  - **Track environmental manufacturing footprint**
  - **Measurement of process efficiency**
- Quantify improvements throughout process development life-cycle
- To be more transparent; basis for objective comparison
  - **Increasing expectations from internal and external audiences to describe progress, demonstrate improvement**
- Benchmark
  - **Allows a simple comparison to the on-going green efforts throughout the industry in the pursuit of mass efficient pharmaceutical processes.**
- **Insight in sustainability of overall manufacturing process**, **from bulk chemicals to API**, **is required.**

Composition of PMI—Pharma Benchmarking



PMI by Development Phase
Median Values - 2008



The Next Logical Step…
Involve Suppliers

- Measure PMI for all steps from commodity raw materials
- Use one tool for consistency across the industry

PMI Calculator Tool

Step Name/Number	1	
	Value	Units
Physical Batch Size		
Assay Purity		
Assay Batch Size		
Yield		
Assay Kg product		
Product Purity		

Raw Materials	Physical Charge (kg)
Substrates	
Reagents	
Solvents	
Aqueous	

PROCESS STEP METRICS	
Mass Substrate (kg)	0
Mass Reagents (kg)	0
Mass Solvents (kg)	0
Mass Aqueous (kg)	
Step PMI	#DIV/0!
Step PMI Excluding H2O	#DIV/0!
Cumulative PMI	#DIV/0!
Cumulative PMI Excluding H2O	#DIV/0!

PMI Calculator Tool

- Spreadsheet with embedded calculations
- Only need to fill in amounts of reagents, solvents, and aq.
- Spreadsheet calculates step and overall PMI for linear sequences
- Calculates overall PMI as well as separate PMI for solvents, water, and reagents

Located on ACS GCI Pharmaceutical Roundtable website: www.acs.org/gcipharmaroundtable

Example

Isentress (raltegravir) 9 step process

Cumulative PMI	**114**
Cumulative PMI Substrate, Reagents, Solvents	**78**
Cumulative PMI Substrates and Reagents	**9**
Cumulative PMI Solvents	**69**
Cumulative PMI Water	**36**

For a copy of the PMI calculator tool, see the excel file available at www.acs.org/gcipharmaroundtable.

Going Forward

- Encouraging suppliers to calculate and provide PMI data
  - For all APIs and API intermediates
  - At all stages of development
  - Include breakdown of solvent, reagents, and water PMI

Find the PMI Calculator Tool at www.acs.org/gcipharmaroundtable
Questions/comments: gcipr@acs.org

Any comments, suggestions or questions are greatly appreciated.

Thank you!

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www.acs.org/gcipharmaroundtable