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

## ACS Green Chemistry Institute® Pharmaceutical Roundtable

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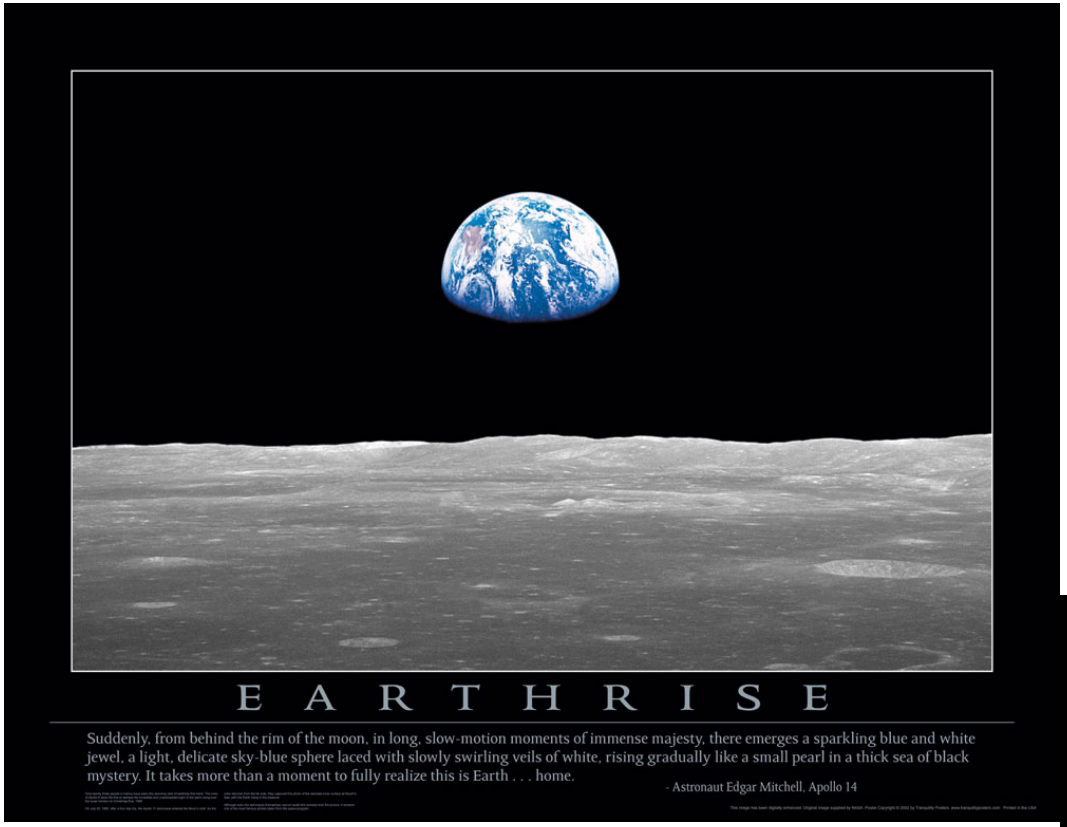
# Pharma and Suppliers: Collaborating on Green Chemistry. Launch of PMI tool

- **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.*

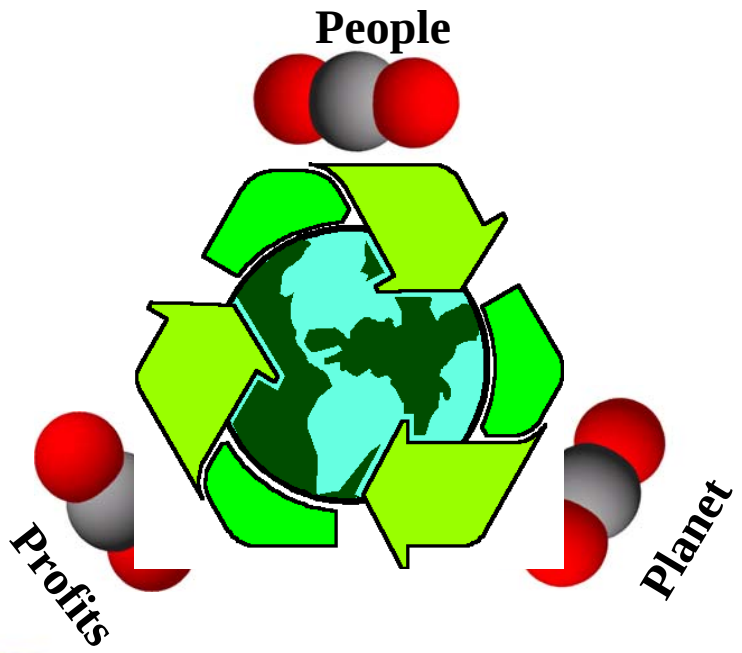
**Balance Social, Environmental & Economic Needs**
***Globally and Across Generations***

# 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









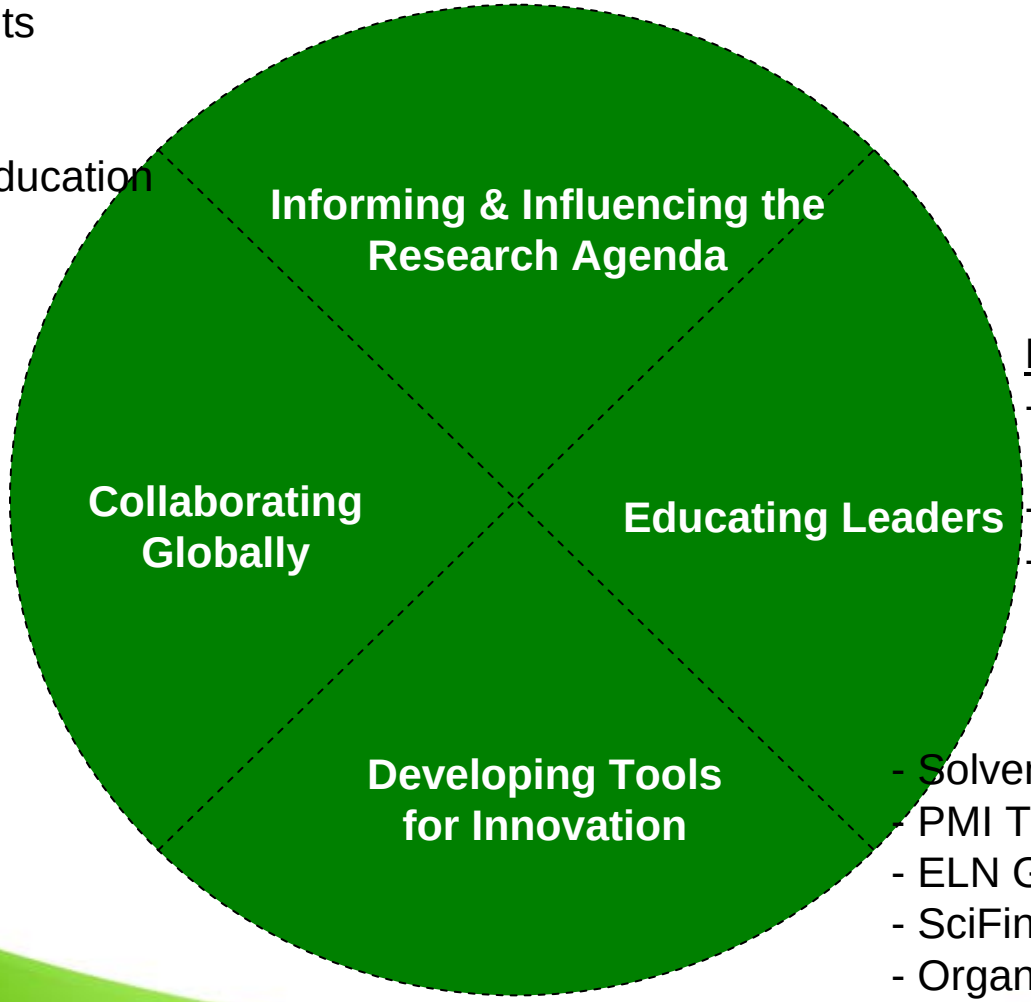







# Strategic Priorities of ACS GCI Pharmaceutical Roundtable

~$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")

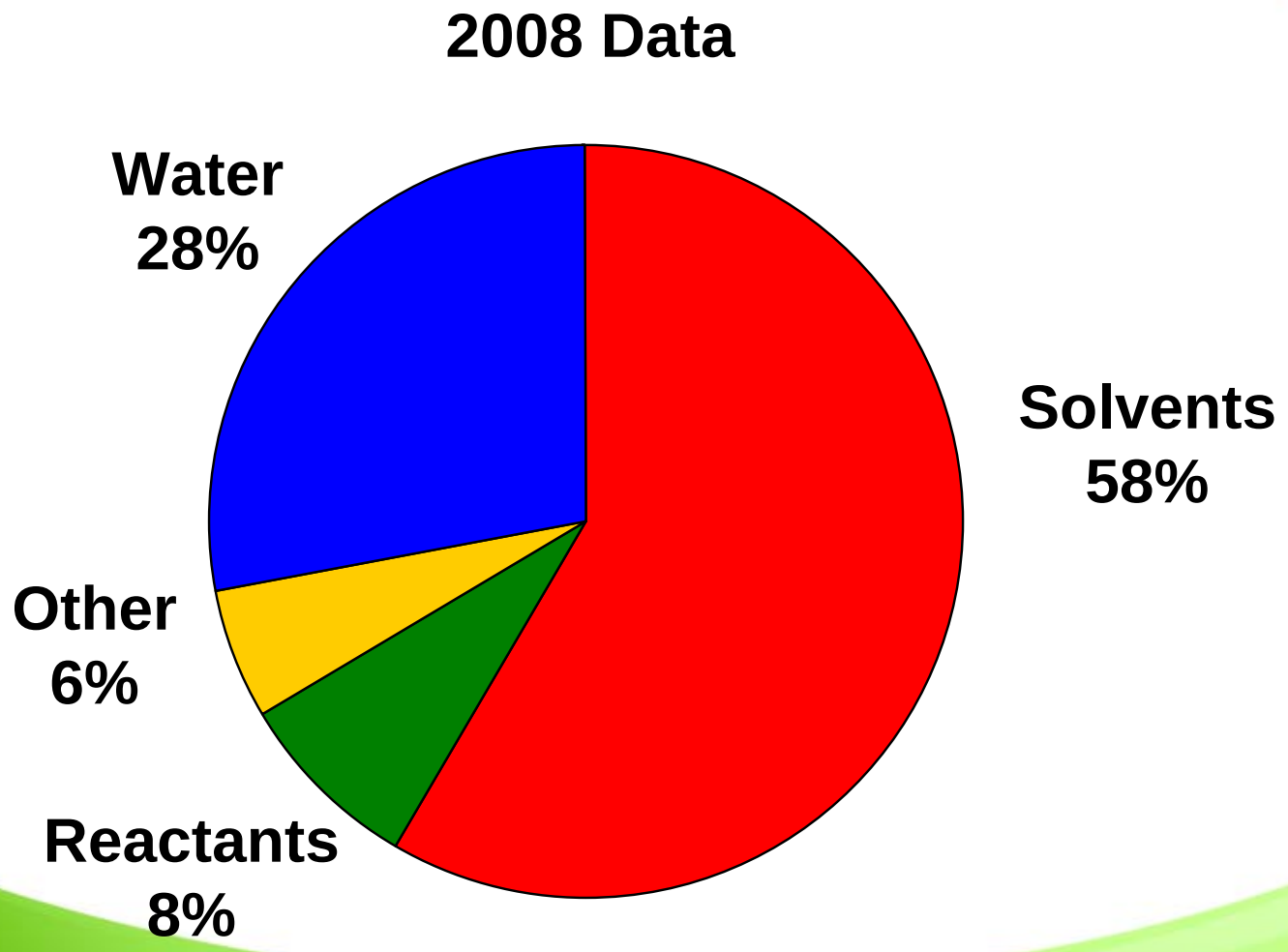
**Raw Materials** are all materials including water that are used directly in the process of synthesizing, isolating, and purifying the API final form

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

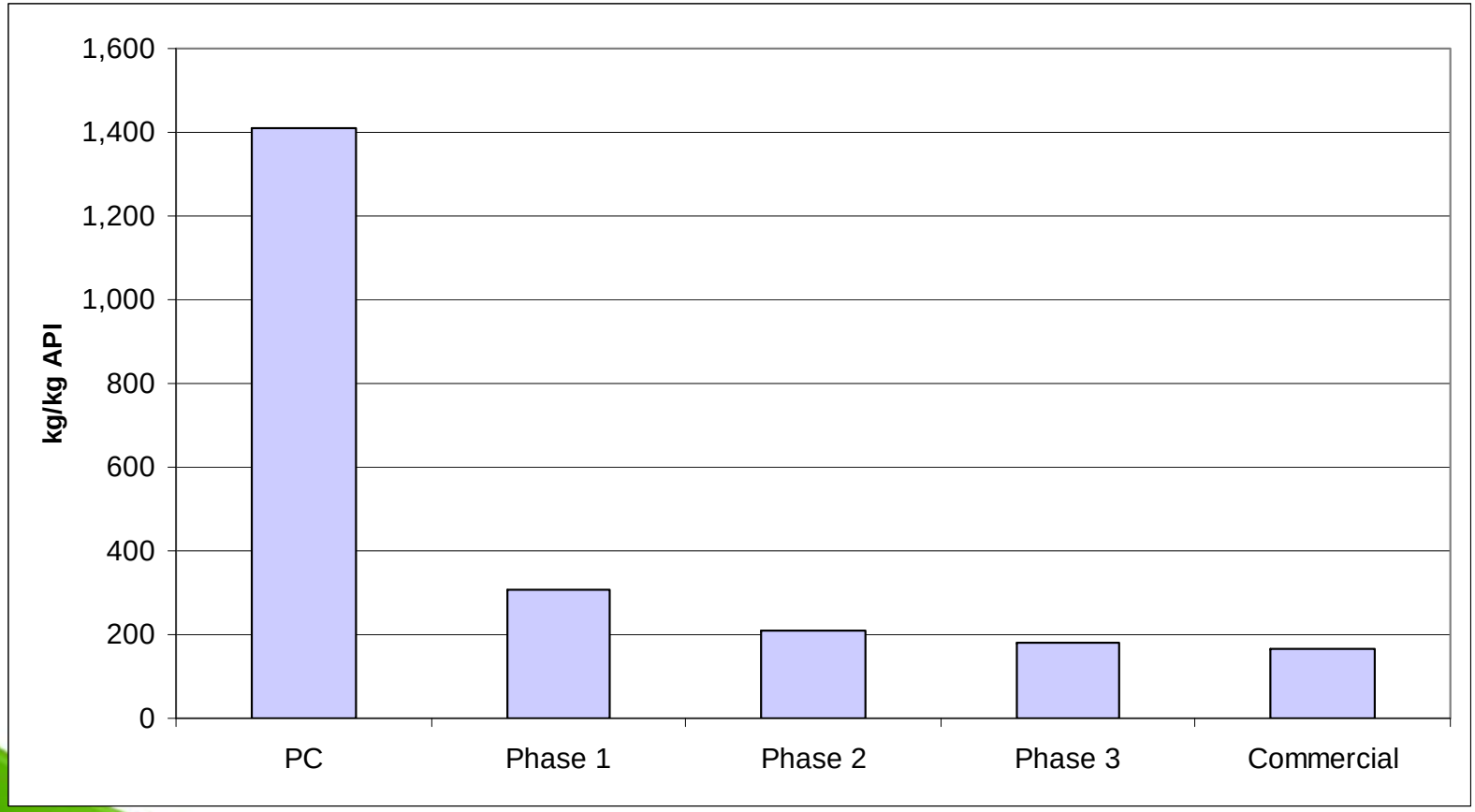
# Why measure PMI?

- 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!

gcipr@acs.org

www.acs.org/gcipharmaroundtable