50 Years after *Silent Spring*: The Past, Present and Future of the Global Chemical Enterprise

An Overview of Green Chemistry in the Pharmaceutical Industry: Pfizer and the ACS Green Chemistry Institute Pharmaceutical Roundtable

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Outline

• At the company level
  – Pfizer example of green chemistry practices

• At the industry sector level
  – ACS Green Chemistry Institute Pharmaceutical Roundtable example of green chemistry practices
The 13th Principle of Green Chemistry

It must make economic sense

$$$$
Our Green Chemistry Program: Commitments and Actions

Pfizer is finding innovative ways to ease our impact on the environment during manufacturing and is continuing to "green" the process.

Goals and commitments:

- Continue developing and applying Green Chemistry practices
- Share Green Chemistry knowledge within our organization, as well as by educating current and future generations of scientists and engineers
- Apply innovative science to improve world health

Notable projects embracing Green Chemistry principles:

- "Naturalizing" Lyrica®: Taking advantage of nature's own chemical catalysts (enzymes) through biosynthesis. The enzymatic synthesis of oxycodone will save more than 300,000
Pfizer Green Chemistry Mission

- To introduce, educate and promote the application of Green Chemistry across Pfizer.
- Key Philosophy: Voluntary restraint is better than enforced constraint.
- Green Chemistry includes protection of the environment and worker safety.
- Informing and influencing the Green Chemistry research agenda.
Pfizer Green Chemistry - What Does it Encompass?

- **Spans R&D and Manufacturing**
  - Research scale synthesis of small molecules to make potential new medicines (lab scale)
  - Scale up synthesis to make supplies of pre-clinical and clinical study materials (kilo & pilot plant scale)
  - Manufacturing of new medicines (typically batch production)

- **Includes and goes beyond synthetic chemistry**
  - Includes engineering (e.g. process technology innovation – continuous processing, PAT, biocatalysts etc)
  - Includes other sciences (e.g. Biology - substitution or reduction of radio-labeled assays).

- **Reaches outside the company**
  - Schools - influence the next generation of science and engineering students.
  - Academia – to positively shape today's chemistry research to solve industry (and society’s) needs is based on chemical reactions established 50-100 years ago!
### Pfizer Emphasized GC’s Economic and Environmental Benefits

Table 1. Green Chemistry principles deliver economic and environmental benefit

<table>
<thead>
<tr>
<th>Thinking Environmental</th>
<th>Thinking Economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>atom economy</td>
<td>minimal byproduct formation.</td>
</tr>
<tr>
<td></td>
<td>reduced environmental burden.</td>
</tr>
<tr>
<td>solvent reduction</td>
<td>less solvent required, less solvent waste.</td>
</tr>
<tr>
<td>reagent optimization</td>
<td>catalytic, low stoichiometry, recyclable.</td>
</tr>
<tr>
<td>convergency</td>
<td>reduced environmental burden related to improved process efficiency.</td>
</tr>
<tr>
<td>energy reduction</td>
<td>reduced environmental burden related to power generation, transport, and use.</td>
</tr>
<tr>
<td>in situ analysis</td>
<td>reduced potential for exposure or release to the environment.</td>
</tr>
<tr>
<td>safety</td>
<td>nonhazardous materials and processes reduce risk of exposure, release, explosions and fires.</td>
</tr>
</tbody>
</table>

more from less, incorporate total value of materials, reduced cost.

减少了容量要求，减少能源需求，降低成本。

更高效率，更高选择性，降低成本。

更高效率，更少操作，降低成本。

增加效率，更短过程，更温和条件，降低成本。

实时数据增加通过时间和效率，更少返工，降低成本。

工人安全和减少停工时间，减少特殊控制措施，降低成本。

Pfizer Web-based Green Chemistry Tools

Fig. 1 Pfizer solvent selection guide for medicinal chemistry.

Fig. 3 Oxidation of primary alcohol to aldehyde.
Internal Recognition of Pfizer Scientists for Green Chemistry Achievements

2003 Groton Labs Green Chemistry Awards

Call for nominations!

The objective of the Green Chemistry Award is to recognize individuals or teams for innovative chemical technologies that reduce or eliminate the use or generation of hazardous substances during the discovery or development of pharmaceutical drug substances.

Refer to the Pipeline article on July 7, 2003 for full details.

Submit nominations to Michael Rottas via e-mail or interoffice mail (MS 4157) no later than October 31, 2003.

5. Donation Made to Chemistry Department

Pfizer made a donation to the Department of Chemistry through Dr. Timothy Lash. His former student, Dan Richter (BS ‘97, MS ‘99), was the winner of an internal corporate “Groton Green Chemistry Award” and was able to designate ISU to receive a $5,000 award. Dan was a winner of the campus-wide Fisher Thesis Award for his MS Thesis.
Pfizer Green Chemistry Results –
External Recognition

- **Green Chemistry Technology Institute of Chemical Engineers (IChemE) in the United Kingdom**
  “*Excellence in Green Chemistry and Engineering Award*” (2006)
  For Lyrica® revised synthesis – significant reductions in waste by using an enzymatic process, and performing reaction steps in water.

- **UK Institute of Chemical Engineers (IChemE)**
  “*Crystal Faraday Award for Green Chemical Technology*” (2003)
  For process redesign of Viagra® (sildenafil citrate) – eliminates use of certain solvents, and recovers those that are used.

- **U.S. Environmental Protection Agency (EPA)**
  “*Presidential Green Chemistry Award*” (2002)
  Revised manufacturing process for Zoloft® (sertraline hydrochloride) – doubled product yield, and significantly reduced environmental impacts (use of resources, waste minimization).

Green Chemistry Triumphs at Environmental Awards

The best in UK environmental excellence was celebrated on 1 July at the 2009 Business Commitment to the Environment (BCE) Environmental Leadership Awards in London. Twelve companies received recognition for their outstanding achievements, but it was Pfizer that successfully scooped the Management Premier Award. Founded by Sir Peter Parker in 1975, the BCE Awards program is one of the world’s longest running environmental award schemes. It celebrates businesses that the BCE independent judging panel recognises as meeting the commercial demands of the present, without compromising the environment for future generations... Read the full story »
Pfizer Green Chemistry Education Workshops
Pfizer Green Chemistry Outcomes

• Green chemistry is firmly established in all aspects of Pfizer’s R&D and commercial manufacturing.
  – Drug discovery, chemical development and global supply chain.
  – Pfizer product processes => 5σ
• Pfizer spokesperson reports their weighted-average E-factor is 25 (industry average > 100)
  – Educated guess value ≈ $200-400 million/year
• Pfizer is recognized globally as a leader in industrial green chemistry
• Pfizer has provided strong support for green chemistry education for more than a decade
• Pfizer’s green chemistry model has been adopted by other pharmaceutical companies.
ACS Green Chemistry Institute
Pharmaceutical Roundtable

• **Mission:** To catalyze the implementation of green chemistry and engineering in the pharmaceutical industry globally.

• **Strategic Priorities**
  – Informing and Influencing the Research Agenda
    • Finding greener reactions and supporting academic R&D funding
  – Defining and Delivering Tools for Innovation
    • Solvent selection guide
    • Reaction selection tool
    • Expand CAS search capability
  – Educating Leaders
    • Workshops, conferences, business case studies
  – Collaborating Globally
Stocking the Pharma Green Chemistry “Tool Box”

• Only 25% or so of chemistry used by Pharma is green, another 25% could be made greener with a small effort, leaving half requiring innovative solutions.
• The GCIPR has awarded almost $1.5 million in research money to academic researchers globally to find these solutions.
• The GCIPR assesses all new published chemistry 2X/yr and reports through a publication their findings about the greenest synthetic options.
• The GCIPR has persuaded the NSF and NIGMS to support and fund research with a green chemistry outcome.
• The GCIPR has persuaded editors of several prestigious journals to require green assessments and metrics for articles submitted.
• Still, far too few universities where chemists and engineers are trained, require green chemistry coursework.
  – Except in China and India!
ACS GCIPR Reagent Selection Guide

Chemical Development:
Scalability

Medicinal Chemistry:
Broad Applicability

A
B
C

Manufacturing Greenness
## ACS GCI Pharmaceutical Roundtable Solvent Selection Guide

**Version 2.0 April 1, 2011**

### Substance Information

<table>
<thead>
<tr>
<th>Solvent Name</th>
<th>CAS Number</th>
<th>Safety</th>
<th>Health</th>
<th>Env (Air)</th>
<th>Env (Water)</th>
<th>Env (Waste)</th>
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<td>ETHYLENE GLYCOL</td>
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</tr>
</tbody>
</table>

### Scoring Information

- **Safety**: 1 (Least Safe) to 5 (Most Safe)
- **Health**: 1 (Least Impact) to 5 (Most Impact)
- **Env (Air)**: 1 (Least Impact) to 6 (Most Impact)
- **Env (Water)**: 1 (Least Impact) to 6 (Most Impact)
- **Env (Waste)**: 1 (Least Impact) to 6 (Most Impact)

*Guiding the selection of safer/greener solvents for chemical reactions.*

[www.acs.org/gcipharmaroundtable](http://www.acs.org/gcipharmaroundtable)
ACS GCI Pharmaceutical Roundtable Outcomes

• Today, all major pharmaceutical companies (Big Pharma) practice green chemistry in the design of drug manufacturing processes
  – Of the $900B in global sales, more than half comes from GCIPR member companies
  – Manufacturing cost savings can run up to $15million/year for a major drug (>1B sales p.a.)
  – Starting to see interest in generics, OTC’s, small pharma and biopharma sectors
• Through the GCIPR, progress is being made towards stocking the green chemistry tool box
• The GCIPR has exerted its influence with major chemistry journal editors to secure greener outcomes
• The success of the GCIPR has led to the creation of two roundtable clones: Formulated Products and Chemical Manufacturers
• Stay tuned!