



Green Chemistry at Pfizer



**Green Chemistry Symposium II
Sacramento, CA
June 19th, 2007**



Agenda

- **Introduction to Green Chemistry at Pfizer**
 - ✓ What it is, what it encompasses
- **Making a Difference through Green Chemistry**
 - ✓ Engagement and alignment across the company
 - ✓ Internal tools – helping chemists “go green”
 - ✓ Education
 - ✓ Supporting and influencing academic research
 - ✓ Results - in Research, Chemical R&D & Manufacturing
- **Take Away Messages**



Pfizer Overview

- Number 1 in global pharmaceutical sales
- World's largest biomedical research group
- Products in 150 countries; locations in more than 60 countries
- More than 25 languages represented





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.



Green Chemistry – What is it?

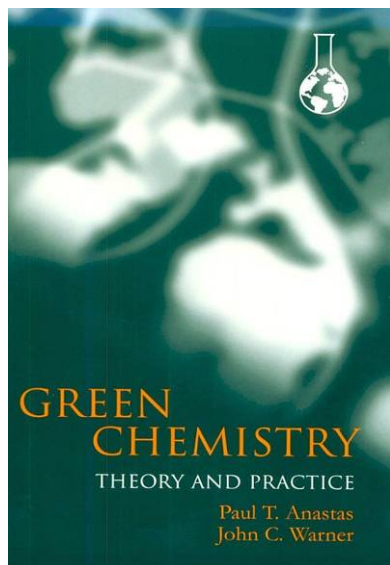
- Green Chemistry efficiently utilizes (preferably renewable) raw materials, eliminates waste and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products.

Roger Sheldon

Green Chem 2005, 7, 267-278



Principles of Green Chemistry Include:



- ✓ Waste prevention
- ✓ Atom economy
- ✓ Less hazardous chemical synthesis
- ✓ Safety solvents and auxiliaries
- ✓ Design for energy efficiency
- ✓ Use renewable feedstocks
- ✓ Catalysis
- ✓ Inherently safer chemistry for accident prevention

**Source: Paul T. Anastas and John C. Warner, Green Chemistry: Theory and Practice*



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 Green Chemistry – Engagement & Alignment

- **Success required attention to Green Chemistry across all our locations: research, scale-up, and manufacturing facilities.**
- **We have:**
 - ✓ A full-time GC leader with a company-wide responsibility
 - ✓ A company GC Policy and Steering Committee (*responsible for the strategic plan, communications plans, key policy decisions, and monitoring of performance*).
 - ✓ Research site GC teams – Chemistry and EHS colleagues, set annual objectives, manage site-based awards programs, raise awareness, and drive behavior change.
 - ✓ Integrated GC into our co-development process with manufacturing and initiated a Manufacturing GC Award.



Use of Internal Tools – Pfizer Solvent Selection Guide

Water

Acetone

Ethanol

2-Propanol

1-Propanol

Heptane

Ethyl Acetate

Isopropyl acetate

Methanol

MEK

1-Butanol

t-Butanol

Cyclohexane

Toluene

Methylcyclohexane

TBME

Isooctane

Acetonitrile

2-MeTHF

THF

Xylenes

DMSO

Acetic Acid

Ethylene Glycol

Pentane

Hexane(s)

Di-isopropyl ether

Diethyl ether

Dichloromethane

Dichloroethane

Chloroform

NMP

DMF

Pyridine

DMAc

Dioxane

Dimethoxyethane



Pfizer Solvent Replacement Table

Red Solvents	Alternative
Pentane	Heptane
Hexane(s)	Heptane
Di-isopropyl ether or ether	2-MeTHF or t-Butyl methyl ether
Dioxane or dimethoxyethane	2-MeTHF or t-Butyl methyl ether
Chloroform, dichloroethane or carbon tetrachloride	DCM
DMF NMP or DMAc	Acetonitrile
Pyridine	Et ₃ N (if pyridine used as base)
DCM (extractions)	EtOAc, MTBE, toluene, 2-MeTHF
DCM (chromatography)	EtOAc / Heptanes
Benzene	Toluene



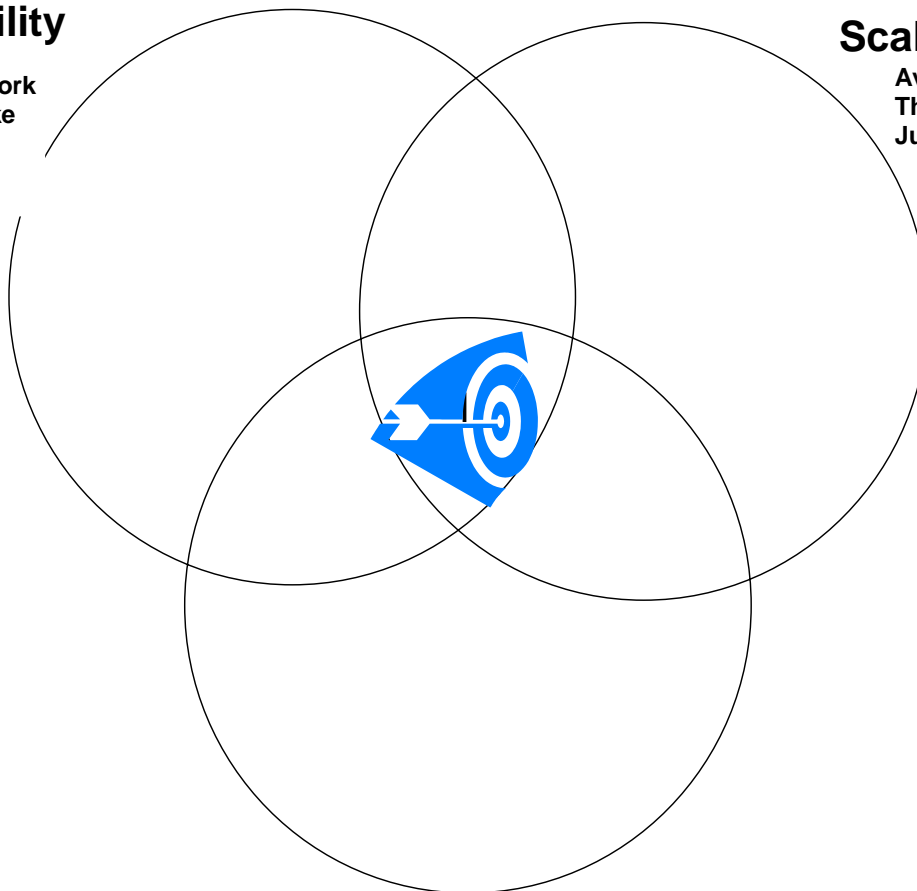
Pfizer Green Chemistry – Reagent Selection Guide

Wide Utility

The ability of a reagent to work On a wide variety of drug like Molecules. As judged by experienced Discovery Scientists

Scalability

Availability, Lack of Major Thermal or Tox Hazards. As Judged by API-Supply Chain



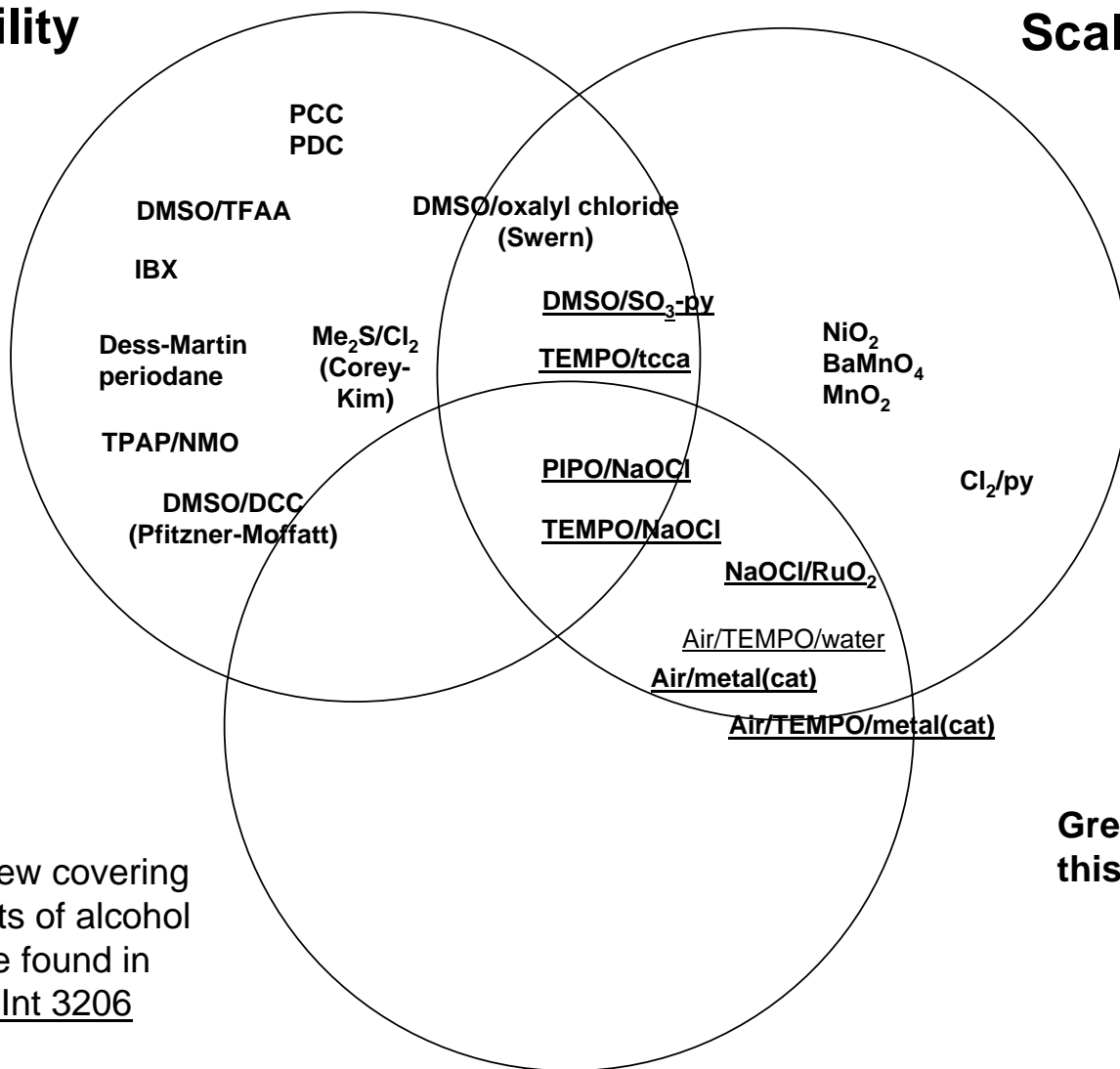
"Greenness" Criteria clearly laid out For each transformation



Example: Oxidation of Primary Alcohol to Aldehyde

Wide Utility

Scalability



An excellent review covering the Green aspects of alcohol oxidations can be found in 2006 Ang Chem Int 3206

Green Criteria for this Transformation



Microsoft Word Document

"Greenness"



And some simple Common Sense Advice...

- **Extractions**
 - **If you need to use DCM measure it! (don't just fill up the separating funnel)**
- **Chromatography**
 - **Consumes large volumes of solvent; is recrystallization or distillation an alternative?**
- **Need heat? Try to microwave (vs. oil bath heating)**
- **Evaporation**
 - **When stripping down methylene chloride on a rotary evaporator, transfer the evaporated solvent to the waste container periodically.**



Green Chemistry - Pfizer's Support and Influence on Academic Research

- Membership in the ACS GCI Pharmaceutical Roundtable
 - Let Academics and Govt agencies know of some of the key challenges in Pharmaceutical Manufacturing so they can be addressed (*see P.J. Dunn et al, Green Chemistry, 2007, 9, 411-420*)
- Identify commonly used reactions in Pharmaceutical Manufacturing.
- Inform research community, encourage funding agencies.
- Selectively fund key research areas.
(*e.g., Amide Formation, OH activation, Amide Reduction, Green Mitsunobu reactions, Oxidation/Epoxidations*)



Pfizer Green Chemistry - Education

- Pfizer believes education is a key to changing behaviors – of present colleagues and *future* scientists
- We ...
 - ✓ Hold **GC seminars** at all our research sites - by chemists for chemists with prominent chemistry speakers (*including CA, UK, PR, CT, MI*).
 - ✓ Hold **GC workshops** for university students in the areas where Pfizer is based
 - ✓ Share success internally and promote externally, (*e.g. Presidential Award Winning Green Chemistry*)
 - ✓ Have worked with educational partners to develop a middle school green chemistry (sustainability) curriculum:

<http://www.pfizer.com/pfizer/subsites/philanthropy/caring/science.education.greenchem.jsp>



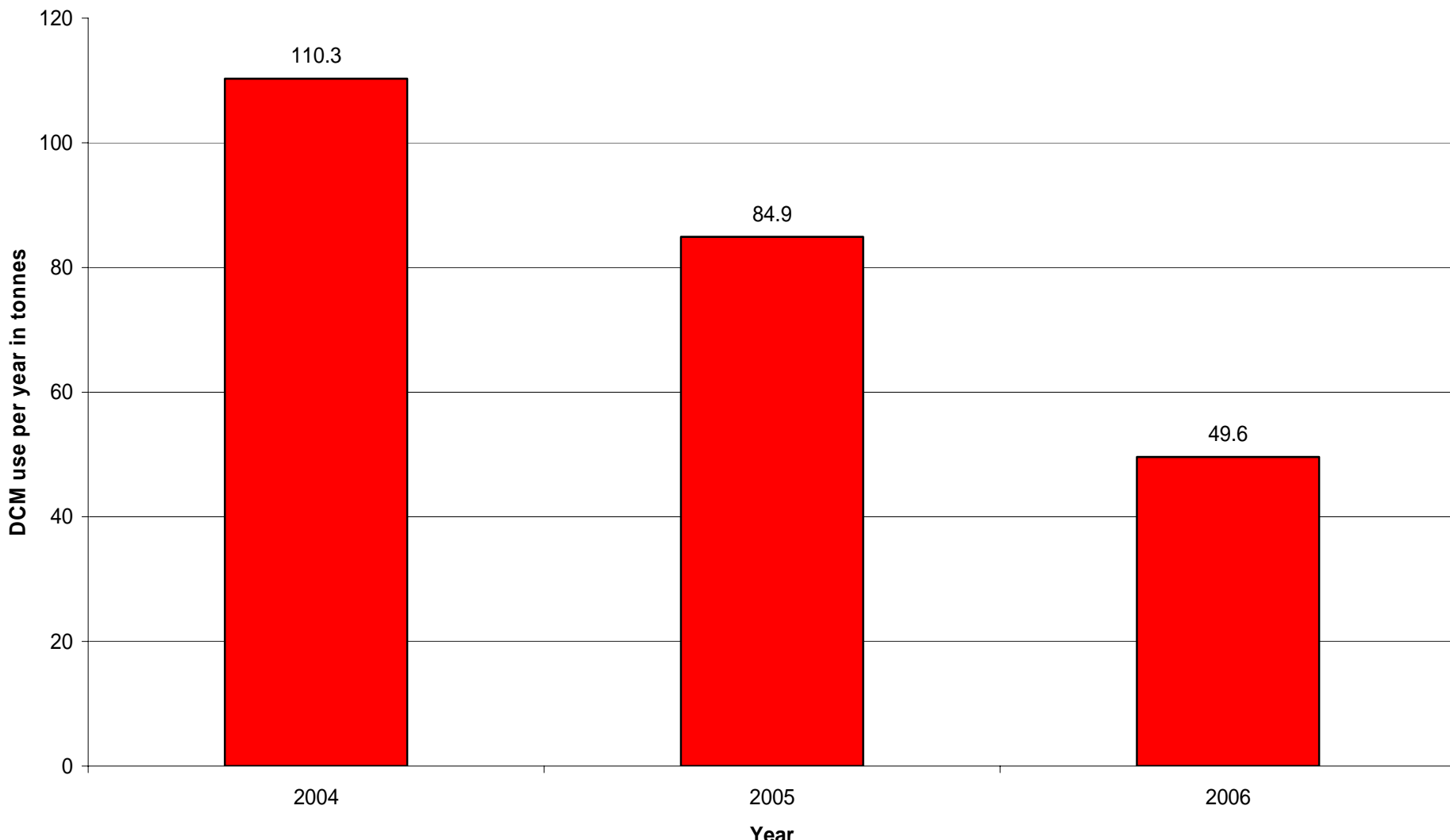
Green Chemistry Middle School Curriculum – Video Clip (3 minutes)

[Click here for the Green Chemistry Inspire Young Minds video clip](#)



Pfizer Green Chemistry Results – Some Examples

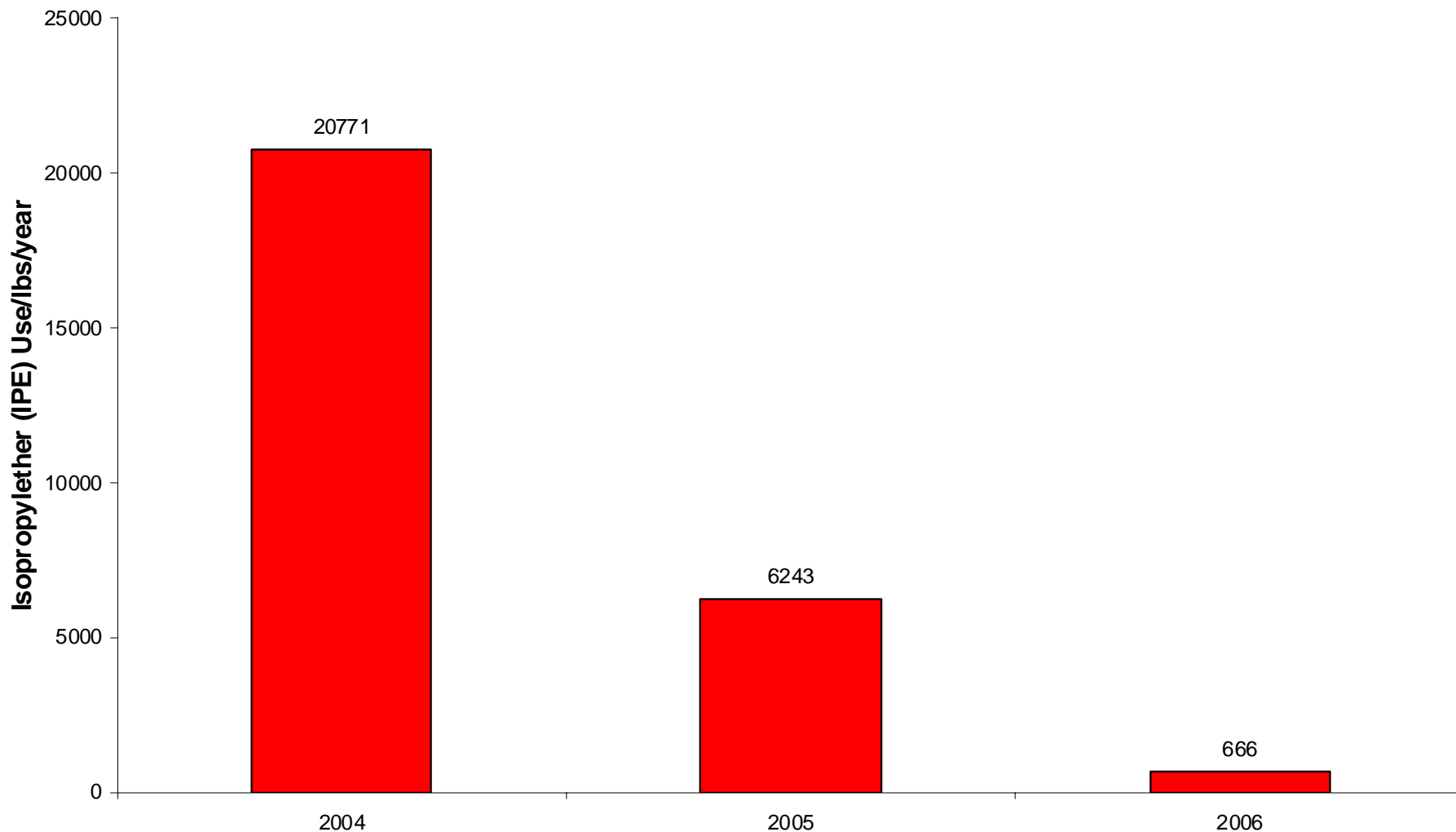
Combined Groton and Sandwich DCM use 2004 - 2006





Pfizer Solvent Switching Program

PGRD Global Diisopropylether Use





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 a 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)



Take Away Messages

- Leadership, colleagues and stakeholders care - Pfizer is committed to effective environmental management.
- Integrating GC provides the opportunity to do that through the core of our business - discovery, development and manufacture of new medicines.
- GC has resulted in significant environmental benefits (reduced use of resources, minimized waste and emissions, energy efficiency, cleaner and safer processing, a healthier workplace....)
- Provides cost effective solutions
 - Even at lab scale cost savings can be realized
 - Manufacturing scale process changes save \$MMs



Q&A

Thank You!

- To our many Pfizer colleagues
- To our partners in education and research
- To YOU – today's audience!