Green Chemistry in Materials Design

John C. Warner

President and Chief Technology Officer Warner Babcock Institute for Green Chemistry, LLC

President Beyond Benign









BROMINATED FLAME RETARDANTS

KOUCHNECK 4

PHTHALATES

ROUGHNEO

BISPHENOLA

ROUCHNEOK &







Asking the Right Questions

Why would a chemist make a hazardous material?

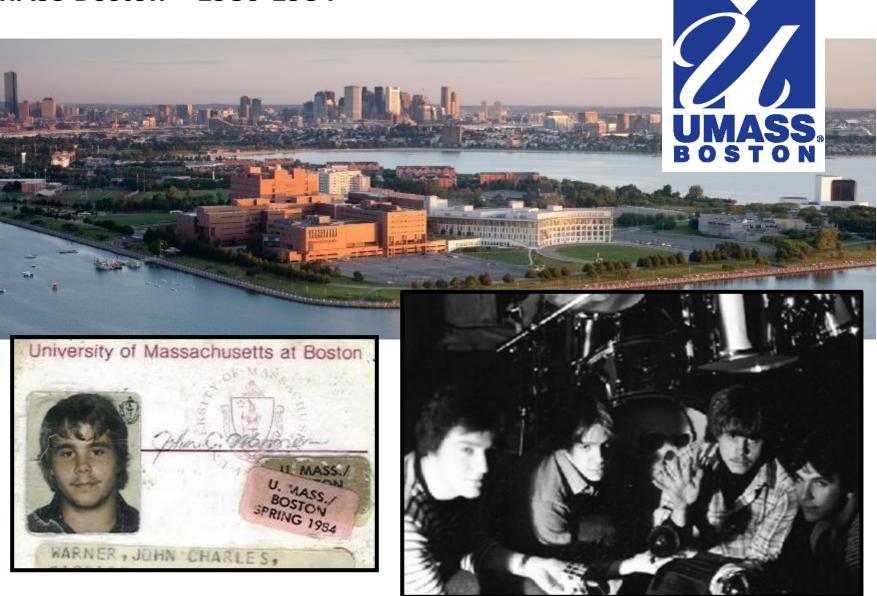
How do we train chemists?





Becoming a Chemist...

UMASS Boston – 1980-1984











Professor J.-P. Anselme

"N-Nitrosamines from the Reaction of N-Chlorodialkylamines with Sodium Nitrite." Nakajima, M.; Warner, J. C.; Anselme, J.-P. J. Chem. Soc., Chem. Commun., **1984**, 451.

"N-Nitrosamines *via* the Phase-Transfer mediated Nitrosation of Secondary Amines with Sodium Nitrite and N-Haloamides." Nakajima, M.; Warner, J. C.; Anselme, J.-P. *Tetrahedron Lett.*, **1984**, *25*, 2619.

"N-Nitrosamines from the Reaction of Sulfamoyl Chlorides with Sodium Nitrite." Warner, J. C.; Nakajima, M.; Anselme, J.-P. *Bull. Soc. Chim. Belges*, **1984**, *93*, 919.

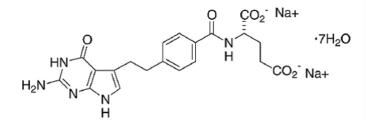
"The Wittig Reaction in the Undergraduate Organic Laboratory." Warner, J. C.; Anastas, P. T.; Anselme, J.-P. *J. Chem. Ed.*, **1985**, *62*, 346.

"Benzoyl Phenyl 1-Methylpyrazoles. Synthesis, Characterization, and Spectra." Kano, K.; Scarpetti, D.; Warner, J. C.; Anselme, J.-P.; Springer, J. P.; Arison, B. H. *Can. J. Chem.*, **1986**, *64*, 2211.





Princeton University – 1984-1988







Professor E. C. Taylor

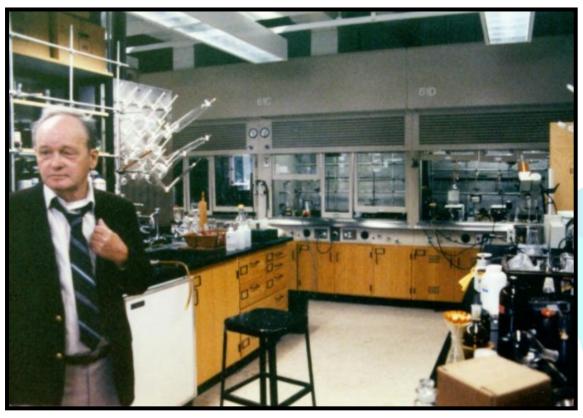


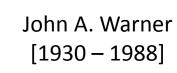
Natalie Warner [1932 – 2002]



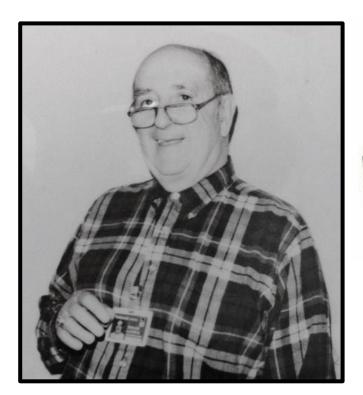












Lloyd D. Taylor

Polaroid Corporation – 1988-1997

POLARCID LAND CAMERA









For over 180 years of "Modern Chemistry"...



Heat things under high temperature

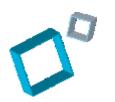
Runs reactions at "room" temperature

Apply high pressures

Runs reactions at ambient pressure

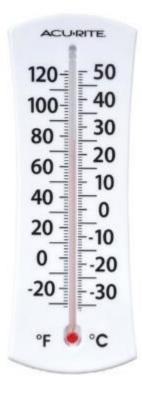
Use organic solvents

Uses water as a solvent





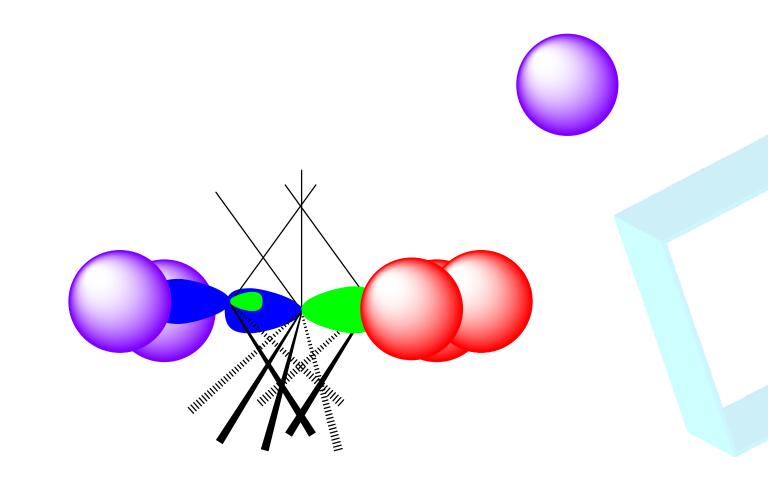
A thermometer is a molecular speedometer...

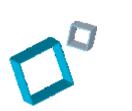






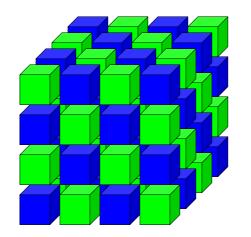




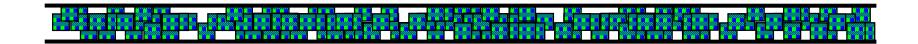




Non Covalent Derivatization













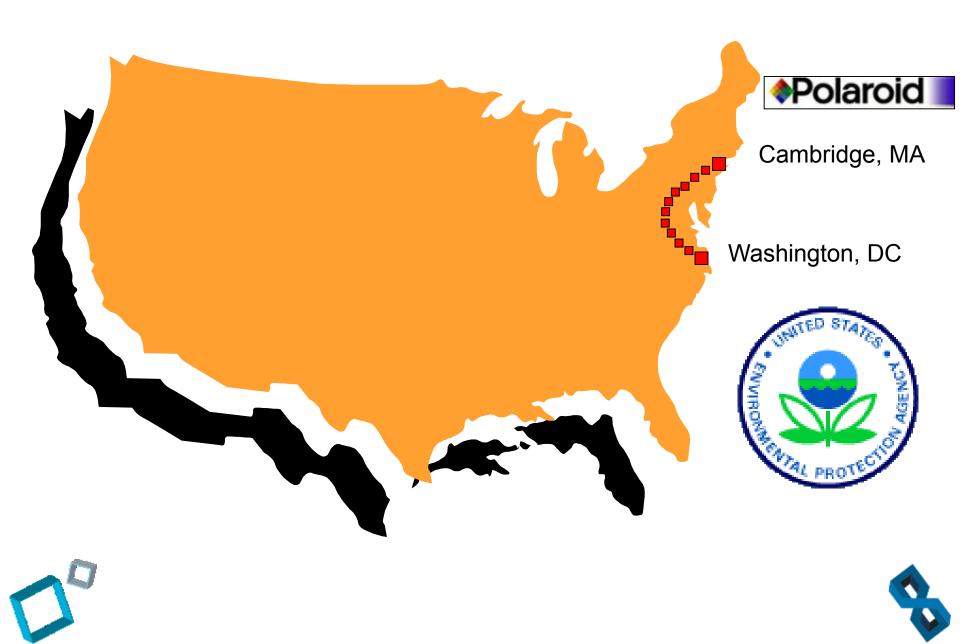
EPA Approval Low Volume Exemption PreManufacturing Notification

"Small particles"?

"Molecular Complexes"?

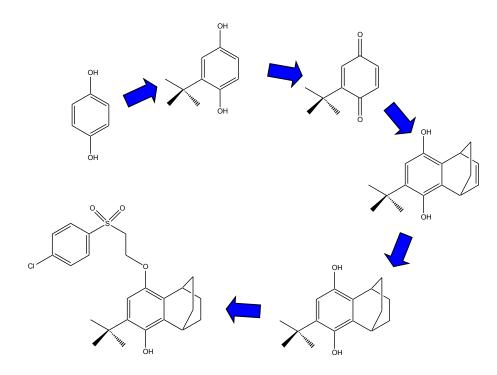


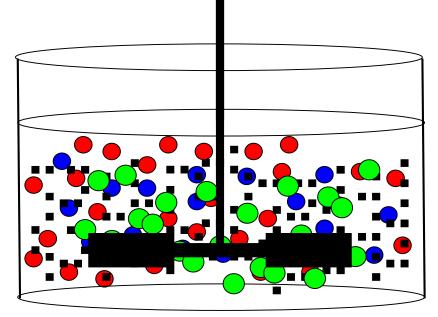










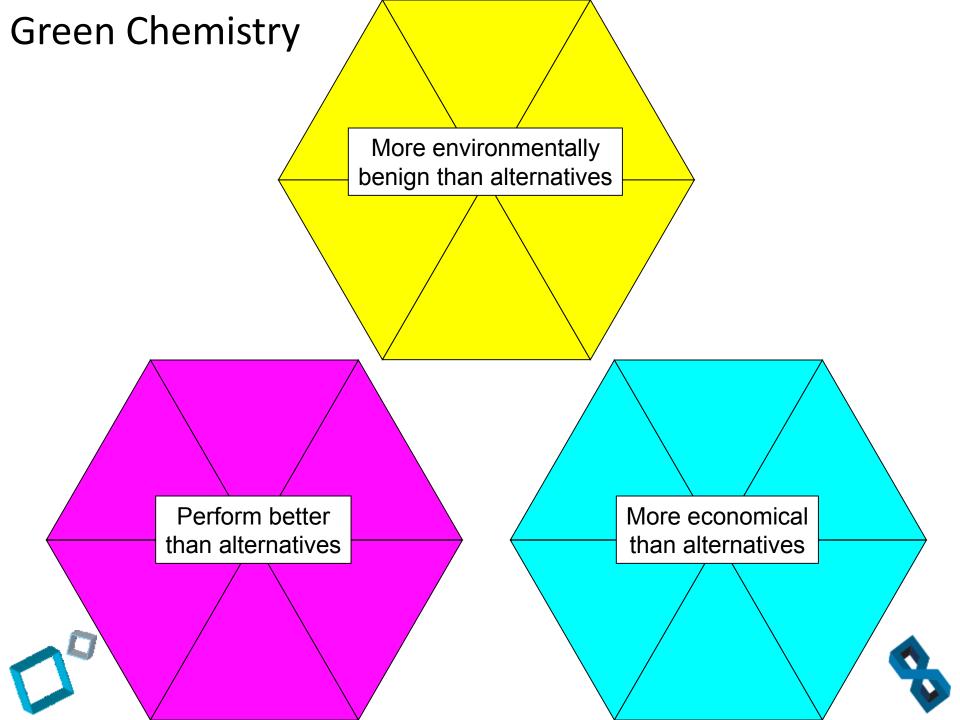


Old Technology Several Solvents High Energies Hazardous Reagents

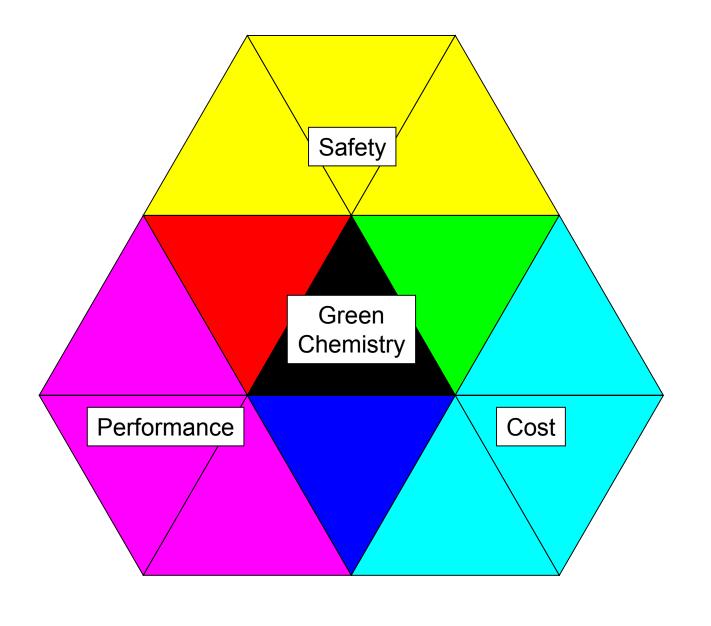
New Technology

Aqueous Conditions Low Energies Non-hazardous Reagents





Green Chemistry







Green Chemistry is the *design* of chemical products and processes that reduce or eliminate the *use and/or generation* of hazardous substances.





The Twelve Principles of Green Chemistry

1. Prevention. It is better to prevent waste than to treat or clean up waste after it is formed.

2. Atom Economy. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. Less Hazardous Chemical Synthesis. Whenever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. Designing Safer Chemicals. Chemical products should be designed to preserve efficacy of the function while reducing toxicity.

5. Safer Solvents and Auxiliaries. The use of auxiliary substances (solvents, separation agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.

6. Design for Energy Efficiency. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

7. Use of Renewable Feedstocks. A raw material or feedstock should be renewable rather than depleting whenever technically and economically practical.

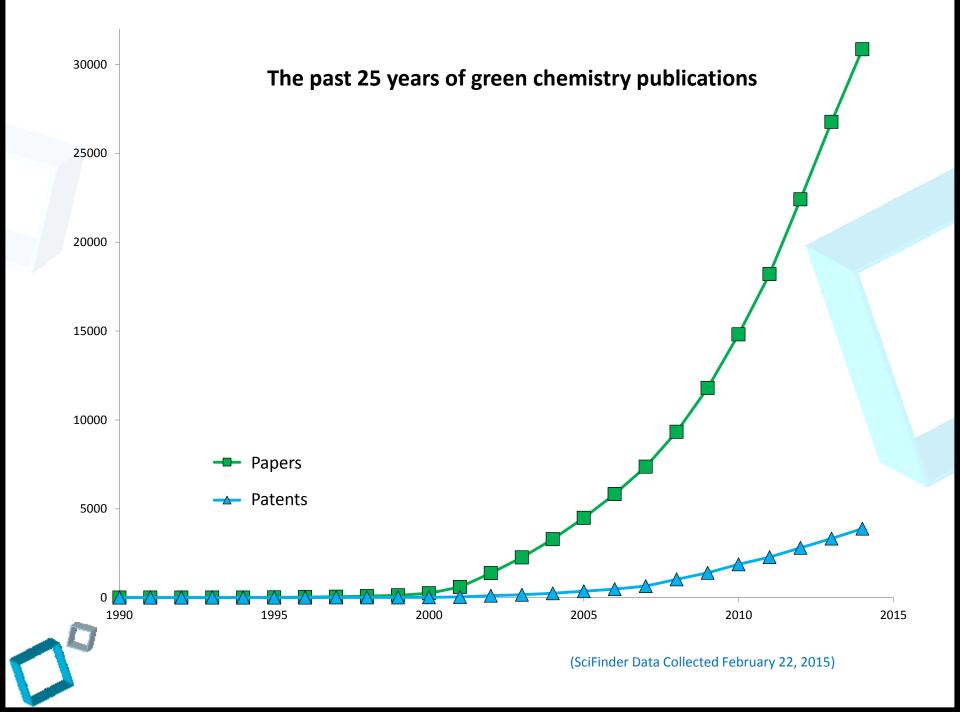
8. Reduce Derivatives. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible .

9. Catalysis. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for Degradation. Chemical products should be designed so that at the end of their function they do not persist in the environment and instead break down into innocuous degradation products.

11. Real-time Analysis for Pollution Prevention. Analytical methodologies need to be further developed to allow for real-time inprocess monitoring and control prior to the formation of hazardous substances.

12. Inherently Safer Chemistry for Accident Prevention. Substance and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.





1988-1997

Lloyd Taylor

"Thermographic Recording Film." Dombrowski, Edward J.; Guarrera, Donna J.; Jones, Robert L.; Mischke, Mark R.; Warner, John C.; Yang, Jiyue, US Patent 5,750,464. May 12, **1998**.

"Thermographic Recording Films." Dombrowski, Edward J.; Jones, Robert L.; Warner, John C.; Yang, Jiyue, US Patent 5,750,463. May 12, **1998**.

"Process for Fixing an Image, and Medium for Use Therin." Marshall, John L.; Shon Baker, Rita S.; Takiff, Larry C.; Telfer, Stephen J.; Warner, John C., US Patent 5,741,630. April 21, **1998**.

"Copolymers Having Pendant Functional Thymine Groups." Grasshoff, J. Michael; Taylor, Lloyd D.; Warner, John C., US Patent 5,708,106. January 13, **1998**.

"Photographic Development" Guarrera, Donna J.; Mattucci, Neil C.; Mehta, Avinash C.; Taylor, Lloyd D.; Warner, John C. US Patent 5,705,312. January 6, **1998**.

"Photographic System" Guarrera, Donna J.; Mattucci, Neil C.; Mehta, Avinash C.; Taylor, Lloyd D.; Warner, John C. PCT Int. Appl. WO 9,729,405. August 14, **1997**.

"Method of Imaging Using a Polymeric Photoresist Having Pendant Vinylbenzyl Thymine Groups"
Grasshoff, J. Michael; Taylor, Lloyd D.; Warner, John C., US Patent 5,616,451. April 1, 1997.
"Process for Fixing an Image, and Medium for Use Therin." Marshall, John L.; Shon Baker, Rita S.; Takiff, Larry C.; Telfer, Stephen J.; Warner, John C., US Patent 5,582,956. December 10, 1996.
"Low-Volatility, Substituted 2-Phenyl-4,6-bis[Halomethyl]-1,3,5-triazine for Lithographic Printing Plates." Fitzgerald, Maurice J.; Kearney, Frederick R.; Liang, Rong-Chang; Schwarzel, William C.; Guarrera, Donna, J.; Hardin, John M.; Warner, John C., US Patent 5,561,029. October 1, 1996.
"Process for Fixing an Image, and Medium for Use Therin." Marshall, John L.; Shon Baker, Rita S.; Takiff, Larry C.; Telfer, Stephen J.; Warner, John C., PCT Int. Appl. WO 9,529,067. Nov 2, 1995.
"Vinylbenzyl Thymine Monomers and Their Use in Photoresists." Grasshoff, J. Michael; Taylor, Lloyd D.; Warner, John C., US Patent 5,459.

"Imaging Medium and Process." Fehervari, Agota F.; Gaudiana, Russell A.; Kolb, Eric S.; Mehta, Parag G.; Taylor, Lloyd D.; Warner, John C., US Patent 5,424,268. June 13, **1995**.

"Thermally-Processable Image Recording Materials Including Substituted Purine Compounds." Ford, M.; Guarrera, D. J.; Mischke, M.; Pai, R.; Warner, John C., US Patent 5,411,929. May 2, **1995**. "Copolymeric Mordants and Photographic Products and Processes Containing Same." Grasshoff, J. Michael; Tailan Have D.; Warner, John C., US Patent 5,395,731. March 7, **1995**.

"Process and Composition for Use in Photographic Materials Containing Hydroquinones. Cont in Part." Taylor, Lloyd D.; Warner, John. C., US Patent 5,338,644. August 16, **1994**. "Process and Composition for Use in Photographic Materials Containing Hydroquinones." Taylor,

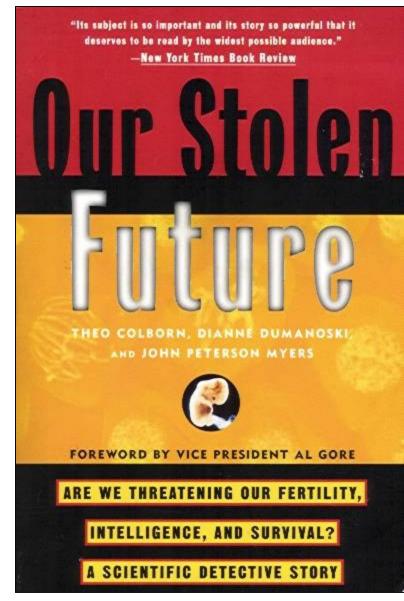
Lloyd D.; Warner, John. C., US Patent 5,177,262. January 5, 1993.







John Patrick Warner [Nov 12, 1991- Mar 20 1993]





I have synthesized over 2500 compounds!!!!!





I have synthesized over 2500 compounds!

I have never been taught what makes a chemical toxic! I have no idea what makes a chemical an environmental hazard!

I have synthesized over 2500 compounds!

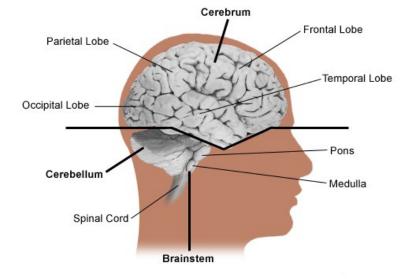
I HAVE NO IDEA WHAT MAKES A CHEMICAL TOXIC!







Stanford Hospital & Clinics



What causes brain tumors?

The majority of brain tumors have abnormalities of genes involved in cell cycle control, causing uncontrolled cell growth. These abnormalities are caused by alterations directly in the genes, or by chromosome rearrangements which change the function of a gene.

Patients with certain genetic conditions (i.e., neurofibromatosis, von Hippel-Lindau disease, Li-Fraumeni syndrome, and retinoblastoma) also have an increased risk to develop tumors of the central nervous system. There have also been some reports of people in the same family developing brain tumors who do not have any of these genetic syndromes.

Research has been investigating parents of children with brain tumors and their past exposure to certain chemicals. Some chemicals may change the structure of a gene that protects the body from diseases and cancer. Workers in oil refining, rubber manufacturing, and chemists have a higher incidence of certain types of tumors. Which, if any, chemical toxin is related to this increase in tumors is unknown at this time.

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http://cancer.stanfordhospital.com/healthInfo/cancerTypes/brain/default



Recent scientific research has clearly demonstrated an association between organochlorines and breast cancer. An analysis of chemical plant workers in Hamburg, Germany discovered a two-fold increase in breast cancer among the women workers who had been exposed to dioxin contamination. Significantly higher levels of breast cancer have been found in separate studies of women living near organochlorine chemical plants in Minnesota and Long Island. **Other studies have revealed elevated breast cancer mortality among professional chemists.**

http://www.fwhc.org/health/xeno.htm

"Its subject is so important and its story so powerful that it deserves to be read by the widest possible audience." --New York Times Book Review

THEO COLBORN, DIANNE DUMANOSKI, AND JOHN PETERSON MYERS FOREWORD BY VICE PRESIDENT AL GORE ARE WE THREATENING OUR FERTILITY, INTELLIGENCE, AND SURVIVAL?

A SCIENTIFIC DETECTIVE STORY

Olsson, H. and L. Brandt (1981). **"Supradiaphragmatic presentation of non-Hodgkin's lymphoma in men occupationally exposed to organic solvents**." Acta Med Scand 210(5): 415-8.

Walrath, J., F. P. Li, et al. (1985). **"Causes of death among female chemists**." Am J Public Health 75(8): 883-5.

Christie, D., K. Robinson, et al. (1991). **"A prospective study in the Australian petroleum industry. II. Incidence of cancer**." Br J Ind Med 48(8): 511-4.

Persson, B., M. Fredriksson, et al. (1993). **"Some occupational exposures as risk factors for malignant lymphomas**." Cancer 72(5): 1773-8.

Berlin, K., C. Edling, et al. (1995). **"Cancer incidence and mortality of patients with suspected solvent- related disorders**." Scand J Work Environ Health 21(5): 362-7.

Persson, B. (1996). "Occupational exposure and malignant lymphoma." Int J Occup Med Environ Health 9(4): 309-21.

Lynge, E., A. Anttila, et al. (1997). "Organic solvents and cancer (review)." Cancer Causes Control 8(3): 406-19.



Every Year: (United States)

Chemistry and Chemical Engineering Graduates

15,000 Undergraduate Degrees

3,000 Masters Degrees

3,000 Doctoral Degrees

50.9 % Women Undergraduate Degrees (2004)





To get a degree in Chemistry...

No universities require any demonstration of knowledge regarding toxicity or environmental impact!





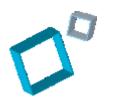
UMASS - 1996-2007







1997 Assistant Professor 1998 Associate Professor (Tenure) 1999 Director of Biochemistry 2000 Full Professor 2001 Chair Chemistry Department 2001 Director Green Chemistry PhD Program 2004 Professor Plastics Engineering (UML)





EDUCATION



GREEN CHEMISTRY EARNS A PH.D.

The University of Massachusetts, Boston, now offers a Ph.D. track in green chemistry

Sity of Massachusetts, Boston (UMB), has been accepting students into a new program called the green chemistry Ph.D. track. It is offered by the department of environmental sciences but administered by the department of chemistry

The first of its kind in the world, the program is the brainchild of its director, UMB chemistry professor John C. Warner. Students in the program, he explains, will be trained much like other Ph.D. chemistry students, although their education will emphasize skills to design materials and processes that have minimal impact on human health and the environment. Areas of concentration include environmentally benign synthesis, environmental monitoring and detection, biodegradation, and bioremediation.

What makes the program different from anything else available so far, Warner says, is the requirement of courses in toxicology, environmental law and policy, environmental fate and transport, and industrial chemistry. Through these courses, he explains, "we broaden the students' understanding of environmental realities such as what makes a molecule toxic, what laws have been established to govern synthetic procedures, and what happens in the environment—which conventional chemistry programs don't teach."

Terrence J. Collins, a chemistry profes-

sor at Carnegie Mellon University, notes that "we do not live in a sustainable civilization, sustainability meaning that what we do every day can be carried on to the indefinite future without causing damage." Collins was a recipient of the 1999 Presidential Green Chemistry Challenge Academic Award. The UMB program, he tells C&EN, is one way to call attention to the fact that "a sustainable civilization needs the intimate engagement of chemistry."

The UMB program "is timely, as there has been a distinct shift in focus in chemistry," says Janet Scott, deputy director of the Centre for Green Chemistry at Monash University, in Australia, "Even those who might not consider themselves' green chemists' are beginning to focus on issues of sustainability and the design of benign products and processes to prevent pollution at the source. The chemical industry is beginning to demand a wider knowledge of and attention to issues of sustainability."

Mary Kirchboff, assistant director of the Green Chemistry Institute, in Washington, D.C., agrees that the time is right for a green chemistry Ph.D. program. It might have been met with skepticism 10 years ago, when the term "green chemistry" first surfaced, she tells C&EN. Warner is the ideal person to lead such a program, she adds. "He's got the research credentials, the teaching credentials, the commitment to students, and the passion." Particularly in organic synthesis, forINCUBATOR The University of Massachusetts, Boston, houses the first Ph.D. program in green chemistry.

mal green chemistry training will force chemists to change how they think.

"One of the things that makes organic synthesis so exciting is that, if you draw a molecule, there are probably an infinite number of synthetic pathways that you can follow to make that molecule," Warner says. Traditionally, the focus has been on maximizing yields and stereoselectivities. Considerations of environmental and toxicological impact rarely come into play.

"IF ONE STEP in a synthetic sequence requires a hazardous reagent that's regulared by the federal government, that sequence could be more expensive than an alternative route that might give less yield," Warmer explains. Regulatory and environmental realities often decide the economic viability of a synthetic route, he adds.

Chemists usually learn of such considerations when they're working for a company, Warner says. "Industry would like people to come in with some understanding of these issues, because there's economic benefit if processes designed in labs do not have to be reworked to satisfy regulatory requirements."

A green chemistry Ph.D. would be a big plus for chemists interested in process development, notes Berkeley Cae, vice president of pharmaceutical sciences at Pfizer Global Research & Development, Groton, Conn. "What we try to incorporate into the design of manufacturing processes—such as safety, efficient use of raw materials, minimal use of solvents, and online analysis—are aligned to the concepts that Warner and people like him are teaching." he explains. "We just didn't call it green chemistry. We called it process development."

Amy Cannon is the first student enrolled in UMB's green chemistry Ph.D. program. She's working on constructing solar energy devices in a more environmentally benign manner. Currently, she explains, producing solar cells consumes so much energy that a solar panel has to operate for years before it generates as much energy as was used to make it.

"Alternative energy is one of the most important areas in terms of sustainability," Cannon tells C&EN. Having just completedber master's degree under Wamer's guidance, Cannon is passionate about green chemistry. "What could be better than this," she asks, "given that my big goal in life is to help save the world by doing what I can where I am?" – MAUREEN ROUH

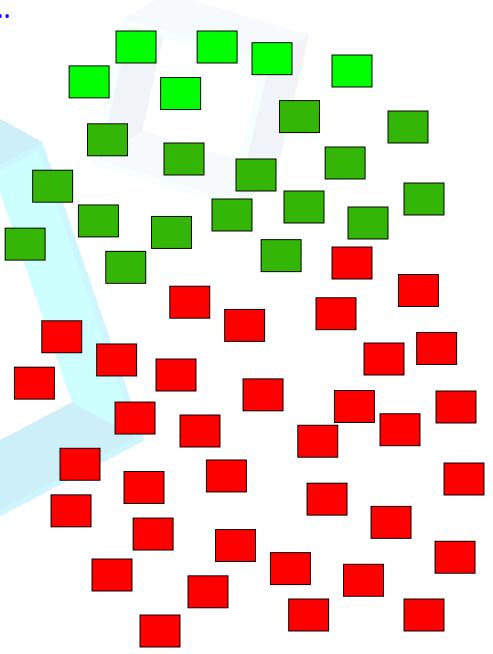


Of all the products and processes...

Maybe 10% are benign...

Maybe 25% have alternatives available...

65% Still have to be invented!



How does Green Chemistry fit into the big picture of Sustainability.





United States Environmental Protection Agency

Learn the Issues

Science & Technology

Laws & Regulations

About EPA



Green Chemistry

Basics of Green Chemistry

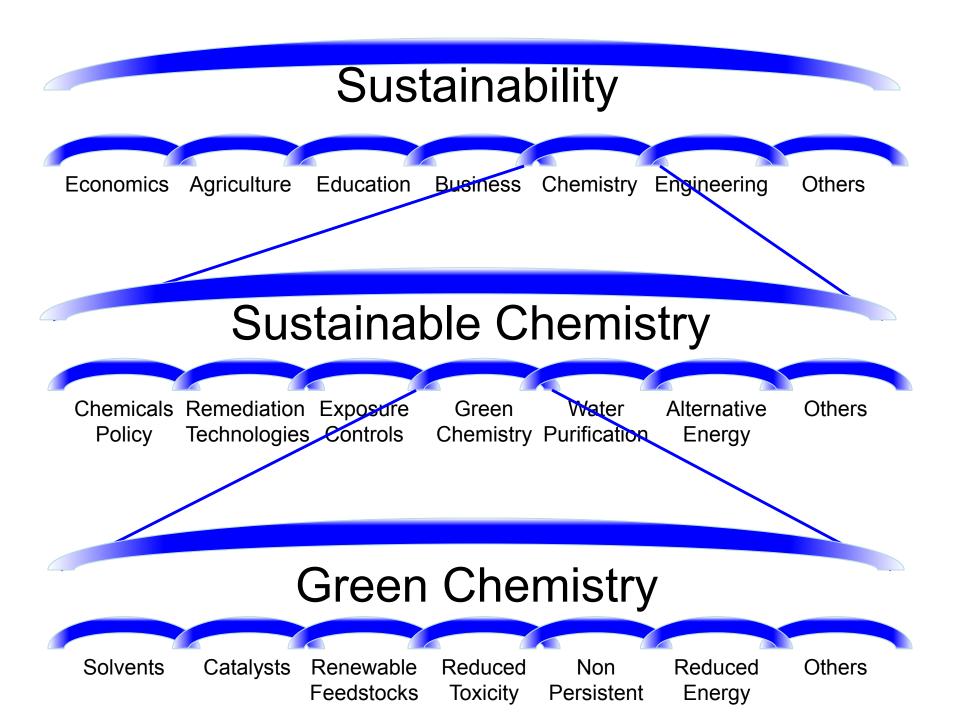
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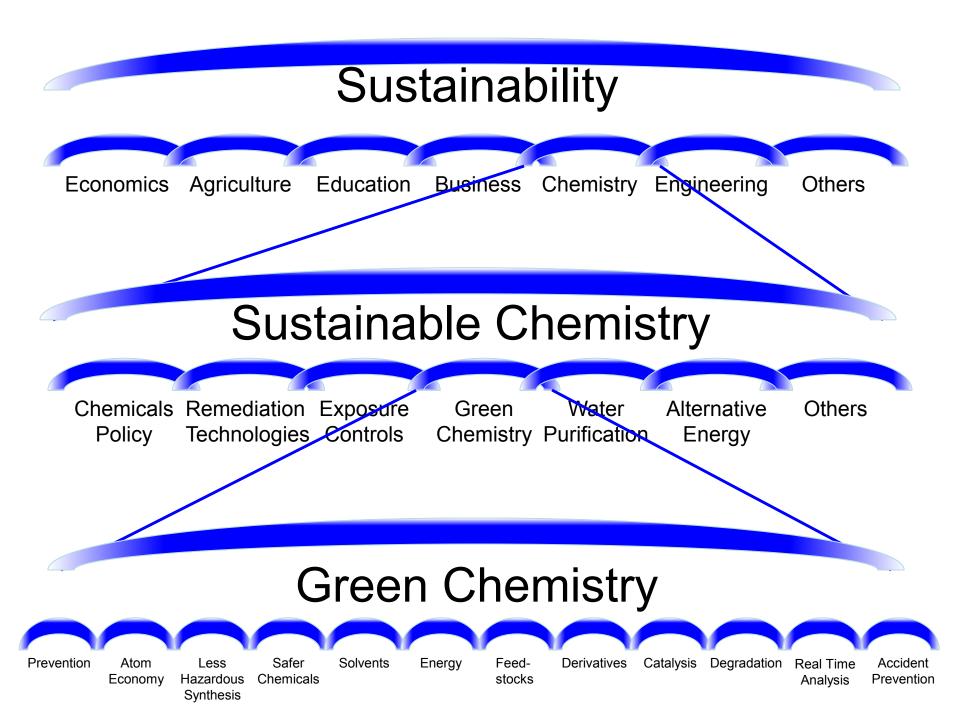
- Definition of green chemistry
- How green ch
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- Twelve princip
- Green chemis as sustainable chemistry.

Definition of green chemistry

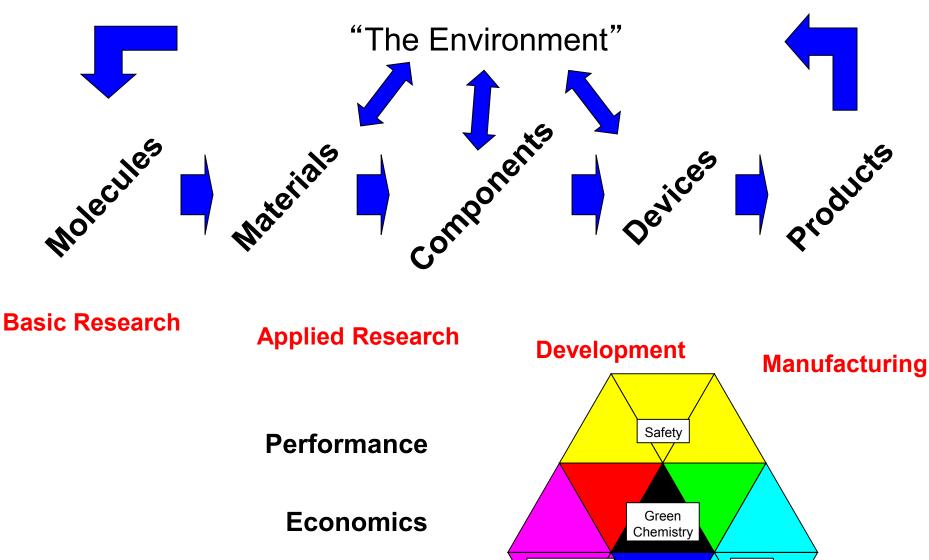
Green chemistry is the design of chemical products and processes that reduce or eliminate the use or generation of hazar ous substances. Geen chemistry applies across the life cycle of a chemical product, including its design, manufacture, use, and ultimate disposal.

Green chemistry:





Where do products come from?



Performance

Cost

Social Implications



"The Environment"

Green Chemistry

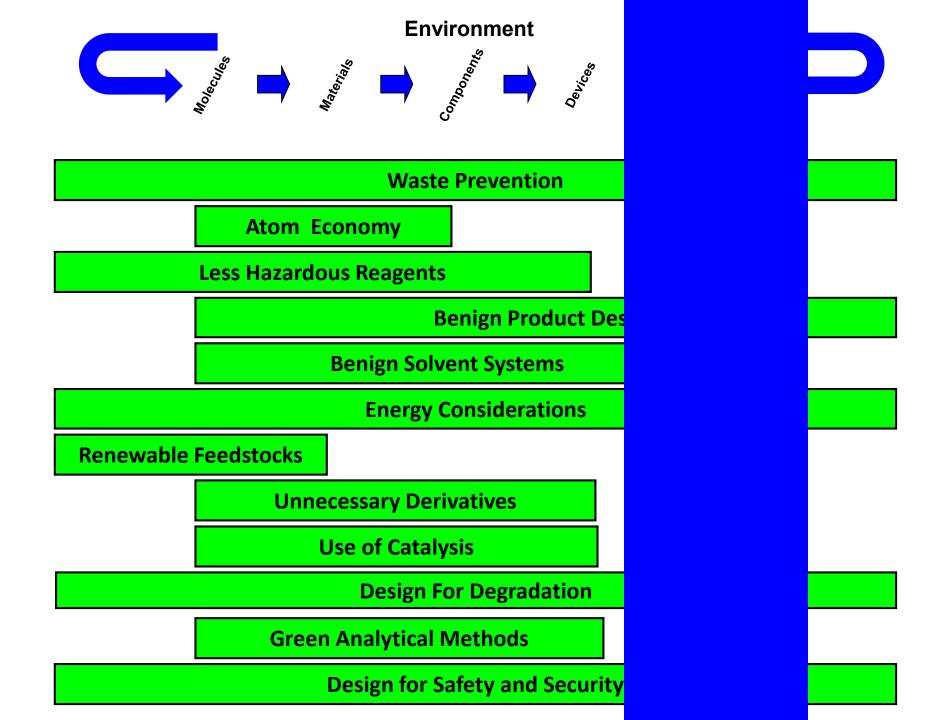


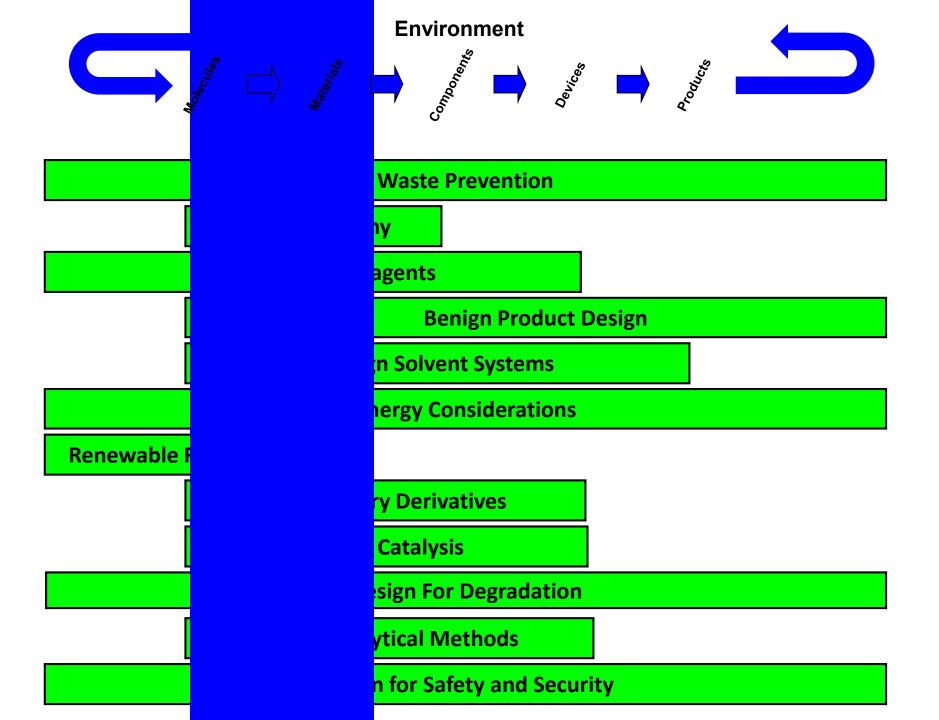


How does Green Chemistry relate to Life Cycle Analyses?









Chemists have ALWAYS cared about Human Health and the Environment.











Risk = Exposure x Hazard





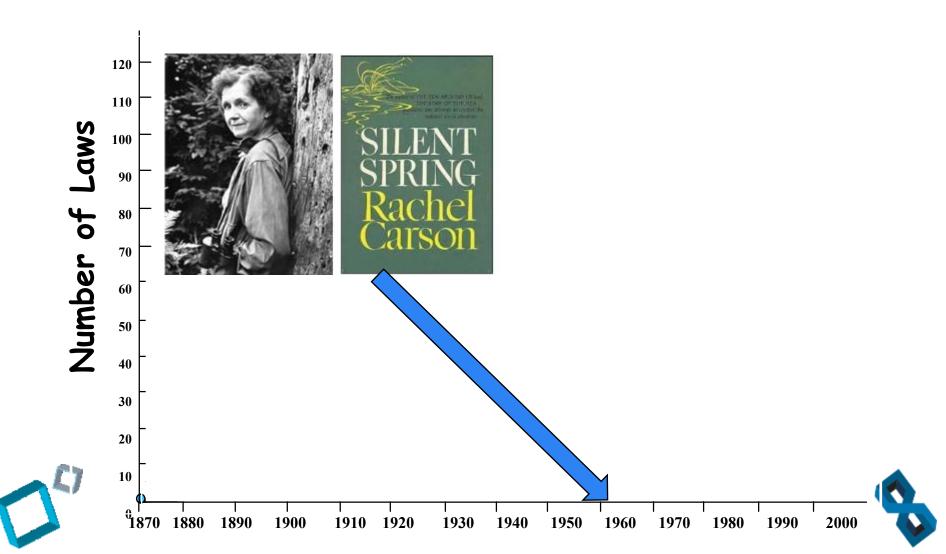
The cost of using hazardous materials:

Storage Transportation Treatment Disposal **Regulatory Costs** Liability **Worker Health and Safety Corporate Reputation Community Relations New Employee Recruitment**





Environmental Regulations





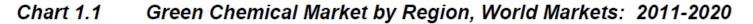


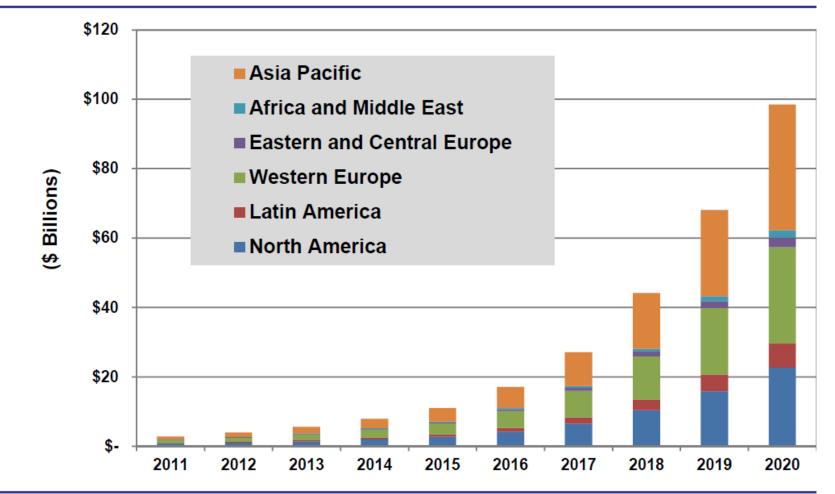
Green Alternatives





Traditional Processes





(Source: Pike Research)





2007 onward...







John Warner Amy Cannon

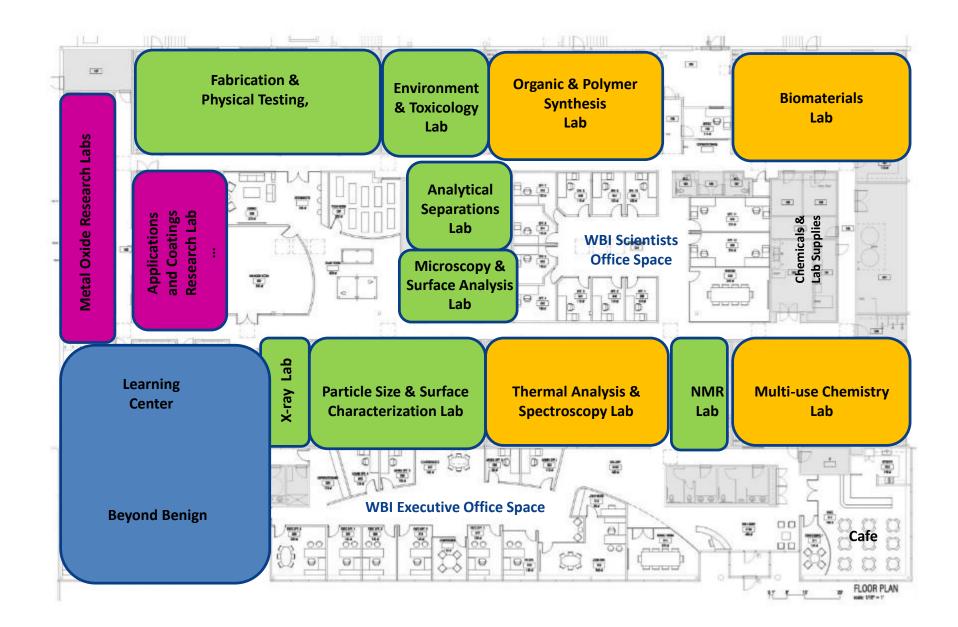
Lawrence warner babcock beyondbenign Nes Bever Billerica 95 Salem Woburn West Lynn Concord Mede Waltham Boston gh Newton M ramingham Quincy Dedham Braintree Norwood



Jim Babcock Joe Pont, CEO

100 Research Drive Wilmington, MA 01887





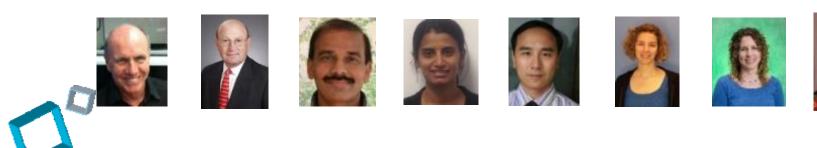










































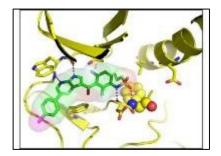






Business Sectors at WBI

Pharmaceuticals, Agriculture and Biotechnology





Chemical Sciences, Development and Manufacturing

Textiles, Materials and Coatings





Energy, Natural Resources and Environment

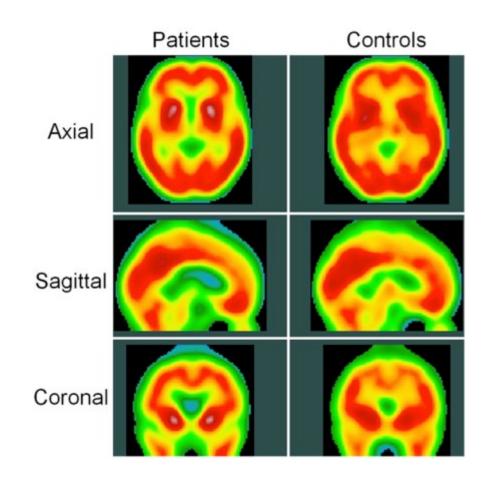
10

Cosmetics, Personal Care and Consumer



Pharmaceuticals: Neurochemistry

- WBI and its sister company, Collaborative Medicinal Development LLC, are advancing into Phase I clinical trials leads for Parkinson's disease, amyotrophic lateral sclerosis (ALS) and cancer
- WBI has substantially contributed to these programs through formulation development and the creation of new compositions of matter





"Non-Covalent Derivatives of Metal Complexes and Methods of Treatment" Warner, John C., Cheruku. Srinivasa R.; US Pat Application No. 61/932,348 January 28, **2014**. "Copper (II) bis(N-alkyl-hydrazinecarbothioamide) Complexes as Non-Covalent Derivatives for the Treatment of CNS Conditions" Warner, John C., Cheruku. Srinivasa R.; US Pat Application No. 61/902,682 November 11, **2013**.

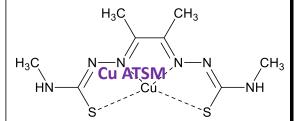


Parkinson's Disease Therapeutic



THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH





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PARKINSON'S FUNDED GRANT

Lead Optimization for a Parkinson's Disease Therapeutic

GRANT ABSTRACT

Objective/Rationale:

CuII(atsm) has the potential to delay disease progression in Parkinson's disease, based on extensive pre-clinical model data. CuII(atsm) has been shown to significantly improve motor function in standard models of Parkinson's disease. The observed motor improvement correlates with preservation of dopaminergic neurons in the brain and biomarkers of neuronal health and function.

Project Description:

CuII(atsm) is sparingly soluble and requires formulation for oral administration prior to entering human clinical development. Procypra will pursue two parallel approaches to develop a proprietary oral formulation: (1) Procypra will work with the Warner Babcock Institute for Green Chemistry to develop a proprietary formulation of CuII(atsm) incorporating GRAS (Generally Regarded As Safe) excipients; and (2) Procypra will evaluate the solubility of proprietary CuII(atsm) analogues. The utility of these formulations will be evaluated using standard solubility and bioavailability assays and efficacy will be compared to the parent formulation in the MPTP toxic lesion pre-clinical model of Parkinson's disease.

Relevance to Diagnosis/Treatment of Parkinson's Disease:

Current Students Staff Library Contact & Maps

CuII(atsm) has the potential to delay disease progression in Parkinson's disease. Successful clinical development of an optimized formulation of CuII(atsm) would provide Parkinson's disease patients, on diagnosis, the opportunity to delay the progression of their disease and maintain their quality of life for a much extended period of time. In (atsm) with

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The Melbourne Newsroom

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University Activities Medicine and Health Science

University of Melbourne enters agreement to develop therapy for Parkinson's disease



11 October 2013

University Home

MELBOURNE

parent drug show an how promise emonstrating usina n the cypra son's disease.

the

will have directed



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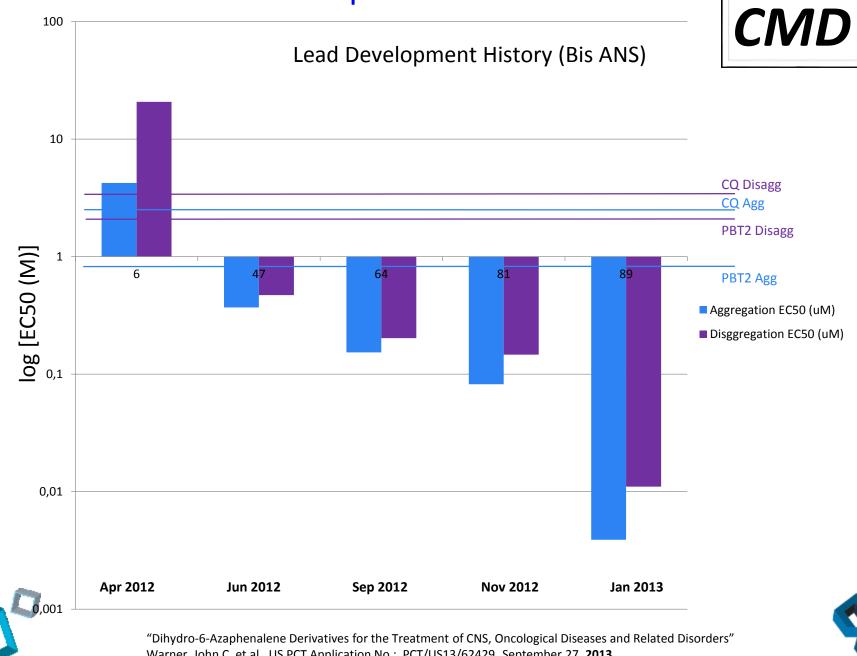
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Alzheimer's Disease Therapeutic



Warner, John C. et al., US PCT Application No.: PCT/US13/62429. September 27, 2013.

Construction Materials: Asphalt Paving



Delta S Asphalt Rejuvenator

- WBI has created a low-cost, environmentally sustainable asphalt rejuvenator that enables the use of substantial quantities of recycled asphalt pavement and shingles
- Several successful use-tests have been conducted on New England roads and driveways
- WBI spin-off, Collaborative Aggre LLC, currently evaluating commercialization options, e.g. licensing vs. direct sales







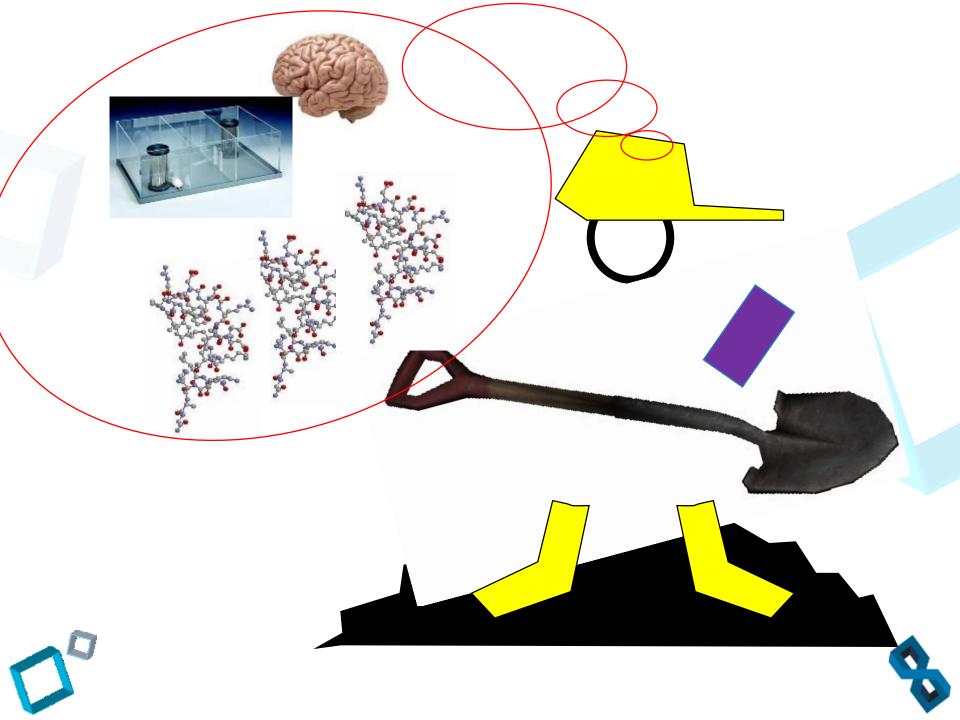
Paving with 113°C (236°F) asphalt at Centerdale School in Providence, RI



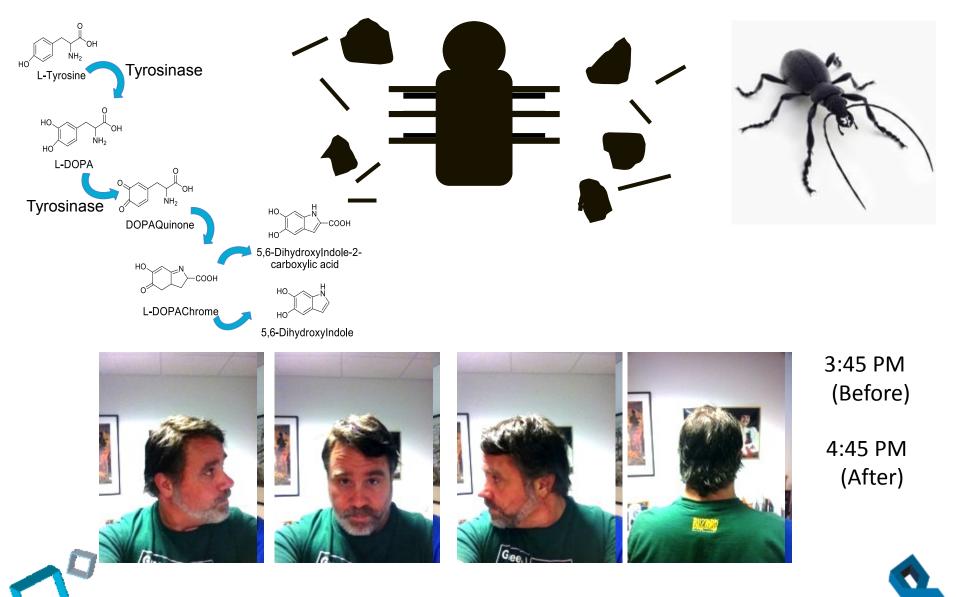
Paving on November 25, 2013 in -8°C (17°F) weather in Wilmington, MA







Personal Care: Hair Color Restoration

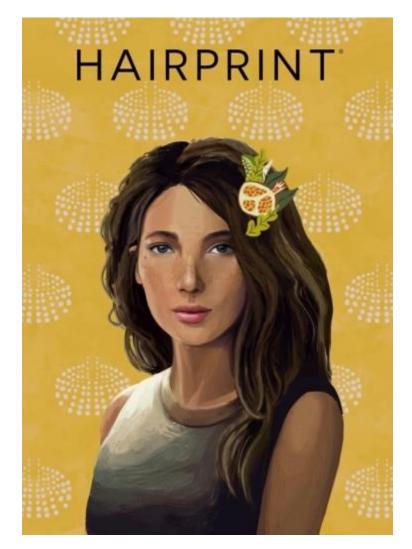


"Formulation and Processes for Hair Coloring" Warner, John C.; Muollo, Laura; Stewart, Amie, U.S. (2014), US 8828100 B1 20140909 filed Oct. 14, **2013.**

Hairprint[®] hair color restoration

- Foundational IP created at WBI through inspiration from coloring processes in the natural world
- WBI's licensee, Nature of Hair LLC, funded optimization work at WBI to yield commercialization-ready Hairprint[™] technology
- Nature of Hair is sublicensing Hairprint[™] to global personal care players.







Construction Materials: Wood Composites

- WBI has created a low-cost, environmentally sustainable adhesive technology for use in wood-composite applications
- The technology enables the replacement of expensive, formaldehyde-based incumbent products
- Collaborative Aggregates LLC and WBI currently engaged in pilot-scale usetesting and technology optimization







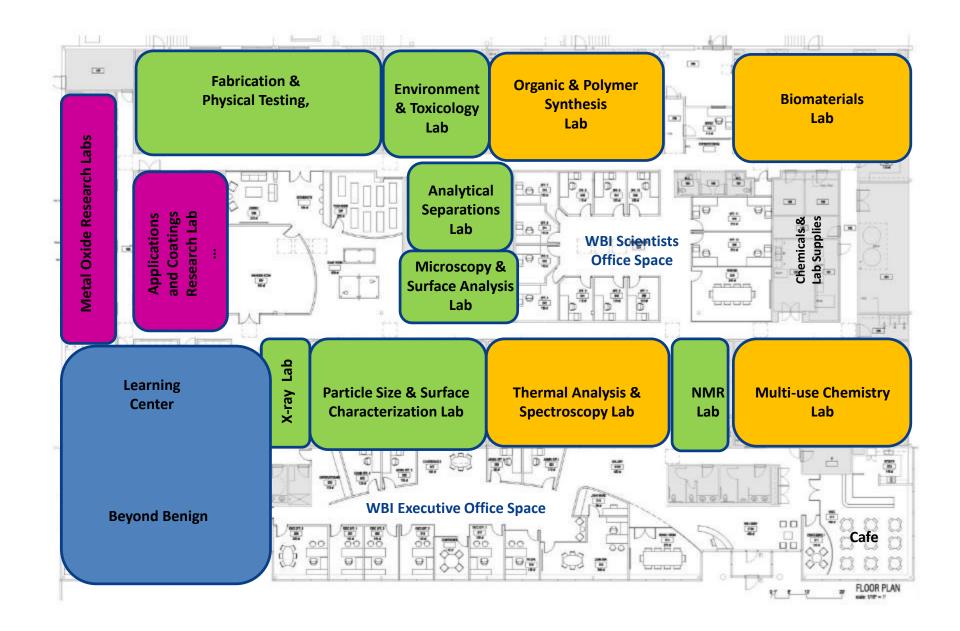


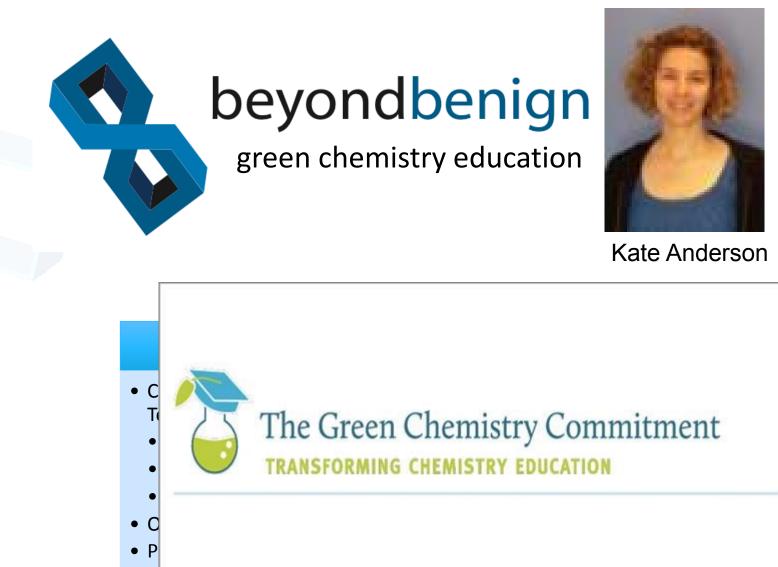
To get a degree in Chemistry...

No universities require any demonstration of knowledge regarding toxicity or environmental impact!









- K-12 and Community Outreach
- College Student Fellows program



Amy Cannon

ment







green chemistry education

