Green Chemistry and Engineering: Towards a Sustainable Future

A white paper reporting on the green chemistry philosophy of reducing waste, toxicity and hazards, and its application on an industrial scale.
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ABOUT THE AUTHOR
Melissae Fellet has written about chemistry for New Scientist, Chemical & Engineering News and Chemistry World. She graduated from the Science Communication program at the University of California, Santa Cruz and holds a Ph.D. in chemistry from Washington University in St. Louis.
I. Executive Summary

The slogan “benign by design” summarizes the ethos of green chemistry, and 12 principles guide its implementation. In short, the main goals and applications of green chemistry are to reduce environmental, human health and safety risks of chemicals by redesigning toxic molecules, synthetic routes, and industrial processes.

Green chemistry is an interdisciplinary field, drawing on knowledge from chemistry, chemical engineering, toxicology, and ecology. Chemists can design new catalysts that reduce the amount of reagents used and thus reduce the amount of waste generated in reactions. Chemical engineers can design a production line to recycle certain reagents and minimize energy consumption. Toxicologists and ecologists provide information about the toxic characteristics and effects of molecules so that chemists can then work to design new molecules that avoid structures linked to toxicity.

Green chemistry researchers develop new catalysts, test new solvents, and experiment with microscale flow processes. Some of this research is adopted by the chemical industry, particularly in pharmaceuticals. Through annual green chemistry awards, the American Chemical Society and the U.S. Environmental Protection Agency reward successful applications of green chemistry in industry. The Royal Society of Chemistry in the United Kingdom offers a green chemistry award every two years.

Educating future chemists is also an important part of the philosophy of green chemistry. Green chemistry experiments, with their low-risk ingredients and connection to sustainability, can be used as demonstrations for school groups. Green chemistry experiments are working their way into undergraduate teaching laboratories as well. And as the next generation of chemists learns these principles, perhaps one day green chemistry will not be an additional consideration when designing a synthetic route or industrial process. It might just be how things are done.
II. What Does It Mean To Be Green?

The 12 principles of green chemistry (see Appendix A), outlined in 1998, ask chemists to prevent waste, minimize energy use, use renewable raw materials, design biodegradable products, and choose chemicals to minimize potential accidents. But putting those principles into practice often requires trade-offs, especially when you’re trying to determine the “greenness” of an entire process.

For example, a reaction with a hazardous reagent is not attractive for a process scale because of the inherent safety risks. But sometimes using such a reagent can shorten a reaction sequence, reducing costs, waste and solvent use. Jeffrey V. Mitten of Novasep, a company that specializes in chemical process development, described how the company handled this situation when converting a hydroxyester to an aminoalcohol using diborane gas, which can ignite in humid air. Novasep’s chemists and engineers created a way to generate diborane on site and meter it into the reaction. With the hazards contained, this route eliminated protection and deprotection steps, shortening a five-step sequence to two steps. By using this new route, costs were reduced by 60%, and the product yield was improved from 59% to 81%.

Hazardous, But Greener

Novasep’s route to aminoalcohols defies green chemistry principles by using hazardous diborane gas as a reagent. The process makes up for the transgression by reducing the reaction to two steps, generating less waste, and reducing costs.

Initial process:

Greener process:

$Z = \text{CH}_2$, NH, O, or S; PG = protecting group; Ms = methanesulfonyl
Green metrics seek to quantify the abstract concept of sustainability.(3) These measurements can help scientists compare processes for their overall "greenness," although trade-offs exist here as well. Optimizing a process for environmental effect might reduce its safety, for example. One easily calculated metric is the E-factor, which is the mass of waste per mass of product. This ratio, typically up to 100 for pharmaceuticals(4), reflects the amount of waste generated in a process. In contrast, petrochemicals have an E-factor around 0.1, near the ideal waste-free value of zero.(2)

There's also a need for qualitative metrics too. "You could have an E-factor of 20, which would be low by pharmaceutical standards, but if the solvent in every single step in the process is benzene, it's not a green process," Berkeley W. Cue Jr., chair of the ACS Green Chemistry Institute Governing Board, told Chemical & Engineering News in 2012.(4) Many pharmaceutical companies use a different green metric: process mass intensity (PMI). This value reflects the total mass of material in a process per mass of product. The ideal PMI is 1, indicating that all reagents are converted into product. It provides a broader indication of process efficiency than just tracking waste using the E-factor.

However, any single metric cannot describe the range of factors — from sources of raw materials to energy use and water consumption — that affect sustainability of a particular process. Thus, the ACS Green Chemistry Institute spearheaded the Greener Chemical Products & Processes Standard to develop common measurements that chemists, consumers, and policymakers can use to evaluate the environmental aspects of a particular product.(5)

"Ecolabels" on cleaners also attempt to describe sustainability. But these labels, or ingredient lists ranked by toxicity, are not as comprehensive as the proposed standards. Industry trade groups or environmental groups often develop the current ecolabels and product guides. Though the rankings may reflect products with reduced toxicity, they may not account for other sources of environmental damage, like using water and energy when washing clothes or dishes.(6)
Environmental life cycle assessment (LCA) tracks the environmental impact of a product from the origin of its raw materials through its production, distribution, use, and disposal. Such an analysis allows scientists to identify destructive points in the life cycle and make changes to stem the damage. Early LCAs in the 1970s looked at ingredients, emissions, and waste produced by different beverage containers. Now a variety of analyses allows scientists to estimate a range of potential ecological consequences, like global warming, nutrient overloading, or environmental toxicity. Other analyses track product resource use and human toxicity of a particular process.

These analyses provide a view of the environmental impacts and trade-offs of a particular process that is more accurate than just looking at a single metric, such as waste. That's because an LCA inherently accounts for the connections between different steps of production, distribution, and utilization. Collecting enough data about a particular process can be time-consuming and expensive. And the methods of data collection, any models used, and any assumptions employed in an LCA need to be known before an organization changes its policies based on information in the analysis.

There are several ways to analyze a product over its life cycle without doing a full LCA. Process mass intensity (PMI), a common green metric, can be used to quickly estimate life cycle impacts, as it correlates with global warming potential for compounds under development at the pharmaceutical company GlaxoSmithKline (GSK). Chemists at GSK have also developed several specific LCA tools. One allows for quick comparisons of synthetic routes from experimental stages through to manufacturing. Another combines this streamlined LCA tool with a PMI calculator developed by Merck to be a standard quick LCA for the pharmaceutical industry.

An online resource, iSustain.com, helps scientists and students quickly estimate how a product fits with the 12 principles of green chemistry. Users input information about the materials that enter a process and the waste that comes out. The site generates a Green Chemistry Index rating that reflects a quick snapshot of process efficiency, without doing a full LCA.

CRADLE-TO-CRADLE DESIGN

The cradle-to-cradle engineering philosophy involves considering the life cycle of a product, from raw material to disposal. Industrial and academic labs that add this framework to the 12 principles of green engineering (see Appendix B) build biodegradable, renewable products that require less energy for production. Recyclable carpet tiles are one practical application resulting from this union. Carpet fibers are often made of recyclable nylon 6, while the backing is commonly made from rigid polyvinylchloride plastics. In 1996, Shaw Industries started to redesign the backing to be made from a recyclable polymer as well, primarily a low-density polyethylene. The new backing composition also created carpet tiles with better flame-retardant characteristics than traditional carpet treated with arsenic or aluminum oxides. The new tiles are fully recyclable, once the fibers are separated from the backing, and building
blocks of each polymer can be used to make new carpet tiles. The product won a U.S. Environmental Protection Agency (EPA) Presidential Green Chemistry Challenge Award for Designing Greener Chemicals in 2003. To encourage their customers to recycle the tile, the company also provides free collection and recycling of used tiles.

Along with carpet, plastics are another major component of landfills. Polylactic acid (PLA) plastics made from corn are the leading biorenewable plastics, but breaking them down requires high temperatures and agitation at commercial composting sites. Plastic that isn’t recycled or deposited in a landfill washes out to sea and disintegrates into tiny pieces that harm wildlife. The X Prize Foundation is developing a project challenging researchers to create plastics that degrade in the ocean.

A researcher at the University of Florida is already working on building plastics that break down in water. He has designed a new way to make plastic that installs an acid-sensitive functional group, an acetal, throughout a polydecreline plastic made from a fatty acid in castor seeds. Plastics made with this method degrade faster than PLA plastics in acidic tetrahydrofuran solution, a preliminary test for water degradability. However, these materials are still too soft to replace current PLA plastics.

FIVE EASY THINGS YOU CAN DO TO MAKE YOUR LAB MORE SUSTAINABLE

A certification program at the University of Michigan recognizes laboratory efforts to become more sustainable. At the request of the manager or head of the lab, a staff member from the university’s Office of Campus Sustainability visits the lab and provides recommendations for sustainable practices based on green chemistry principles, waste reduction, and pollution prevention. Sudhakar Reddy, the program’s coordinator, says 45 labs have participated in the program as of March 2013. He shares a few recommendations encouraged by the program:

1. Close fume hoods when not in use to reduce energy use.
2. Run experiments on the microscale to reduce waste.
3. Switch to green solvents: Use 2-methyl tetrahydrofuran in place of methylene chloride, and use cyclopentylmethyl ether in place of tetrahydrofuran, 1,4-dioxane and ether.
4. Neutralize basic phosphate-buffered HPLC waste or acidic HCl waste to pH 7 and pour down the drain.
5. Recycle electronics, ice packs, packaging materials, toner cartridges, pipette tip boxes, and water purification cartridges.

For more information on the program, check out the ACS GCI Nexus blog:

Chemists design safer syntheses by looking for ways to reduce waste from solvents and added reagents. Minimizing reagent hazards and toxicity by running reactions on a small, continuous process is also another way to reduce risk. One classic green synthesis is a route to ibuprofen developed by the BHC Company (now BASF) in 1991 and put into industrial production the next year. This new route condensed a six-step stoichiometric synthesis to a three-step catalytic sequence. This revamped synthesis won the EPA Presidential Green Chemistry Challenge Award for Greener Synthetic Pathways in 1997. This synthesis reduces waste in several ways. About 80% of the atoms in all the reactants end up in the final product, compared to less than 40% in the original synthesis. This increased atom economy inherently reduces reactant waste, as more of the reagents are converted to product. Additionally, all the catalysts in the synthesis — hydrofluoric acid and palladium — are recovered and recycled. No other solvent besides HF is needed.

This section will discuss concepts in four areas of green chemistry research — catalysis, solvents, alternative energy sources for reactions, and continuous processing — and show how these ideas are reaching industry.

**CATALYSIS**

Catalysis dominates the literature on green synthesis, even though it’s an important research area in its own right. The goals of catalyst development dovetail with the principles of green chemistry: Chemists want to build a fast, long-lived, and highly selective catalyst that works under mild conditions. Since a catalyst regenerates itself after a reaction, one molecule of catalyst can perform several transformations. That allows scientists to get high yields from a reaction that uses only a relatively small amount of catalyst.

Traditionally, transition metals like palladium, platinum, and ruthenium are used to build catalysts for carbon-carbon bond-forming reactions. However, these metals are expensive and in low abundances in the Earth’s crust. In some cases, the catalysts require large ligands to control the selectivity of a reaction, which can be considered wasteful according to the 12 principles.

Therefore, researchers look to get the same functionality of these catalysts with a more available and sustainable metal: iron. Iron catalysts can carry out a wide range of cross-coupling reactions, but many of those reactions require flammable Grignard reagents. Currently, that requirement may prompt researchers to avoid using these catalysts on larger scales until more is understood about how they work. Another iron catalyst can make an alkylsilane used in shampoo and to soften denim with greater activity and selectivity than industrial platinum catalysts.
RECYCLING AND REPLACING RARE EARTH ELEMENTS

Much of modern technology contains rare earth elements. Magnets in wind turbines, medical imagers and hard disk drives contain terbium, neodymium, and praseodymium. So do the nickel metal hydride batteries of hybrid cars. Light emitting diodes and energy efficient fluorescent light bulbs contain europium and ytterbium.

The big issue with rare earth elements is not their suggested scarcity. These 17 elements are moderately abundant in the Earth's crust, though they are too dispersed for extraction to be economically efficient. (1) Most of the easily-extracted metal is found in China. Mines in the country provide 97% of the world's supply of rare earth elements, and that supply can be cut off if and when China sets export restrictions. (2) Restricting supply means prices for the metals climb.(3)

New mines in the United States and Australia, along with ones planned in Brazil, Canada and Vietnam, could stabilize the supply of rare earths. But new mines bring radioactive mining waste and potentially more fossil fuel energy needed to recover metal buried in poor ore.

So companies that make products using rare earth elements are looking for ways to recycle and reuse the metals. In 2010, Hitachi developed a method to recycle rare earth metals from hard drives and compressors. In March 2013, Honda announced a process to reuse the metals from batteries in hybrid cars.

University researchers are also creating new materials that can replace those in common products that rely on rare earth elements. An experimental electrode material for lithium ion batteries contains an organic molecule from plants called purpurin.(4) Quantum dots LEDs, made from silicon(5) or other metals, could replace LEDs colored using rare earth elements. Nanostructured films of manganese and gallium can exert magnetic fields of strength similar to rare-earth containing magnets.(6)

Another independent area of research, nanoscience, might provide insights into building green metal catalysts too. Gold-palladium nanocatalysts can generate hydrogen peroxide, an acceptable oxidant for green chemistry, from hydrogen and oxygen.(20) Attaching catalysts to magnetic nanoparticles makes it easy for chemists to separate and recycle the catalyst after a reaction.

Other types of catalysts can reduce safety risks. Acid catalysts attached to silica, for example, reduce the aqueous waste generated by quenching and neutralizing a reaction.(21) Phase transfer catalysts (often ammonium salts) carry an insoluble reactant between the organic and aqueous phases in a mixture. Chemists used tetrabutylammonium bromide to catalyze the displacement of a chloride by a cyanide ion on a process scale. The reaction releases heat, but the researchers could control the exotherm and prevent a temperature spike just by controlling the stirring speed.(22)

Enzymes are commonly used as catalysts in industry, particularly pharmaceuticals, because they work at ambient temperatures and pressures in water.(2) That makes them safe to handle on a process scale. One example is the three-step enzymatic route to the key chiral building block used to make the active ingredient in the cholesterol-lowering drug Lipitor. The process won enzyme company Codexis an EPA Presidential Green Chemistry Challenge Award in 2006. Previous routes to the key intermediate involved separating enantiomers in the first step (at 50% maximum yield) and a final step plagued with byproducts. The enzymatic process gives the desired intermediate in a greater than 90% isolated yield. (23) The overall process has an E-factor about five times smaller than a typical pharmaceutical designed with green chemistry principles.

But in practice, biocatalysts are not necessarily “greener” than chemical catalysts. A streamlined LCA comparing a metal catalyst to an enzymatic reduction of a ketoester revealed that some of the processes and reaction
conditions most impacted the analysis.(24) Including bioprocesses in LCA would help the pharmaceutical industry evaluate these catalysts.

Applications for enzymes can be found outside of the pharmaceutical industry, too. In 2012, a chemical company, Buckman International, won an EPA Presidential Green Chemistry Challenge Award for using enzymes to create stronger paper without added wood pulp or chemical additives. The enzymes connect the fibers of cellulose within the paper, resulting in a stronger end product. The enzymes also allow for increased production. Combined with energy reductions, the new process saves the company an estimated $1 million per year.(25)

**GREEN SOLVENTS**

Green solvent research in academic labs is targeted at finding new solvents. Scientists also develop applications for interesting liquids like water, supercritical carbon dioxide (CO2), and ionic liquids. Water is often not thought of as a potential solvent for organic reactions, because many reagents are water-sensitive or insoluble in water. But some reactions, like an aqueous Diels-Alder reaction between cyclopentadiene and butanone, run faster in water than in organic solvents like methanol.(26, 27) Often the rate enhancement is due to hydrophobic effects and hydrogen bonds that stabilize transition states. Running a reaction in water makes it possible to use enzyme catalysts as well.

A 2007 analysis of green solvents that includes life cycle impacts ranks water and supercritical CO₂ as promising green alternatives to traditional organic solvents.(28) Many chemicals do not dissolve in these solvents, but the researchers write that that fact is “more than counterbalanced” by the ease of handling and separating these solvents, as well as their low environmental impact.

Supercritical CO₂ has properties between that of a gas and a liquid. It’s commonly used as a dry cleaning solvent or to extract caffeine from coffee beans. Scientists can control what compounds dissolve in the supercritical fluid by adjusting its density to tune its polarity. The volatility of CO₂ means that the supercritical fluid is easily removed after a reaction.

Ionic liquids are mentioned in almost half of the green solvent research published in Green Chemistry in 2010.(29) The structure of positive and negative ions in these liquid salts control solubility and guide a reaction. Ionic liquids work as solvents for a variety of reactions (30), and they can be designed to catalyze reactions too.(31) While ionic liquids might be interesting substances from the perspective of basic research, their potential utility in industry is unclear due to as-yet-to-be-determined disposal protocols on a large scale.(32)

The amount of research into various green solvents doesn’t match predicted needs for solvents to reduce environmental damage, writes Philip Jessop of Queen’s University in Canada, in a 2011 perspective in Green Chemistry.(29) While Jessop supports basic research into solvents, he asks his colleagues to consider their research topics carefully if they wish to reduce solvent-caused environmental damage.
Of course, the best way to reduce solvent use is to not use solvents in the first place. It’s often thought that a solvent is needed to increase catalyst efficiency or improve the enantioselectivity of a catalyzed reaction. Some asymmetric reactions, however, can be run just by mixing the reagents together.(33)

**ALTERNATIVE ENERGY SOURCES FOR REACTIONS**

Running reactions can be energy intensive. When chemists boil a reaction, they simultaneously cool the solvent vapors. The resulting droplets fall into the reaction so that the reaction never runs dry. But this standard process requires energy to both heat and cool the reaction, in addition to the water being constantly run through a condenser.

Therefore, some green chemists look to new energy sources to drive reactions. Microwave-assisted reactions can be run in water at a small scale, often with accelerated rates due to temperature and pressure effects. Reactions to build oxygen-, nitrogen- or sulfur-containing rings common in medicinal chemistry can also be driven using microwaves, though these reactions aren’t running on a process scale yet.(34) Alternatively, the energy from grinding reagents together using a mortar and pestle or a ball grinder can be enough to trigger a reaction.(35)

Ultrasound sonication is another energy source with useful applications such as deprotecting an amine, protecting hydroxyls on sugars, or reducing an α,β-unsaturated ketone in a steroid. The sound waves create areas of high and low pressure, much like ripples in a pond, as they travel through liquid. Bubbles form in the low-pressure areas, collapse when they reach high-pressure regions, and send shockwaves through the reaction. Surprisingly, ultrasound sonication can influence the products of a reaction. When chemists stirred a suspension of benzyl bromide and alumina-supported potassium cyanide, they retrieved diphenylmethane, which contains two connected benzene rings, as the product of a Friedel-Crafts reaction. But when they sonicated the reaction, the cyanide ion replaced the bromine atom, giving benzyl cyanide as the product. The researchers suspect that the bubbles generated during sonication masked the metallic catalytic sites on the solid support.(35)

**CONTINUOUS PROCESSING**

Typical syntheses, whether in academic labs or batch processes, proceed through a series of discrete steps and reactors. This creates large amounts of solvent and water waste. Continuous processing, however, carries production in a steady flow by adding reagents to a stream of liquid. Such reactions can address nine of the 12 principles of green chemistry.(36)

These experiments are often performed on the microscale by pumping reactants through small channels. This scale has inherent safety benefits. Chemists can use smaller amounts of potentially hazardous reagents, and the flow system gives them better control over conditions that might otherwise lead to runaway reactions. Continuous processes can even be designed to run short, multistep syntheses.(37)
Microscale reactions can be scaled up by running one reactor for a long time, or by running multiple reactors in parallel. It’s also possible to scale up flow reactions by increasing the width of the tubes, and thus the volume of liquid traveling through them. A pilot-plant project made more than 100 kilograms of 6-hydroxybuspirone over three runs of the flow process.

Continuous production can be hampered by clogs in the lines or mechanical problems, like leaking or valve failures. Thus, monitoring the reactions in the stream for blockages, as well as product formation, helps to keep the flow processing moving. Chemists in Denmark built an industrial-scale inline monitoring system for the production of allylcarbinol using a Grignard reaction. A Grignard reaction as the first step in a pharmaceutical synthesis, for example, needs precise stoichiometric control of the Grignard reagent and ketone substrate to prevent byproducts and yield loss. The monitoring system measures the amount of ketone left in the product, and then controls the flow rate of the Grignard reagent into the reaction to maintain the proper stoichiometry.

In a recent survey, eight of nine pharmaceutical companies reported using continuous processing in pilot plants or on the production scale. However, most companies in the survey responded that they hesitate to build continuous-process plants when existing batch-plant infrastructure meets demands.

IV. Reducing Toxicity By Design

Toxicologists track how chemicals harm the body, by studying their effects on biochemical pathways, cells, and tissues. They also uncover relationships between the dose of a chemical and its physical effect. These dose-response relationships are part of risk assessment and hazard management plans. But one principle of green chemistry aims to do more than manage risks; it challenges chemists to reduce a molecule’s toxicity during the design process, rather than managing the effects after a molecule has been synthesized.

Currently, it’s not possible to fully predict the toxicity of any new molecule. But principles of toxicology can help chemists identify characteristics of a molecule that might impart toxicity. Certain molecular structures bind to metabolic enzymes. Other electron-poor molecules are carcinogenic because they bind to DNA. And fat-soluble molecules can accumulate in fat cells and not be cleared from the body.

Medicinal chemists can exploit some of these structures to help develop killer drugs specific for diseased cells. Green molecular designers, however, want to avoid those structures, as they want to prevent a molecule from causing biological harm.
**REDUCING ENDOCRINE DISRUPTION**

Endocrine disruptors are harmful molecules that behave like hormones in humans and alter the body’s natural signaling system. Endocrine disruptors are thought to be linked to health conditions such as obesity, cancer, diabetes, and infertility. Now a new protocol helps chemists design molecules to reduce their endocrine-disrupting effects.

Bisphenol-A (BPA), a phthalate used as a plasticizer in polycarbonate plastics, is an example of a potentially endocrine-disrupting chemical. It’s also found in the linings of canned food and cash register receipts. Many products advertise that they are BPA-free, due to consumer concerns about ingesting BPA. Chemical companies are searching for molecules to replace BPA for food and beverage applications, but they’re struggling to find something that’s an equally effective replacement.(42)

A new tiered system of tests, developed by a team of 23 scientists, might help chemical companies determine if a new molecule is a potential endocrine disruptor.(43) The first tier involves computer modeling based on physical properties, chemical reactivity, and estimates of biological reactivity using structural similarities. The second tier involves biochemical pathway screening. Then a molecule is tested in tissues of increasing complexity — from cells to whole amphibians to mammals.

The study of endocrine disruption is still a growing field, so protocols will evolve to include assays that incorporate knowledge as it is discovered.(44) For example, a growing body of evidence suggests that chronic, low doses of endocrine disruptors like BPA may cause physical harm.(45) That means a typical interpretation of toxicology — reducing risk by preventing exposure to harmful doses — may not apply to this class of chemicals.
V. Renewable Feedstocks

The ingredients for many chemicals and materials come from petroleum and natural gas processing. One principle of green chemistry calls for using renewable feedstocks when technically and economically possible, instead of drawing on materials that deplete natural resources.

Plants are seen as a source of sugars for biofuel production. Starch from corn is an easily accessible sugar source, but it’s impractical to scale up biofuel production using corn. Every acre of corn destined for biofuel production is one less acre that’s not in agricultural production. However, there are other fast-growing plants like switchgrass and a species of poplar tree that could make attractive sugar sources, while avoiding a “food versus fuel” debate. However, it’s difficult to break apart these woody plants into sugars needed for fuel production. Tough fibrils of lignocellulose reinforce plant cell walls. Releasing the sugars in that lignocellulose is key to getting the maximum amount of fuel from a plant.

Chemical catalysts can convert plant matter to oxygenated fuels like ethanol, furfural, and levulinic acid. Virent, a biofuel company in Wisconsin, converts sugars to hydrocarbons — essentially the same blend as gasoline — using an aqueous process and chemical catalyst. Alternatively, engineered microbes can consume sugars and produce a fatty acid methyl ester or farnesane for biodiesel.

Multiple Highways

Many starting points lead to many end points for biofuels.

**LIGNOCELLULOSE**
- Crop residues
- Forest residues
- Municipal waste
- Energy crops
- Hydrolysis/ enzymes
- Aqueous sugars
- Aqueous-phase processing
- Gasification
- Synthesis gas
- Fischer-Tropsch chemistry
- Fermentation
- Pyrolysis
- Biocrude oil
- Catalytic cracking
- Hydrotreating
- Gasoline
- Diesel fuel
- Jet fuel
- Ethanol

**STARCHES/SUGARS**
- Corn grain
- Sugarcane
- Aqueous sugars
- Fermentation
- Ethanol or butanol
- Diesel fuel or jet fuel
- Gasoline
- Diesel fuel
- Jet fuel

**LIPIDS**
- Soybeans
- Other oilseeds
- Animal fat
- Algae
- Vegetable oil/animal fat
- Esterification
- Hydrotreating
- Diesel fuel
- Jet fuel
Currently the economics of biofuel production still lie in favor of petroleum-based fuel. But a biofuel plant can offset its production of low-value fuel by also producing high-value bulk chemicals. In 2004, the U.S. Department of Energy listed 15 chemicals as top targets to make in a biorefinery. Included on the list were glycerol, succinic acid, aspartic acid, and furandicarboxylic acid. An experimental small scale biorefinery from researchers at the City University of Hong Kong transforms wasted pastries from Starbucks into succinic acid. Companies like BioAmber, an industrial biotechnology firm in Minneapolis, are looking to use more traditional sugar sources, and won a 2011 EPA Presidential Green Chemistry Challenge Award for its microbial production of succinic acid from glucose, corn sugar, and corn stover. BioAmber operates a plant in France that produces 3,000 metric tons of succinic acid a year. It plans to open a larger factory in 2013, capable of producing 11,000 additional metric tons at full capacity. A wave of upcoming factory openings for other biobased chemicals, including isobutyl alcohol, glucaric acid, acetic acid, and farnesene, carves out a place for biobased chemical production in the industry, although the bottom-line profitability of these companies is still unknown.

What is known is that the chemicals being produced are destined for solvents, detergents, and coatings.

Companies large and small are working on developing ingredients for rubber, fragrances, and plastics as well. Polylactic acid (PLA) made from corn sugar is a common biobased plastic used in compostable cups, plates, and utensils. A material that mimics the structure and properties of polyethylene terephthalate (PET) can be made from lignin-derived vanillin and methanol-derived acetic acid.

It’s also possible to make traditional plastics, like polystyrene and PET, at least partially from renewable feedstocks. Again, these traditional plastics from renewable feedstocks cannot yet compete economically with their petroleum-derived relatives. However, interest from large companies like Coca-Cola and Heinz might increase demand for these biobased plastics and might help give the market some momentum.

But a recent LCA of plastics shows that switching to a biobased feedstock doesn’t improve the “greenness” of the process overall. PLA and polyhydroxyalkanoate plastic from corn grain or stover get high marks compared to the petroleum-derived plastics when analyzing their adherence to green design principles. But production of 10 different traditional plastics, like polystyrene, propylene, and polycarbonate, has less environmental impact in terms of nutrient overloading, ecotoxicity, ozone depletion, and carcinogenicity than bioplastic production. That’s because the biobased plastics the researchers analyzed come from corn that requires fertilizer, pesticides, and farmland. Microbial fermentation and other chemical processing steps also contribute to the negative environmental impact from biobased plastic feedstocks. This bioplastics LCA did not include recycling or biodegradation in the analysis; negative environmental impacts might be found to be reduced if recycling and biodegradation were considered in the analysis.
VI. Green Chemistry in Industry

Three roundtables, convened by the ACS Green Chemistry Institute, unite companies in various chemical industries to spread green chemistry principles through their industries. (56) There's a roundtable for manufacturers and one for formulators, companies that mix chemicals to make shampoos, cleaners, and/or cosmetics. The third, and oldest, is the Pharmaceutical Roundtable, started in 2005 as a partnership between Eli Lilly & Co., Merck & Co., and Pfizer. Today the group has grown to 16 members, including enzyme company Codexis and supplier DSM.

Of the different kinds of chemical industries, pharmaceutical companies produce the smallest amount of product and the largest amount of waste. Refining petroleum produces 106 to 108 tons of chemicals each year, compared to tens to thousands of tons of pharmaceuticals. But pharmaceutical production generates up to 1,000 times more waste, as measured by E-factor, than petrochemical production. (57)

Due in part to the efforts of the ACS Pharmaceutical Roundtable, a group of process chemists in the pharmaceutical and fine chemical industry that was convened by ACS Green Chemistry Institute, the principles of green chemistry are spreading through the industry. The roundtable produces biannual reviews of green chemistry literature of interest to the pharmaceutical industry. (58–62) The group also develops tools like solvent selection guides to help chemists make greener choices during product design. It also funds academic green chemistry research applicable to industry and brainstorms new directions for that research. (24, 63)

BIOGAS AND BEER WASTE POWER FOOD FACTORIES

Companies in the food industry, large and small, turn waste into energy for their factories. Straus Family Creamery, a family-owned dairy just north of San Francisco, converts manure to energy that powers the dairy. (1) Workers flush manure and wastewater from rinsing the barns into a holding pond that separates the solids from the liquids. The liquid manure runs into a second pond covered with a tarp, called an anaerobic digester. Bacteria in the pond convert the manure to biogas, which is mostly methane. They collect that methane and use it to run a generator that powers the dairy. Heat from the generator warms water used to clean barns and excess energy is returned to the area's electrical grid.

Anaerobic digesters can also be used on a larger scale. This summer, one will open in Wisconsin to process liquid waste from cheesemaking, called whey, from five cheese factories and a soy food ingredient factory. (2) Thick Greek yogurt gets its consistency due to extra straining, so these yogurt factories also have to dispose of whey. The Fage factory in New York funnels some of its whey waste to an anaerobic digester, which was able to completely power the factory when Hurricane Sandy hit the area last October. (3) The Chobani factory, about 50 miles east of the Fage factory, trucks its sugar-filled liquid waste to farmers who use it as fertilizer.

Dairy waste isn’t the only thing that can be fed to microbes for biogas. The Campbell Soup Company is building an anaerobic digester in Ohio to process waste from soup, sauce and drink production. (4) Switching to this source of renewable energy, the company expects to cut its greenhouse gas emissions due to electricity by the equivalent of 3,000 cars.

Sometimes waste from the food industry can be burned to create power for a plant. The Alaskan Beer company in Juneau is the first craft brewery to use spent grain as the sole fuel source for their steam boiler. (5) Spent grain must first be dried before it can be burned as fuel. But spent grain is not an efficient fuel source if it takes more energy to dry the grain than comes from burning it. The brewery found a way to create drier grain by improving the efficiency of how they remove the mash from the liquid beer. Then they combined their 20-year experience running a grain dryer to help design an efficient grain-powered steam boiler. The company estimates this new process will cut their fuel consumption in half.

A recent survey of 21 pharmaceutical and fine chemical companies showed that about 88% of them had policies regarding green chemistry. 

(4) Green solvents are a priority for all companies surveyed. Process design, energy use, green metrics, and sustainable raw materials were also issues of high importance to the companies. Some of the basic principles of process design — waste minimization, reducing energy use, increasing safety — dovetail with the 12 principles of green engineering. But other green chemistry technologies and approaches need more research to be used in industry. Continuous processing and LCA of bioprocesses are two important green engineering research areas important to the pharmaceutical industry.

SOLVENT USE

At GlaxoSmithKline (GSK), solvents contributed 85-90% of the total mass of non-aqueous materials used to make a drug in 2005. (32) A growing awareness in green chemistry has influenced solvent use among companies in the Pharmaceutical Roundtable. In 2012, about 54% of the mass of a product came from solvents. (4) Many common organic solvents carry inherent environmental, health, and safety risks. Emissions from volatile solvents can destroy the atmospheric ozone layer. Other solvents, like benzene, are classified as carcinogens. Flammable solvents also pose storage risks. In 1998, chemists at GSK developed a solvent selection guide to help their chemists pick solvents to maximize yield and minimize risk. The first version of the chart ranked solvents in terms of their risks to the environment, health, and safety. Now the amount of information involved in the rankings has expanded, while the presentation is still simple and easy to read. The latest edition of the guide ranks 110 solvents by preferred use based on their physical properties, flammability, and waste handling. (65) A quick reference guide explains the rankings. Solvents with a high boiling point are disfavored because they require energy to remove them by distillation. For other solvents, the environmental damage caused during production and transport is greater than that from their emissions alone. The chart also includes an LCA ranking for each solvent to help chemists consider solvent production in their selection. A more detailed version of these rankings is available for process chemists who need more information when choosing solvents compared to medicinal chemists running smaller-scale experiments. Other companies have their own solvent selection guides, too. However, any chemist can access the solvent selection guide created by the ACS GCI Pharmaceutical Roundtable.

Solvent use is declining in industry, particularly for the most harmful chlorinated solvents. Of 21 pharmaceutical and fine chemical companies surveyed in 2011, none use chloroform or carbon tetrachloride. (4) Dichloromethane is used only when necessary as well. Academic
journals are encouraging the use of “greener” solvents too. Editors at Organic Process Research and Development will not publish papers using solvents like benzene, carbon disulfide, or chloroform unless the authors have analyzed alternative solvents or justified the use of those solvents. (66)

Quantitative metrics of solvent selection charts can help chemists improve the “greenness” of processes. But sometimes qualitative determinations of sustainability are a matter of perspective. In the ibuprofen synthesis mentioned at the beginning of this chapter, hydrofluoric acid used in the first step usually would not be considered a low-risk solvent. Its fumes are irritants, and liquid HF can seep through skin and pull calcium out of bones. But in this synthesis, anhydrous HF serves both as reagent and solvent, reducing waste. The liquid is also recycled, thus reducing solvent consumption. (67)

VII. Education

Chemical accidents, like the release of methyl isocyanate in 1984 at a factory in Bhopal, India that killed more than 3,800 people, help foster a negative public perception of chemistry. Green chemistry seeks to prevent such tragedies by reducing hazards and toxicity. Environmentally aware students who may be wary of chemicals can connect to chemistry through the sustainable values of green chemistry.

Beyond Benign, a foundation based in Massachusetts, brings green chemistry concepts to kindergarten through high school students. (68) The foundation also sponsors a fellowship program for undergraduate and graduate students to be green chemistry ambassadors around Boston. The fellows do outreach with local groups and schools and develop their own green chemistry experiment.

The ACS Summer School on Green Chemistry and Sustainable Energy is a week-long program aimed at educating graduate students and postdoctoral scholars from the U.S., Canada, and Latin America on the basic concepts of sustainability, green chemistry and engineering, and sustainable energy technologies. Many students who have participated in the program return to their labs eager to apply the knowledge they’ve gained about green chemistry to their research.

LAB EXPERIMENTS

Integrating green chemistry into an already packed undergraduate curriculum is possible, but it can be challenging. The University of Oregon, for example, has had green chemistry laboratory courses for more than a decade. (69) To further this integration more broadly, Beyond Benign proposed last year that colleges and universities sign a Green Chemistry Commitment, pledging to absorb green chemistry into their curricula. (70)
For introductory general laboratory courses, at least, there are advantages to incorporating experiments from green chemistry. These experiments have less waste, lower liability, and lower energy costs, with the added benefit of increased safety. Green chemistry is especially advantageous for old labs that do not have proper ventilation because the experiments can be performed on bench tops (71).

There are several resources for people interested in learning more about green chemistry experiments. The Greener Educational Materials (GEMs) database, run by the University of Oregon, is an interactive, online collection of chemistry education materials and experiments focused on green chemistry (69). Users can search the database by a specific chemical concept they want to teach, like enzymes, boiling point, or molecular reactivity. They can also search by lab technique, or identify experiments that demonstrate particular principles of green chemistry.

Some experiments teach “greener” lab techniques, like performing a multi-step, small-scale synthesis without metal catalysts. Undergraduates at Harvey Mudd College in California developed a green synthesis of warfarin, a drug that reduces blood’s ability to form clots. (72) The students used an organocatalyst, rather than transition metals, to introduce the stereochemistry needed in the product.

There’s even an opportunity to learn about green chemistry beyond the 15 college programs currently offered in the United States. The University of California, Berkeley Extension offers continuing education for professionals from materials science to environmental science.

### FUNDAMENTALS

**UC Berkeley Extension’s Certificate Program in Green Chemistry includes core courses and electives**

<table>
<thead>
<tr>
<th>REQUIRED COURSES</th>
<th>ELECTIVES</th>
</tr>
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<tbody>
<tr>
<td>Principles of Green Chemistry</td>
<td>Developmental Biology</td>
</tr>
<tr>
<td>Green Chemistry &amp; Chemicals Policy</td>
<td>Introduction to Bioethics</td>
</tr>
<tr>
<td>Business &amp; Financial Planning for Green Chemistry</td>
<td>Sustainability Leadership: Strategies &amp; Paradigms</td>
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<tr>
<td>Current Topics in Green Chemistry</td>
<td>Greening Your Supply Chain: Life Cycle Assessment Tools</td>
</tr>
<tr>
<td>Alternatives Assessment: Chemicals, Materials, Products &amp; Processes</td>
<td>Molecular Endocrinology</td>
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<tr>
<td>Either Toxicology &amp; Risk Assessment, or Decision Making in Comparative Risk Assessment</td>
<td>Biology of Human Cancer</td>
</tr>
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**Source:** UC Berkeley Extension
management to sharpen their knowledge of green chemistry. (73) Eventually all of the courses for the certificate will be available online.

VIII. Conclusions

Green chemistry is spreading from academic labs into industry as a way to reduce costs, as well as environmental, health and safety risks. Applications of the 12 guiding principles are found on scales small and large, from choosing ingredients for reactions that minimize waste and risk to metrics that quantify waste and process efficiency. And principles of engineering and process design lead green chemists to track energy use during production, search for sustainable raw materials, and build biodegradable or recyclable products to prevent waste.

But green chemistry is still not widely implemented. Current estimates put green chemistry products at only 1% of the products from the chemical sector. Several barriers hinder implementation of green chemistry in the United States. (74) The challenge of developing sustainability metrics keeps companies from evaluating their processes and incorporating green chemistry into business decisions. Regulations around drug production and the investment tied up in existing chemical plants hinder the development and implementation of new technologies. The interdisciplinary nature of green chemistry also challenges the specialized knowledge gained in current training and industrial work experience. In the U.S., government policies that forward knowledge sharing or provide economic incentives can help spur green chemistry innovation.

The prospects and barriers for green chemistry are different in a developing country like China. The current growth of the Chinese chemical industry offers great potential for incorporating green chemistry practices as a way to combine the goals of environmental protection and economic growth. (75) Some of the barriers to

SUMMER SCHOOL ON GREEN CHEMISTRY AND SUSTAINABLE ENERGY

The ACS Summer School on Green Chemistry and Sustainable Energy has educated almost 600 graduate students and postdoctoral scholars since it launched in 2003. Participants engage in lectures, case studies, discussions, and poster sessions as they assess the greenness and sustainability of specific technologies. World-class researchers—including Joan Brennecke of the University of Notre Dame, Philip Jessop of Queen’s University, and Eric Beckman of the University of Pittsburgh—share their expertise in green chemistry and sustainable energy throughout the week-long program.

The Summer School has a significant impact on the participants, and a number of former students who are now faculty members have sent their own students to the program. A survey of 274 students who participated in the Summer School from 2003-2007 garnered a 64 percent response rate. Eighty-six percent of the respondents indicated they have used green chemistry in their careers since participating in the Summer School, and 90 percent reported that the Summer School had a positive influence on their career paths. Connections made during the Summer School are remarkably strong, with 80 percent of the survey respondents still in contact with at least one other participant.

Feedback from participants is uniformly positive on post-Summer School surveys. One student who attended the 2010 Summer School commented, “I got more great ideas for my research at this course than I ever have before at any other class or conference. The social aspect was also extremely awesome and I made tons of friends and contacts.” A 2012 Summer School participant observed that the best thing about the course was the “diversity of backgrounds of participants and speakers! I had no idea that students from so many areas of chemistry could all be green chemists!” The 2013 Summer School will once again be held at the Colorado School of Mines with support from the ACS Petroleum Research Fund.
INSPIRING FUTURE CHEMISTS THROUGH GREEN CHEMISTRY K-12 OUTREACH

A common perception of a chemist is a wild-haired person dressed in a lab coat who sets things on fire. Amy Cannon and John Warner, co-founders of the green chemistry education non-profit Beyond Benign, argue that chemists themselves help create this misperception. “When we perform demonstrations to a group of school children to get them excited about science we do exactly what we would hope never happens in the “real world”: explode things and set them on fire,” they write. (1)

Green chemistry experiments offer a way to perform demonstrations showing that chemistry does not have to be hazardous or environmentally damaging. Beyond Benign works to bring green chemistry to K-12 classrooms, through demonstrations, teacher training and curriculum development. Another project brings green chemistry to the broader public by connecting artists and scientists to develop community exhibits.

One classroom project has students build dye-sensitized solar cells using a titanium dioxide semiconductor, blackberries as the dye, and pencil lead as the counter electrode. The experiment is an opportunity to talk about alternative energy and chemical concepts like oxidation and reduction of the electrolyte. Students test their solar cells to see how much energy they can harvest from the sun.

Another program aims to specifically help school-age girls get excited about chemistry. In 2011, Aisling M. O’Connor, at Fitchburg State University in Massachusetts, worked to expand the chemistry activities performed by the nonprofit Science Club for Girls. The students meet for four days during vacation to do experiments related to personal care products. The girls learn about acids, bases and chemical bonding as they make fizzy bath balls from baking soda and citric acid. The final project is to make soap using lye, vegetable oil and lavender oil. Then the girls compare the safety of their ingredients to those used in a few commercially available soaps.

By exposing school-age children to chemistry early in their education, these outreach efforts hope to increase students’ understanding of science by engaging them in activities that connect science to their daily lives.

IX. Works Cited


Cue, B. W. and Zhang, J. “Green process chemistry in the pharmaceutical industry.” *Green Chemistry Letters and Reviews* **2009**, 2, 193–211.


Appendix A: 12 Principles of Green Chemistry

1. **Prevention**
   It is better to prevent waste than to treat or clean up waste after it has been created.

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 Syntheses**
   Wherever practicable, synthetic methods 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 effect their desired function while minimizing their toxicity.

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

6. **Design for Energy Efficiency**
   Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, 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 practicable.

8. **Reduce Derivatives**
   Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

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 break down into innocuous degradation products and do not persist in the environment.

11. **Real-time analysis for Pollution Prevention**
    Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

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

Appendix B: 12 Principles of Green Engineering

1. **Inherent Rather than Circumstantial**
   Designers need to strive to ensure that all materials and energy inputs and outputs are as inherently nonhazardous as possible.

2. **Prevention Instead of Treatment**
   It is better to prevent waste than to treat or clean up waste after it is formed.

3. **Design for Separation**
   Separation and purification operations should be designed to minimize energy consumption and materials use.

4. **Maximize Efficiency**
   Products, processes, and systems should be designed to maximize mass, energy, space, and time efficiency.

5. **Output-Pulled Versus Input-Pushed**
   Products, process and systems should be “output pulled” rather than “input pushed” through the use of energy and materials.

6. **Conserve Complexity**
   Embedded entropy and complexity must be viewed as an investment when making design choices on recycle, reuse, or beneficial disposition.

7. **Durability Rather than Immortality**
   Targeted durability, not immortality, should be a design goal.

8. **Meet Need, Minimize Excess**
   Design for unnecessary capacity or capability (e.g., “one size fits all” solutions) should be considered a design flaw.

9. **Minimize Material Diversity**
   Material diversity in multicomponent products should be minimized to promote disassembly and value retention.

10. **Integrate Material and Energy Flows**
    Design of products, processes, and systems must include integration and interconnectivity with available energy and material flows.

11. **Design for Commercial “Afterlife”**
    Products, processes, and systems should be designed for performance in a commercial “afterlife.”

12. **Renewable Rather Than Depleting**
    Material and energy inputs should be renewable rather than depleting.

Green Chemistry and Engineering: Towards a Sustainable Future

A white paper reporting on the green chemistry philosophy of reducing waste, toxicity and hazards, and its application on an industrial scale.