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IT'S NOT EASY BEING GREEN

In the past two decades, the green-chemistry movement has helped industry become much cleaner. But mindsets change slowly, and the revolution still has a long way to go.

BY KATHARINE SANDERSON

By the latter half of the 1980s, the worldwide chemical industry knew that it had to clean up its act: its environmental reputation was dismal. Still fresh in the public mind was the 1984 disaster at Bhopal, India, where at least 3,000 people died and hundreds of thousands were injured by a toxic gas leak at a Union Carbide pesticide plant. Also fresh were memories of the 1978 Love Canal incident in Niagara Falls, New York, where the discovery of buried toxic waste forced the abandonment of an entire neighbourhood, and the discovery of dioxin contamination a few years later that forced the evacuation of an entire town — Times Beach, Missouri.

Even when companies did try to deal responsibly with their waste, which typically included volatile organic solvents and other hard-to-clean-up agents, the volumes were daunting. Global statistics were, and still are, fragmentary. But in the United States, according to the earliest systematic data gathered by the Environmental Protection Agency (EPA), some 278 million tonnes of hazardous waste were generated in 1991 at more than 24,000 sites. Not all of it came from chemical companies, but much of it did. More than 10% of the total, some 30 million tonnes, came from one firm alone: the Dow Chemical Company, headquartered in Midland, Michigan. And other firms, such as petrochemical giant Amoco, headquartered in Chicago, Illinois, and DuPont, of Wilmington, Delaware, were not far behind.

The result, as chemical companies struggled to deal with increasingly stringent environmental regulations, was an industry-wide move towards what is often called 'green chemistry' — a term introduced in 1991 by Paul Anastas, then a 28-year-old staff chemist with the EPA.

The goal of green chemistry was never just clean-up, explains Anastas, who is currently on leave from Yale University to head the EPA's research division. In his conception, green chemistry is about redesigning chemical processes from the ground up. It's about making industrial chemistry safer, cleaner and more energy-efficient throughout the product's life cycle, from synthesis to clean-up to disposal. It's about using renewable feedstocks wherever possible, carrying out reactions at ambient temperature and pressure — and above all, minimizing or eliminating toxic waste from the outset, instead of constantly paying to clean up messes after the fact. "It's more effective, it's more efficient, it's more elegant, it's simply better chemistry," says Anastas.

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If the green-chemistry ideal is simple to state, however, achieving it has been anything but simple. Yes, says Eric Beckman, a chemical engineer at the University of Pittsburgh in Pennsylvania, "Companies these days are being very attentive to rendering their current processes greener." In 2009, for example, the total US output of hazardous waste was down by an order of magnitude over 1991, to 35 million tonnes. The largest generator in that year, DSM Chemicals in Augusta, Georgia, produced just 3.4 million tonnes.

But the greening of any given process is always a trade-off among benefits, feasibility and cost, says Beckman — and green is not always the winner. Furthermore, he says, industry's adoption of green chemistry has so far been focused mainly on incremental improvements in existing processes.

"It's embryonic at best," says Beckman, who speaks for many observers when he says that the real 'green revolution', in the form of processes redesigned from scratch and plants rebuilt from the ground up, is only just beginning.

The progress of green chemistry so far has been partly a matter of technical feasibility, as researchers have developed less toxic alternatives to conventional methods. A prime example is supercritical carbon dioxide: ordinary, non-toxic carbon dioxide that has been heated and pressurized above its 'critical point' of 31.1 °C and 7.39 megapascals, beyond which it behaves like both a gas and a liquid, and readily serves as a solvent for a wide range of organic and inorganic reactions. Other non-toxic replacements for solvents have been found among the ionic liquids: exotic cousins to ordinary table salt that happen to be liquid at or near room temperature.

THE E-FACTOR

Green chemistry's progress has also benefited from an awareness campaign by Anastas and his allies. A key first step was the 1991 coining of the name itself, says John Warner, president of the Warner-Babcock Institute for Green Chemistry in Wilmington, Massachusetts, who at the time was director of exploratory research at the Polaroid Corporation in Minnetonka, Minnesota. "Identifying green chemistry as a field of science differentiated it from a political and social movement," he says.

Another key step was the drawing up by Anastas and Warner of a set of principles intended to help scientists define and practise green chemistry (see 'The twelve principles of green chemistry'). And yet another came in 1995, when Anastas helped to persuade US President Bill Clinton to launch the Presidential Green Chemistry Challenge, which still awards five citations each year to companies and academics who have done an outstanding job of implementing the principles.

Mostly, however, green chemistry's progress has been a matter of corporate buy-in, as epitomized by its promotion by the chemical industry's own voluntary initiative, Responsible Care (www.responsiblecare.org), which works with national industry associations to improve the industry's health, safety and environmental performance. Founded in Canada in 1985, membership has grown from 6 national associations to 53.

The pharmaceutical sector has embraced green chemistry most enthusiastically, perhaps because it has the most to gain. Pharmaceutical plants typically generate 25 to 100 kilograms of waste per kilogram of product, a ratio known as the environmental factor, or 'E-factor'. So there is plenty of room to increase efficiency — and cut costs.

At drug-maker Pfizer, for example, the first laboratory synthesis of its anti-impotence drug sildenafil citrate (Viagra) had an E-factor of 105. But long before Viagra went on the market in 1998, a team at Pfizer's plant in Sandwich, UK, was rigorously re-examining every step of the synthesis. The researchers replaced all the chlorinated solvents with less toxic alternatives, and then introduced measures to recover and reuse these solvents. They eliminated the need to use hydrogen peroxide, which can cause burns. They also eliminated any requirement for oxalyl chloride, a reagent that produces carbon monoxide in reactions and is therefore a safety concern. Eventually, Pfizer's researchers cut Viagra's E-factor to 8.

After that success, Peter Dunn, the leader of the Viagra synthesis team, became head of the more systematic green-chemistry drive started by Pfizer in 2001. Dunn says he is not free to talk about specific cash savings, but can point to sweeping changes made across the company. Pfizer has reduced the E-factor of the anticonvulsant pregabalin (Lyrica) from 86 to 9, he says, and has made similar improvements for the antidepressant sertraline and the non-steroidal anti-inflammatory celecoxib. "These three products alone have eliminated more than half a million metric tons of chemical waste," says Dunn.

CREATIVE CHEMISTRY

Nor is Pfizer alone; the pharmaceutical sector is so competitive that no company can afford to ignore green chemistry's potential savings. The Pharmaceutical Roundtable, first convened in 2005 by the American Chemical Society's Green Chemistry Institute, now has 14 member companies that jointly fund academic research in the field and share pre-competitive information.

In 2002, the chemicals giant BASF, based in Ludwigshafen, Germany, introduced an industrial-scale process that uses ambient-temperature ionic liquids to remove acid by-products from reaction mixtures — a common chemical manufacturing step that had previously been much more cumbersome. But BASF's embrace of green chemistry (which the company prefers to call 'sustainable chemistry') goes much further, notes Pete Licence, a green chemist at the University of Nottingham, UK. "You're getting sensible and joined-up thinking about the way that chemical plants are created," he says. "They have this integrated reaction system where the products and the by-products of reactions are actually the starting materials for the plant that is next door." The plants are also designed to maximize energy efficiency, Licence says: "Waste heat from one process is the warm-up for the feedstock for the next."

But the comprehensive restructuring required illustrates why the shift to green chemistry has been comparatively slow among bulk-chemicals manufacturers. These firms deal with products that are made in much larger volumes than pharmaceuticals, and their industrial processes are already highly optimized, with E-factors typically in the range of 1 to 5. Although it is possible to go much lower — E-factors for petrochemicals are on the 0.1 scale — doing so is not always economic. "Once you have a plant, it will run for 30 or 40 years because you have made a huge investment," says Walter Leitner at the Institute for Technical and Macromolecular Chemistry at the University of Aachen, Germany.

IT'S MORE EFFECTIVE, IT'S MORE EFFICIENT, IT'S MORE ELEGANT, IT'S SIMPLY BETTER CHEMISTRY.

Nor does it always pay to be green in the speciality chemicals sector — as Thomas Swan and Company in Consett, UK, learned the hard way. In 2001, building on the work of chemist Martyn Poliakoff at Nottingham University, it opened the world's first continuous-flow reactor using supercritical carbon dioxide as a solvent. "It looked as if it could have been game-changing within the industry," says managing director Harry Swan. But when no government subsidies were forthcoming, the plant could not provide chemicals more cheaply than those made by the standard non-green methods, he says. So the facility was mothballed, and may soon be decommissioned and dismantled.

Other roadblocks to the adoption of green chemistry are technical. For example, even after decades of research, green solvents are not always more efficient than the widely used chlorinated solvents. Nor have chemists completely eliminated the need for catalysts containing precious or toxic metals — although Dunn, for one, is optimistic that this may eventually be possible through advances in enzyme technology. And how to make bulk chemicals from biomass and other renewable feedstocks, rather than from crude oil, is still an open challenge. "It's

THE TWELVE PRINCIPLES OF GREEN CHEMISTRY

Paul Anastas and John Warner formulated these guidelines in the 1990s to provide a roadmap for chemists trying to implement green chemistry.

1 WASTE PREVENTION
Prevent waste from the start rather than treating or cleaning it up afterwards.

2 ATOM ECONOMY
Design synthetic methods to maximize the incorporation of intermediate materials into the final product.

3 SAFER SYNTHESES
Design synthetic methods to minimize the use and generation of toxic substances.

4 SAFER PRODUCTS
Design chemical products to carry out their function while minimizing their toxicity.

5 SAFER AUXILIARIES
Minimize the use of solvents and other auxiliary substances, and make them as innocuous as possible.

6 ENERGY EFFICIENCY
Minimize the energy used in chemical processes, and if possible, carry them out at ambient temperature and pressure.

7 RENEWABLE FEEDSTOCKS
Use biomass and other renewable raw materials whenever practicable.

8 DERIVATIVE REDUCTION
Minimize the potentially wasteful use of blocking groups and other temporary modifications of intermediates.

9 CATALYSIS
Prefer catalytic reagents — as selective as possible — over stoichiometric reagents.

10 DEGRADABILITY
Design chemical products for eventual disposal, so that they break down into innocuous compounds that do not persist in the environment.

11 POLLUTION PREVENTION
Develop methods for real-time monitoring and control of chemical processes that might form hazardous substances.

12 ACCIDENT PREVENTION
Choose processes and practices that minimize the potential for chemical accidents, including releases, explosions and fires.

a different way of looking at a chemical synthesis," says Leitner, who points out that the conventional problem gets turned on its head. Instead of starting out with a relatively simple hydrocarbon extracted from oil, and then adding side groups to the molecule to give it the desired properties, chemists have to start with the incredibly complex mixture of biomolecules typical of most renewable feedstocks, and get to what they want by snipping off pieces in a controlled manner.

But many advocates say that the most fundamental barrier to the wider adoption of green chemistry is mindset — which largely reflects the way chemists are taught. "In the United States, chemists get trained rigorously in chemistry, but don't see any engineering, product design, or life-cycle analysis," says Beckman. Or, as Anastas puts it, "you usually get the safety course that says, 'Wear your goggles and your coat, and don't blow things up — and by the way, here's the number to call if you do.' But I don't think that's the same as treating the consequences of what we do as an intrinsic part of our work".

This curricular conservatism may well reflect the often negative reactions of academic chemists to green chemistry. Especially in its early years, the field was seen as fuzzy and non-rigorous, recalls Neil Winterton of the University of Liverpool, UK, a former critic who has since become more accepting of the movement. The word 'green' conveyed the impression that certain techniques were being promoted for reasons of political correctness, he says. "It needed a little bit more fundamental underpinning to establish whether what was being proposed was or wasn't a major contribution to improving the efficiency of chemical processes."

Sceptics also questioned whether green chemistry was anything more than a trendy new buzzword used to get money for projects of dubious environmental value. "It's something that can dupe the public, it can dupe other scientists working in the area, and much, much more importantly, it can dupe decision-makers", concedes Licence.

Scepticism hasn't gone away entirely; a mention of green chemistry in a gathering of chemists can still provoke sighs and eye-rolling, says Warner. But scepticism has lessened as research has improved.

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GREEN CHEMISTRY SHOULD JUST BE SECOND NATURE, THE DEFAULT VALUE.

The EPA, for example, has made notable progress in lifting one barrier to effective green chemistry, which is that researchers trying to create a new, non-toxic manufacturing process often don't know if a given compound is 'green' or not. No one has had the time or money to gather the toxicity data, which typically requires expensive animal testing.

The EPA's answer is a high-throughput screening project called ToxCast, which has been running at its Research Triangle Park facility in North Carolina since 2007. The ToxCast team has applied a battery of standard high-throughput biochemical assays, which measure such things as binding to cellular receptors, to 1,000 chemicals that already have animal toxicology data. These data have then been used to build statistical and computational models that attempt to predict any compound's toxicity from the assays alone.

A ToxCast prediction costs US$20,000 per chemical, compared with the $6 million to $12 million typical of animal toxicology tests, says Robert Kavlock, who oversees the project as head of the EPA's National Center for Computational Toxicology at Research Triangle Park. So if these models can be made reliable enough, he says, "then we've got a way to address the chemicals that we can't afford to test in animals" — and in the process, help companies to choose compounds that will make their chemistry truly green.

Now that Anastas is the EPA's research chief, he has been trying to spread the green-chemistry approach through staff meetings at the agency's labs across the country. He wants to move the EPA away from a culture of regulating and banning to one where products are designed to be synthesized in a way that reduces or eliminates the use of hazardous substances in the first place. As EPA chief Lisa Jackson puts it: "It's the difference between treating disease and pursuing wellness."

If that change in attitude happens, says Anastas, it will represent a "seismic shift" at the agency — "the culmination of the work of my career". But in a sense, he adds, it will also be just the beginning: "I believe that the ultimate goal for green chemistry is for the term to go away, because it is simply the way chemistry is always done. Green chemistry should just be second nature, the default value." ■

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