Imagine how great it would be to be invited by Ferrari, Mercedes, or Tesla to help design their next new car. From the steering wheel to the engine, sound system, cup holders, and everything else, you would be able to have everything just how you want it. Then you could have the best car builders in the world produce what you have helped them design. For a car enthusiast, it would perhaps be a dream come true, but what if you are not into cars? What if your interests lean more toward the scientific and you are more into, say, chemicals? (Difficult to admit, but you know who you are.) Well, the opportunity to design the next generation of chemicals is precisely what the people that synthesize chemicals are offering and they need assistance.

The field of green chemistry has emerged over the past 20+ years to become a major force in how chemistry is conducted. There are now at least five scientific journals dedicated to green chemistry. University courses and even degree programs are being offered around the world in the subject. Nearly every chemicals-related company has some version of a green chemistry program. Most of the work in green chemistry, however, has been devoted to the way that chemicals are made, e.g., their manufacturing processes, the feedstocks, and the solvents that are used. What has not been at the forefront of work in green chemistry is what molecules are made even though it is explicitly a part of the field. Principle 4 of the Twelve Principles of Green Chemistry states that, “Chemical products should preserve efficacy of function while reducing or eliminating inherent toxicity” (Anastas and Warner, 1998). Yet this one of two tenets that explicitly mentions toxicity has been one of the more under-represented efforts in the thriving field of green chemistry.

How could this be? How could eliminating toxicity be low on the priority of chemical design? It is because chemists are not toxicologists and not appreciative of the discipline of toxicology. The skill set of toxicologists to deeply understand the nature, causes, and mechanisms of toxicity is something to which chemists are almost never exposed. In all of the professional training that a chemist receives either in college or in graduate school they are not required to know, much less master, any of the fundamental principles of toxicology. It is unusual to almost the point of being bizarre that a profession that is creating new things is not required to be aware of the potential adverse consequences of what they are making. Can you imagine chefs and cooks not being instructed on the proper storage and preparation of food to prevent spoilage or food poisoning due to salmonella or botulism? Or an architect who was not trained about structural integrity and how materials fail?

Green chemistry is trying to change this by encouraging (requiring?) chemists to understand the basics of toxicology. The goal is not to turn chemists into toxicologists, but rather to facilitate interaction between chemists and toxicologists so that they understand each other's discipline. Green chemists want to make the next generation of molecules as safe to human health and the environment as possible, but these require and understanding of toxicology and interaction with its practitioners.

Herein lies the opportunity for leadership in toxicology. The opportunity for collaboration is timely and important. As the field of toxicology has developed over the decades, it has evolved from a descriptive science to a mechanistic science becoming increasingly molecular in the process. The problems that toxicologists are seeking to understand are the same ones that the
green chemists are seeking to solve. One could argue that the main reason to deeply understand a problem is to inform and empower its solution. Closer collaboration of toxicologists with the synthetic chemists in the green chemistry community provides that possibility.

In recent years, there has been an encouragingly increased focus on the rational design of chemicals for reduced toxicity in some chemical sectors. Taking many of the same approaches and tools used in drug design to make therapeutic molecules, chemists have sought to use these tools to ensure that the vast majority of molecules that are not drugs are not biologically active. New computational methods are being developed that rely on large amounts of toxicological data. New centers are being formed such as the Molecular Design Research Network (MoDRN) that bring together toxicologists and chemists, but more has to be done. The following initiatives would help stimulate the interactions between the fields and their respective stakeholders:

- **Joint workshops, meetings, and conferences.** In recent years, scientific societies, government agencies, and NGOs (e.g., National Academies of Science, American Chemical Society, Society for Environmental Toxicology and Chemistry, The Heinz Center, and National Institute of Environmental Health Sciences) have help workshops to discuss the integration of toxicology and synthetic chemical design. We need to solicit and conduct more workshops and symposia at the Society of Toxicology Annual Meeting and other appropriate venues to advance this issue.

- **Joint solicitations and proposals.** As the toxicology of green chemistry spans multiple disciplines, this requires research programs to span funding agencies. Although there has been some recent initial investment by the National Science Foundation in collaboration with the United States Environmental Protection Agency, this good beginning needs to be significantly expanded to include agencies such as the National Institutes of Health, Food and Drug Administration, Department of Energy, Consumer Product Safety Commission, and others.

- **Data generation and sharing.** In many cases, data exist in the laboratories of toxicologists that could be critical to enabling safer chemical design but the synthetic chemists are not aware of it. Conversely, structural manipulations that would reduce toxicity exist in the toolbox of synthetic chemists but the toxicologists are unaware of them. We must establish systems that allow for the sharing of expensive data, information, and knowledge.

- **Removing barriers of nomenclature, terminology, and jargon.** There are many terms that toxicologists use differently or have important nuances that need to be clarified for productive collaboration. Terms such as “mechanism,” “pathway,” “target,” are just a few that could benefit from common understanding.

- **Design charrettes—the toxicologist at the design table.** Toxicologists need to take advantage of the opportunity to participate in the chemical design process. Toxicologists possess the critical knowledge about the mechanisms of adverse biological effects. Providing this knowledge during design will have the maximum influence over the intended and unintended consequences of the chemicals and materials we make.

- **Community expansion.** Toxicological Sciences welcomes submissions that address the toxicology of green chemistry. Ultimately, as this interfacial field grows, a new journal may be required to address this important need.

Toxicology is never simply an “academic” exercise. The discipline exists to provide information to the medical, public health, and regulatory communities to protect our biosphere. As our field learns more about the adverse effects of the tens of thousands of chemicals in our environment, it is essential to get the data, information, knowledge, and insight into the hands of the people who can use it to make a difference in protecting health and the environment. Toxicologists are quite familiar with the public health and regulatory communities that need this information, but we have been remiss in getting this information into the hands of the people that are actually making the chemicals themselves. Historically, toxicology has been a reactive discipline, responding to what industries and societies introduce into the environment. However, a more powerful role would be to work with the chemists designing the molecules to which future generations will be exposed. Toxicologists must be at the design table if we as a society are going to avoid the missteps of the past. Society will always need chemicals to control disease-carrying or crop-killing pests, but we must avoid the chemicals that persist in our environment, kill beneficial insects, or contaminate water supplies. The future should rely on targeted pesticides that are benign for other species, enrich the soil, and possess negligible effects the environment. Instead of photovoltaics that are made from depleting, rare earth metals, the future should utilize abundant, nontoxic materials that remove air pollutants while capturing solar energy. As noted above, one of the goals in the field of green chemistry is reducing the inherent toxicity of chemicals. Without knowledge of the toxicological processes this goal cannot be achieved, but the field of toxicology has that knowledge.

As much fun as it would be to design and test drive that new Ferrari, it will have a much greater impact on the world if we design all of the chemicals that go into that Ferrari and every other product that we use to be benign. To accomplish this, the fields of green chemistry and toxicology must interact more closely. What are we waiting for? All of the lights are green.

**REFERENCE**