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Guest editorial: Asking the right questions†

I do not know who said it first. I have heard this statement several times from instructors and colleagues throughout the years. I myself have said it several times. 'The key to quality chemistry education is not teaching the right answers, but teaching how to ask the right questions.' Now, almost 25 years after first calling myself 'a chemist' I believe this more than ever.

I started out as an undergraduate chemistry student doing hands on research at my university. I was what they called a 'lab rat'... a 'research animal'. You know the type, spending more than 60 hours a week in the lab. I published 5 papers as an undergraduate student. I spoke at American Chemical Society National Meetings. I prided myself in my research prowess and productivity. I used to set up 7 or 8 reactions simultaneously. I would work most, if not all, of my reactions up… Isolate and characterize most of my products… I counted in my old laboratory notebooks that I synthesized over 150 compounds as an undergraduate. A large metropolitan area newspaper did a big story on me when I graduated. They called me one of the region's 'best and brightest' college graduates.

My graduate school career continued this productive trend. I started doing research in my first semester. I passed all of my cumulative exams in the first round. I was in a rush to pass into 'candidacy' and more importantly, to get into the lab… Of course, the purpose was to make more compounds. I remember my graduate school days with such fondness. I would get into the lab before the sun came up. I would leave, come back, leave and come back throughout the day, and night, working around the clock. My life and daily activities were aligned to reflux times. Meals, shopping and entertainment were scheduled around the thermodynamics of molecular synthesis. I published more than a dozen papers as a graduate student. I do not have an exact count, but I probably made over 1000 compounds.

I graduated and got a job in industry. I wanted to prove my self-worth. The metric I knew and embraced was measured in 12 dram to 10 dram glass vials with carefully written labels and correlated spectra and analyses. I synthesized more and more new compounds. I put methyl groups and ethyl groups in places where they had never been. This was my pathway to success. And I did it well. I got a bunch of patents. I cranked out countless compounds. I was so very proud of myself. Not only was I making complicated new molecules, whose syntheses were challenging and difficult, but a lot of the compounds that I made actually did what I wanted them to do! I was successful at making stuff and more importantly, I was 'asking the right questions'!

It's funny how things hit you.

I prided myself as being 'a family guy' through all of this. I identified myself first and foremost a member of a large family. My mom had 10 brothers and sisters. I grew up with 35 cousins all within a few miles of my house. Nearly all of my relatives entered the full time workforce immediately from high school, getting jobs and starting families by the time they were 25. I was no exception. My oldest daughter, Joanna was born in my third year of graduate school. My first son, Tom was born just after I started my job in industry. Son number two, John, was born a couple years later. But my son John was born with a serious liver disease. It was called Billiary Atresia. This is one of those diseases that no one quite knows what the cause is. John was born perfectly healthy and normal, but within a week after birth he began to show signs of jaundice. His billiary system was not functional, in fact, it wasn't even there! No bile secretions [necessary for adequate nutritional uptake] could pass from his liver to his GI tract. A surgical procedure called a 'Kasai Junction' was performed on him in order to artificially connect his liver to his small intestines. This 'fix' remained functional for a few months as we waited and waited on a liver transplant list. My son spent an enormous amount of time in the hospital. I stayed over night with him quite a bit. At this time I had several scientists reporting to me in my industrial job. I kept a laptop computer with me, to monitor the progress of 'my people' at work and to keep track of the molecules they were making and testing. I remember going back and forth between excel spreadsheet files in the wee hours of the night. One file showed my son's blood electrolyte levels and another file showed performance results of a series of compounds that were synthesized at work. By this time in my career I figure I must have synthesized over 2500 compounds.

This story doesn't have a happy ending. My son died after receiving his liver transplant. I can't begin to describe the anguish that followed. Lying awake at night, I would wonder 'what causes this kind of thing to happen? Could it possibly be that some chemical that I had previously worked with might have had something to do with this?' I understand that the physiological causes for this disease are complicated—and it is very likely that my son's illness and subsequent death had nothing to do with anything that I ever interacted with in the lab. But a father can come up with a great deal of methods to apply self-blame when an infant son dies.

I began to think more and more about this situation. I had prided myself with my ability to make compounds. I prided myself on my ability to solve complicated scientific problems. I prided myself on the ability 'to ask myself the right questions'. At no time in my chemistry education could I remember learning about toxicity or environmental impact of chemistry or chemicals. Sure I was constantly reminded about safe lab techniques and proper waste disposal protocols. But this was handled as a 'housekeeping' part of chemistry, like taking out the trash at home and filling out tax forms, something you had to do… but in the background.

I consider myself fortunate to have had the opportunity to study with a few of the most brilliant chemists I have ever known. And these people were of the most compassionate of human beings. I do not fault the education that I received or the people who educated me. 'We' as a science have somehow followed a path and got to the point where 'making stuff' is the focus of what we do. The 'right questions' involve the ingenuity of chemical synthesis and design. Issues such as toxicity and

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environmental impact… Well, the EH&S people and the industrial engineers can handle that stuff! I think the most important question, the right question that has not been asked, a simple little question really…. 'Why?'

Isn't it funny that the people society entrusts with the job of inventing the next generation's materials and products are not taught how to make these materials safely? Isn't it strange that a really good chemist can develop dozens of synthetic schemes to prepare new and different molecules, but it is unlikely that they can assess, at any level, the relative risks of their methods and materials to human health and the environment? Why is this acceptable?

My guess is that chemical risk is very different from almost any other type of risk we might expose ourselves to. On occasion I try to do some cooking in the kitchen. Talk about risk! I use a knife to cut up my food. There is a good chance that I will cut myself! But I accept this risk because the function of the knife is to cut. Cut food, cut me. *The risk and function are intimately connected*. Same with the stove. It gets hot. I might burn the food. I might burn myself. But that is what the stove is supposed to do, heat things up. Again, the function and the risk are closely related. Chemistry is different. Lets say that I want to synthesize a red dye. I know that I will want to assemble a planar system with a few conjugated double bonds. I will want to have an electron donating group on one side, and an electron withdrawing group on the other side. If I put this molecule together correctly, it will have appreciable broad absorbance around 500 to 600 nm, and I will have a red dye. If the molecule that I make happens to also be carcinogenic, it will have nothing to do with the fact that it is red. The ability of the molecule to be red has no relationship with it being carcinogenic. *The risk and function are not intimately connected*. It is unlikely that there is some hidden scientific truth that states that all red molecules must be carcinogenic. I, as a synthetic organic chemist, know how to make a red molecule, but I do not know what makes a molecule carcinogenic.

We need to re-evaluate the 'machinery of chemistry'. We need to take a look at our relationship with the community we serve. We need to think about how we teach chemistry to future chemists and to the general community. I do not expect that we can convert all practicing chemists to fully functioning toxicologists. There is still a lot we do not know about mechanisms of toxicity. But we do know some things. And if we want to learn more, then we need to be placing a stronger emphasis on this. We need to link the function of making molecules with a better assessment of their risk. Maybe we need to ask ourselves some better questions, like 'Why do I make things the way I do?' Or perhaps, 'Is there a way to make these molecules that will not be harmful to human health or the environment?' I believe that there are answers. The growing field of Green Chemistry is testament to the interest in answering these questions. There are researchers who understand this quite well. Some may argue it is out of financial incentive. Obviously, it is much less expensive to work with, and manufacture, environmentally benign materials that do not have associated regulatory and disposal costs. I would like to think there is more to it than that.

Things really need to move more quickly. I worry that in some places these important questions are not being asked enough. And perhaps more troubling, the response to these important questions might remain unspoken, but ring through some research hallways…. 'But that's not the way we've always done it!' And that is exactly the point.

John C. Warner
Professor of Chemistry
University of Massachusetts Boston