Mike Pikal is one of the very few pharmaceutical scientists in the world equally comfortable, and equally successful, in both industrial and academic settings. He is held in high regard by both groups because his research career has been a shining example of the application of scientific rigor to problems associated with development and manufacture of pharmaceutical dosage forms. In the busyness of day-to-day life in the pharmaceutical industry, most scientists deal with these problems by, frankly, “throwing a patch on them and hoping they’ll go away.” Mike has steadfastly—and at times perhaps stubbornly—resisted this approach. In doing so, he has done the pharmaceutical science community a real service by educating us on the importance of understanding what’s going on at a fundamental level, even on problems that, on the surface, may appear mundane.

SCIENTIST

Mike is a physical chemist-turned pharmaceutical scientist. After receiving his B.S. degree in chemistry from St. John’s University (Minnesota), he earned a Ph.D. in physical chemistry at Iowa State University. Following a post-doctoral fellowship in solution thermodynamics at the Lawrence Livermore Laboratory, he took a position as assistant professor at the University of Tennessee in Knoxville. Eli Lilly recruited Mike away from academics in 1972, and he stayed at Lilly for the next 24 years. His first real impact as a pharmaceutical scientist was a natural outgrowth of his training as a physical chemist—measurement of vapor pressure of nitroglycerin and the application of this knowledge to physical stability of nitroglycerin tablets. His work on nitroglycerin stability (J. Pharm. Sci., 65:1278 (1976)) led to his first major recognition by the pharmaceutical world—the Ebert Prize in 1977. His early work in stability assessment of solid oral dosage forms, particularly cephalosporins, led to a better appreciation for the role of the physical state of a drug in
chemical stability where, for some molecules, there is a two order of magnitude difference in stability between crystalline and amorphous forms (J. Pharm. Sci., 66:1312 (1977)). This led to a high-impact paper in 1978 on quantitative crystallinity determinations using solution calorimetry (J. Pharm. Sci., 67:767).

Mike’s introduction to pharmaceutical freeze drying in the early 1980s was again in response to production related problems, and again he eschewed “quick and dirty” solutions to these problems. This led within a few years to Mike becoming an internationally recognized authority on the science and technology of freeze drying. His large list of publications on the subject includes some excellent examples of his ability to apply good science to problems that many pharmaceutical scientists would consider not worthy of their best effort. Subtle effects of the heat transfer characteristics of glass vials were shown to have a measurable impact on product quality attributes in his paper “Mass and Heat Transfer in Freeze Drying of Pharmaceuticals: Role of the Vial” (J. Pharm. Sci., 73:1224 (1984)). His entire body of work on heat and mass transfer in freeze drying stands head and shoulders above any related work done before or since. This work is very significant in light of the high cost, and inefficiency, of freeze drying as a unit operation, where the major sources of this inefficiency are limitations associated with both heat and mass transfer.

His research in freeze drying progressed to the study of the role of viscoelastic properties of predominantly amorphous systems on physical and chemical stability of freeze-dried solids—particularly proteins. This is a challenging area of research, and a very important one. Definitive answers are still lacking, and may be for some time to come, but Dr. Pikal’s publications on the subject support the idea that a high glass transition temperature (relative to the storage temperature) of an amorphous freeze-dried solid is a necessary, but not sufficient, quality attribute of that product. Again, his work in characterization of amorphous systems has served to make the pharmaceutical science community aware of concepts such as glass fragility, fictive temperature, and how these ideas might be important in rational design of freeze-dried formulations.

Another area of Mike’s research that is worthy of note is the work on process monitoring and control of freeze drying, including a well recognized paper on evaluation of an electronic hygrometer (J. Parenteral Sci. Technol., 43:60 (1989)) and a less well recognized, but more significant, paper on a technique called manometric temperature measurement (J. Parenteral Sci. Technol. 51:7 (1997)). This technique, based on a mathematical model of heat and mass transfer in freeze drying, allows measurement of product temperature without the need to place thermocouples in individual vials of product (a very significant problem in production operations). This technique has the added benefit of providing data on resistance to mass transfer and the vial heat transfer coefficient. This work has evolved into the “Smart Freeze Dryer” project, the goal of which is optimization of a freeze drying cycle in as little as one trial batch. It was in Mike’s lab at the University of Connecticut that the application of tunable diode laser absorption spectroscopy as an in-process mass flow meter was demonstrated (J. Pharm. Sci., 96:1776 (2007)). This technique shows tremendous promise as a technology that will enhance a Quality by Design approach to development and manufacture of freeze-dried dosage forms.

**FAMILY MAN**

For all of Mike’s enthusiasm for science and technology (it is generally recognized that he only needs a microphone in the largest of speaking venues), he is even more enthusiastic when the subject turns to family, and it becomes apparent that his family is the true center of his life. While still a graduate student, he married Janice Klein of Bluffton, Minnesota, and they had two children (Mary and Jon) by the time he graduated. By the time he finished his post-doctoral assignment, they had child number three—Rob. While Mike was on the Chemistry faculty at the University of Tennessee, child number four—Kathy—came along. They weren’t finished yet. The fifth, and last child—Amy—arrived shortly after Mike started his industrial career at Eli Lilly.

Mike and Janice have instilled a respect for learning and a love of science in their children and, not surprisingly, they have all done exceptionally well. Mary, the oldest, received a B.S. degree in Biochemical Engineering from Purdue, and has worked at Eli Lilly in a variety of technical and management positions for about 13 years. Jon earned a Ph.D. in electrical engineering from Colorado State University, and is currently Associate Professor of Electrical Engineering at the University of Wyoming. Rob is a
physician (B.S. in Biochemistry and MD from Indiana University, specializing in internal medicine) currently practicing in Pontiac, Michigan. Kathy received her Ph.D. in Pharmaceutical Science from the University of Colorado, and is currently working for a consulting firm in the San Francisco bay area. Amy, the youngest, received her B.S. degree in Biology from Notre Dame (where she was a cheerleader for Mike’s beloved football team), and her Doctor of Optometry degree from Indiana University. Amy, recently married, is currently practicing in West Palm Beach, Florida.

EDUCATOR

Dr. Pikal did the pharmaceutical science and technology community another favor when he retired early from Eli Lilly in 1996 and joined the University of Connecticut. Dr. Pikal is the kind of scientist that graduate students should be exposed to early and often, primarily because he sets a wonderful example of how to be both a good scientist and a productive contributor to the mission of all research based pharmaceutical companies. He is setting a good example for pharmaceutical educators by emphasizing a basic science approach to formulation and processing and, in so doing, elevating the status of the subject within the graduate curriculum. Other schools, as well as the pharmaceutical industry, would benefit by following his superb example.

Probably the crowning achievement of Mike’s career was being named Pfizer Distinguished Professor of Pharmaceutical Technology in 2007. This is not only a well-deserved honor for Mike, but it is also much-needed recognition of pharmaceutical technology as a discipline worthy of the best efforts of pharmaceutical scientists, both in industry and in academics.

We’ve asked Mike to respond to some questions about his career and about his views of the future of pharmaceutics:

Your research career has emphasized the application of fundamental physical science to pharmaceutical systems, with emphasis on formulation and manufacturing aspects. With decreased emphasis on physical science in graduate pharmaceutical education, are people such as yourself a vanishing breed? If so, what would you propose be done about it?

Unfortunately, unless something changes, I think the answer is “yes”. The decreased emphasis is largely due to changes in funding patterns. The huge sums of money available from Federal sources, particularly the NIH, are not available to those of us who emphasize the physical science of pharmaceutical systems. Moreover, we are typically “too health science oriented” and applied for the basic sciences within NSF. It is true there are some exceptions, but what I have stated is a very good approximation to reality. Historically, and still today, industry has funded most of the work focused on physical science of pharmaceutical systems. Unfortunately, particularly with all the mergers in big Pharma, even this relatively low level of funding seems to be decreasing, so the picture is not at all bright for a young pharmaceutical scientist seeking a career in academia. Of course, bringing new products to market will still demand the application of physical science, and one way or another, industry will need to have significant efforts in the physical science of dosage form development and manufacturing. With fewer new research workers appropriately trained in the universities for these tasks, and the trend in industry to focus more and more on pushing projects and less on development of the skill sets of their scientists, the level of expertise applied to development problems will certainly decrease in the coming years—unless something does indeed change. The answer to the problem lies mostly in finding increased funding for university research in “physical science of pharmaceutical systems”, whether this comes from federal sources or industry. My own view is that while industrial support is necessary and is likely to continue at somewhere near the current low levels, industry will not commit to the level of funding needed. Therefore, a program such as the National Institute of Pharmaceutical Technology and Education (NIPTE), which is focused on generating significant levels of federal support for research and education efforts in pharmaceutical technology, is essential:

Having been highly successful as both an industrial pharmaceutical scientist and an academic scientist, how would you compare and contrast the critical factors for success in both arenas?

There is much common ground in the success factors. After all, both require the application of good science to problems of significance, perseverance, a sprinkling of innovation, and the ability
to work with others and communicate results in both oral and written form. Of course, the focus in industry is on development. In academia, while some development is often done as a service to industry, the focus is clearly on research. However, at least in pharmaceutical technology, the research is generally applied research in the sense that we know why we are interested in generating the information. Industrial R&D is more dependent on teamwork, particularly within project teams, than is the typical academic position. While the ability to describe and “sell” your research ideas is important in industry, it is much more critical in academia. The big difference between industry and academia is that in the university setting, you have almost complete control over your own situation—as long as you can pay for everything yourself! Thus, at least for a research oriented university, survival depends on your ability to obtain funding to support your students and your research program. In academia, you choose your research projects, and often do so with considerable attention to whether or not the project is “doable”; after all, the student must eventually graduate. In industry, you are generally assigned a project because of potential economic benefit to the company. While certainly most such projects are “doable”, the order of difficulty is not a consideration. That is, you don’t say, “I don’t want that project because I don’t think I can finish on schedule”:

You left academics at University of Tennessee after a fairly short time. What attracted you to the pharmaceutical industry? In retrospect, what were the most pleasing, and the most disappointing, aspects of industrial pharmaceutical science?

The early 1970s were a difficult time for science, particularly for physical chemistry. Students could not find jobs, and I often wondered whether or not anyone except those other academics working in my research area really cared much about what it was I was doing; after all, they did not want to hire my students. I was looking for an opportunity to do good physical chemistry in the pursuit of something useful. Also, I was working part time at Oak Ridge National Laboratory, in the same lab as Sig Lindenbaum, and one day Sig announced that he was going to the University of Kansas to interview for an academic position in “Pharmaceutical Science”. I asked, “what is pharmaceutical science”? Sig responded with, “I don’t know, but maybe I can tell you when I get back”. Well, Sig got back, he told me a little about Pharmaceutical Science, and it seemed to me that this field might be a fruitful area for application of physical chemistry to something useful-health care. Of course, Sig accepted the position at Kansas, and I fired off a number of letters to Big Pharma. Lilly came through with a good offer, and I spent over 24 years at Lilly in the scientific ranks. I think the most pleasing aspect of industrial R&D was the opportunity to work on problems of importance that required good scientific thought. Of course, not all projects were scientifically interesting or challenging, but most were, and I was lucky in that much of what I did was use my particular expertise in “trouble-shooting” problems that developed in other projects; that is, essentially using my specialized technical skills serving projects I was not formally assigned. Most of what I did would be classified as development, but I also did a fair amount of research or what came to be known as “technology development”. I think the balance between development and research was important because it allowed me to develop the knowledge and skills that both kept me interested and motivated and also allowed me to solve problems of importance to Lilly. Disappointments were generally caused by what I perceived as “short sighted” policy decisions that came from management, particularly during difficult economic times. This often took the form of ill conceived reorganization plans and de-emphasis of professional development in the name of “focus”. Fortunately, the “good decisions” outnumbered the silly ones, which is why I remained in one company for so long:

Are you optimistic about the future of academic pharmaceutics (or pharmaceutical technology, or pharmaceutical engineering)? Will such academic units exist a generation from now? How can academic departments that choose to maintain a strong physical science orientation best position themselves for continued research funding?

I am cautiously optimistic, but this optimism is based on the expectation that NIPTE will dramatically change the funding situation. NIPTE is a consortium of 11 universities (including UConn) with significant strength in pharmaceutical technology and has been in existence for about 4 years. The objective is to obtain significant levels of funding from federal sources for support of research in pharmaceutical technology and development of a combined science-engineering
education program. A “Pharmaceutical Technology Roadmap” has been developed, with assistance and input from industry, the FDA, and academics throughout the US. An “Education Roadmap” that attempts to develop a curriculum that is a blend of engineering and pharmaceutical science is currently being developed. This program is directed at both undergraduate and graduate education as well as special education programs for the FDA and Industry. The funding level needed is roughly twice what is currently spent on academic research in pharmaceutical technology throughout the USA and would be partly spent on programs at participating NIPTE institutions and partly to support research and education efforts at any non-profit university in the USA. In fact, if the downward trend in pharmaceutical technology activity in universities is to be reversed, the availability of funds to universities outside of NIPTE is critical. Unfortunately, NIPTE has yet to succeed. There have been partial successes, particularly with collaborations with the FDA, but we have yet to secure anywhere near the level of funding that is necessary to ensure the future of pharmaceutical technology:

What should a “core” curriculum in pharmaceutics consist of? In other words, what are the key components of a knowledge base that all pharmaceutics Ph.D.s should possess, irrespective of the university they choose?

This is a difficult question given the extreme diversity of what currently is called pharmaceutics. The focus of pharmaceutics in the distant past was “physical science” but has certainly changed over the years. Pharmaceutics today might mean biochemistry or molecular biology, might mean chemical engineering, or might mean the more classical materials science and physical chemistry of pharmaceutical dosage forms. The reality is that most pharmaceutics programs have moved away from physical science toward the biology of drug delivery; only a few institutions have maintained an emphasis on the physical sciences or engineering. Thus, I don’t think one can really define a “core” curriculum for pharmaceutics that recognizes the vastly different research directions in the units that call themselves pharmaceutics. I think one could attempt to define a “core” curriculum for those students headed for the typical industrial job, and that is indeed what NIPTE is trying to do. In my view, such a core would consist of: (1) applied statistics, (2) thermodynamics and materials science, (3) kinetics and stability, (4) transport phenomena, (5) processing of dosage forms, (6) biopharmaceutical principles:

Did you ever think you would see a Distinguished Professorship of Pharmaceutical Technology during your career?

No, certainly not. First, it is remarkable that Pfizer decided to provide the funds that established the endowed chair in pharmaceutical technology. This shows a commitment to academic pharmaceutical technology that is not common in the pharmaceutical industry. It should be common, and perhaps other companies will eventually follow the Pfizer lead. Secondly, I never expected that I would be honored by appointment to a Distinguished Professorship. You certainly don’t plan for such things, but I have been fortunate over the years, and I am grateful to Lilly and UConn for providing opportunities for the professional growth that ultimately resulted in this honor:

Who have been your most influential mentors throughout your career, and why?

The first very influential mentor was Kenneth Bronson, who was my high school math and science teacher. He was the one who developed my interest in science, and it was his encouragement that led me to the decision to major in chemistry. The second mentor who influenced me greatly was Mark Hughes, who was the chemistry professor at St. John’s (Minnesota) who taught what became my favorite subject in college, physical chemistry. He not only was a great teacher, but he provided sound advice regarding graduate school and career choices, and was the one who influenced me to attend Iowa State University and major in physical chemistry. He not only was a great teacher, but he provided sound advice regarding graduate school and career choices, and was the one who influenced me to attend Iowa State University and major in physical chemistry. At Iowa State, my major advisor, Frank Spedding, of course, had a significant influence on my development, but there were two other Professors, Bob Hansen in chemistry and Rolland Good in physics, that were outstanding teachers that I learned a great deal from. Bob Hansen taught thermodynamics, statistical thermodynamics (my favorite course), and surface chemistry. Rolland Good taught quantum physics, which was a course that really developed my quantitative skills. It was a difficult course, and I recall one day in class, in response to a complaint from one of the students that the material was difficult, he said: don’t worry, you
can’t expect to fully understand quantum physics until after the second time you have taught the course. That was the third time he taught the course. My post-doc mentor, Don Miller, also had a significant impact on my career. It was with Don that I developed an interest in non-equilibrium thermodynamics and an interest in an academic career, which I did pursue early at Tennessee and now later at UConn. Although not a mentor, I also need to acknowledge the impact of a friend, Sam Yalkowsky, in my early years in pharmaceutical science. I first met Sam at a Gordon Conference dealing with plastic crystals. Most of the conference attendees were physicists or physical chemists, and as I recall, Sam and I were the only ones from the pharmaceutical industry who attended. At the time, Sam was at Upjohn. Sort of in self-defense, Sam and I spent a fair amount of time together talking about science in the pharmaceutical industry, and thereafter for a number of years, Sam introduced me to the “movers and shakers” in pharmaceutics at the Academy of Pharmaceutical Science meetings. Through these contacts, I learned a great deal about the nature of pharmaceutics and got to meet most of the top scientists in the field.

COLLEAGUE AND FRIEND

Many of us look at Mike’s research productivity over the course of his career, and wonder what kind of performance-enhancing substances this fellow takes, and where we might be able to get some. What’s much closer to the truth, though, is that Mike is just in a different league than most of the rest of us. One of the many things we love about him is that he never makes us feel that way.