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ACADEMIC ROUTES TO WORKING WITH PHARMA

University **PROCESS DEVELOPMENT PROGRAMS** are a means to meeting academic and industry needs

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DRUG INDUSTRY MANAGERS often observe that nobody learns chemistry process development in school. Many managers say they simply look to hire graduates with solid backgrounds in science and good problem-solving skills. Once inside a company, new hires get the training they need and learn the ropes after being thrown into process chemistry and engineering work.

Some university researchers are seeing ways they can take on some of the educational role the pharmaceutical industry has subsumed. Doing so, they say, promises to remove the pressure of bringing new employees up to speed in companies already dealing with time and cost constraints.

At the same time, academic mentors hope that practical knowledge and relevant experience will put their students at an advantage in the job market. Teachers are taking different approaches, ranging from industry-sponsored, single-investigator projects to university/industry consortia to even more unique business-like models. And they are targeting students at different stages of their education.

At Rowan University, in Glassboro, N.J., all chemical engineering students must complete four semesters of junior/senior "clinic work." Because Rowan is primarily an undergraduate institution with a small master's degree program in engineering, almost all the research is done by college students. Modeled after medical school training, "the clinic model is a really good way to tackle projects, and we look for real-world problems," chemical engineering professor C. Stewart Slater says.

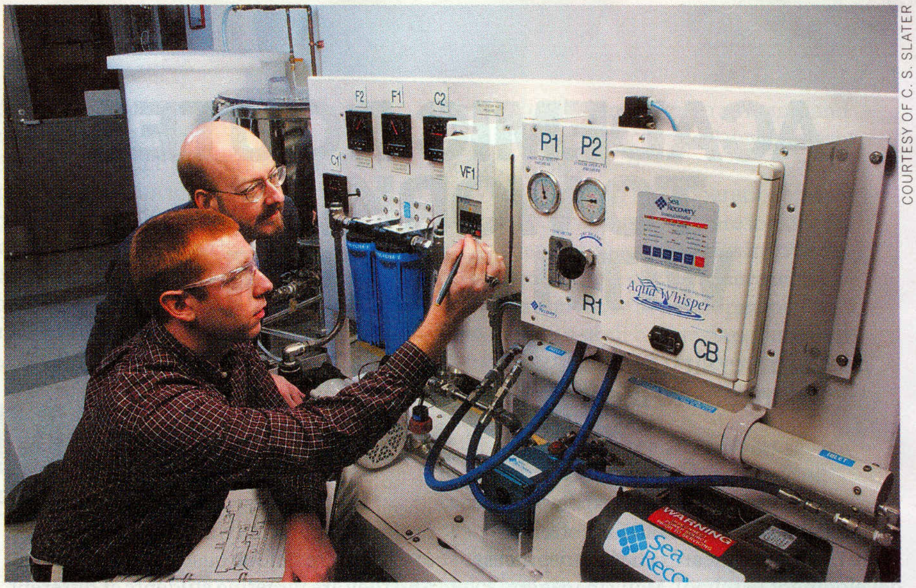
In recent years, Slater says, he and his Rowan colleagues have had great success interacting with Bristol-Myers Squibb (BMS), Pfizer, and Novartis. In addition to industry support, the Environmental Protection Agency has funded much of their work on greener processes for pharmaceutical production. In April, EPA Region 2 recognized Slater and Rowan colleague Mariano J. Savelski with an Environmental Quality Award for their clinic program and their dissemination of green engineering principles to the drug industry, to students in training, and to the international R&D community.

In 2005, the school's first project with BMS had students evaluating the process development of an oncology drug from discovery through pilot-scale production. They created a computer-based solvent selection table to enable more environmentally benign choices (*J. Environ. Sci. Health, Part A* 2007, *42*, 1595).

Work with Pfizer centered on an actual drug in large-scale manufacturing—the analgesic celecoxib, marketed as Celebrex—and looked at opportunities for solvent recovery at a plant in Puerto Rico. According to Slater, students interacted closely with the company's manufacturing, engineering, and plant groups. They were able to attend meetings and make presentations to company managers while learning about factors that influence industrial process work.

TODAY, as part of learning about process development, students are likely to be introduced to the related principles of green chemistry and green engineering. Because both are aimed at creating cost-efficient and cleaner processes, they are valued by industry managers (see page 13).

In the Pfizer project, Savelski says, "we used life-cycle assessment tools to ana-



COURTESY OF C. S. SLATER

GREEN ENGINEERING Rowan University's Slater (back) and student Joshua MacMillian work on a reverse-osmosis membrane process. [redacted]

lyze the feasibility of, and improvements possible through, alternative engineering technologies." The options included distillation, extraction, molecular-sieve adsorption, and membrane pervaporation.

For the work, a Rowan student team won the 12th Annual Green Chemistry & Engineering Conference student paper competition in 2008. Subsequently, membrane technology has been applied in another project with BMS. Meanwhile, a project with Novartis explored an adsorption process for catalyst removal.

"One of the things we look for is to expand the tool kit," says Stephan P. B. Taylor, a process director at BMS. The work with Rowan has been more about developing technologies that can be applied to many different projects. "We're also interested in helping the students get a feel for what life in industry is like," he adds.

The Rowan researchers have found the companies to be receptive to working with the university. "The pharmaceutical industry is really behind these types of initiatives, and that helps projects succeed," Slater says. "You can have all these great ideas, but if you don't have a champion for green chemistry or green engineering at a company, you are not going to get far."

At the University of Leeds, in England, the Institute of Process R&D (iPRD), which launched just over a year ago, works closely with industry to find relevant technical challenges and to prepare students through a master's degree program in chemical process R&D. More than a dozen Leeds faculty members from both the chemistry department and School of Process, Environment & Materials Engineering make up the institute's core team. Its first crop of seven M.Sc. students will graduate this fall, iPRD Director John Blacker says.

Because the students take both chemistry and engineering courses, "they are able to talk to both cohorts in companies," a skill that will prepare them for industrial jobs, says Leeds chemistry professor Christopher M. Rayner. Another high point of the program has been a series of lectures given by company representatives.

THE PARTICIPATING companies are mostly part of iPRD's industrial club, which includes about 12 small and large pharmaceutical and fine chemicals firms. The institute has been meeting with the companies to determine what problems they have in common that can be best tackled by leveraging resources within a consortium, Blacker explains. Companies may also initiate projects with individual investigators.

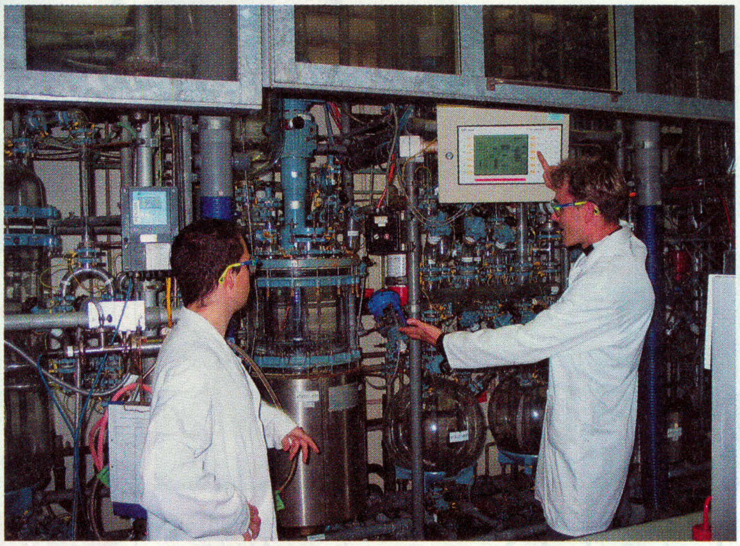
Many of the problems are the same ones identified by the Pharmaceutical Roundtable of the American Chemical Society's Green Chemistry Institute. "For example, we've got Ph.D. students working in the area of mild hydrogenations and two postdocs looking at alkylations using nongenotoxic materials," Blacker says. Willing to look outside the institute for expertise, iPRD is collaborating with University of Bath researchers in the alkylation work.

Despite the interest in the industrial club, both Blacker and Rayner noted how quickly company funding has declined in recent years. "But that has not stopped us doing what we want to do," Blacker says. "In fact, one consequence is that rather than putting cash into projects, companies are making in-kind contributions. That can be more valuable because it means they are committing their own people, and you get a much better interaction and collaboration."

In turn, Rayner points out, government funding has become even more important. Working with companies and other universities, iPRD has applied for two government grants totaling about $4.75 million to fund projects in controlled crystal growth and in catalyst recycling and recovery. And Rayner has a grant from the Wolfson Foundation, a U.K.-based charity, for a lab dedicated to carbon dioxide chemistry that will be built jointly with Leeds's engineering department and be affiliated with iPRD.

The institute also has funding from a regional development agency that will allow it to set up a process development lab. Included in the $12.5 million grant will be an analytical lab at the nearby University of Huddersfield. In return, the schools will help support small companies in the region. iPRD will use the lab for technology development, training, and small-scale contract manufacturing.

Contract manufacturing is the primary way that the Laboratory for Process Research (LPF) at the University of Zurich (UZH) supports itself. For more than a decade, UZH has had facilities capable of industrial-scale synthesis. It developed them with Cilag, part of Johnson & Johnson, to support current Good Manufacturing Practices (cGMP)-compliant production. The process chemistry firm Carbogen is also a UZH spin-off and predecessor of LPF. In 2003, the university assumed full control of LPF and recruited chemistry professor Jay S. Siegel to run it.



LPF/U OF ZURICH

IN-HOUSE PROCESS The Laboratory for Process Research at the University of Zurich has its own production plant.

[redacted]

LPF has two missions, Siegel says. It is a cGMP contract research provider certified by Swissmedic, the Swiss agency that authorizes and supervises therapeutic products, "but we also are dedicated to the training of postdocs in process chemistry research," he explains. Under contract with outside companies, LPF develops synthetic methods, conducts scale-up, and can prepare tens of kilograms of cGMP-quality material to support clinical testing. In addition to a core staff of about 12 across R&D, production, and analytical areas, the lab brings in a handful of postdocs every year—for a total of about 12 working at any one time—who spend two years at LPF before moving on to industrial jobs.

Over the past several years, about 25–30 postdocs have completed the program. "We're very much an academic institution in our dedication to developing human resources. You wouldn't normally have a business model where you are turning over your staff every few years if career development was not important," Siegel points out. "But we are not funded by the university or government at all, so we have to make this business model work."

This setup, Siegel says, makes the learning experience unique because trainees get to work on projects where they face real industrial concerns and deadlines. Another key aspect of their training comes from using LPF's facilities because few, if any, university labs maintain cGMP regulatory standards, he believes.

"Most people will tell you that when they entered the process lab, they had no idea what process chemistry was about," Siegel says. "They may have heard about it, but they certainly had never worked under conditions where the whole process is paramount." There is even talk with some companies about sending new hires to LPF for initial training and to work on projects of interest to the firms, he says.

DOCTORAL STUDENTS are not directly part of the LPF program because the lab must respect traditional business concerns. "We can't really put a graduate student into an environment where the Ph.D. information might be held as confidential," Siegel explains. Graduate students can, however, interact with LPF. "We offer seminars and exposure to process chemistry," he adds.

Although LPF is open to a diverse range of projects, for reasons of the complexity of the chemistry, regulatory issues, and patent positioning, it may choose some over others. For example, it has worked closely for many years with Cilag and with the Swiss generic drug firm AZAD Pharma.

"Although we have to be cost-effective, we are not trying to work margins to the extreme," Siegel says. "What we offer to a major company is that we are improving the human resource, generating intellectual property, and delivering product."

This attitude gives LPF a level of freedom in choosing projects that a highly competitive contract manufacturer may not enjoy. In addition, the number of projects LPF needs to run in any year is modest. "Our capacity is small, and it is not our intention to run a company that is going to have 200 employees someday," Siegel continues. "If we can produce several good-quality postdocs a year, then we are doing our mission."

Gary P. Pisano, a Harvard Business School professor who focuses on technology management, believes LPF is unusual in the scientific world. He says the closest academic analogy is the teaching hospital, which is associated with a medical school and brings in business, treats real patients, and trains doctors. "There's real money coming into the institution, and it should generate enough cash flow to maintain itself but not necessarily with the primary purpose of being profitable," he explains.

LPF intends to shift its business model soon, Siegel says. The plan is to form a holding company that will have an exclusive contract with UZH and will oversee LPF's commercial operations. Shares in this company will be held by a charitable foundation that will invest any surplus in furthering chemistry. Pisano will serve on the board, which will include former process chemistry company executives.

The new model is designed to avoid conflicts that arise when an academic institution runs a business by letting a third party handle legal, marketing, and other commercial details. Taking some of the business-related load off the researchers will also allow them to focus their expertise on chemistry and training, Pisano notes.

Where the boundary lies between university and business roles is a perennial issue. "In the past 20 to 30 years, those boundaries have blurred a lot," Pisano says. "It's important for industry in general to figure out ways to train people." The LPF model, he suggests, might be "interesting for U.S. universities to think about." ■