

CONSULTANCY

Use your skills

In many ways, Beat Widler was ideally placed to start a consultancy. He had spent decades in regulatory affairs and clinical research at Roche, the pharmaceutical firm based in Basel, Switzerland. Most recently, he was global head of clinical quality, ensuring that clinical trials protected human subjects and maintained data integrity. Now, he is a consultant in the same area.

Working out of his home in Zug, Switzerland, Widler takes advantage of a network of contacts in the pharmaceutical industry, contract-research organizations and regulatory agencies. Even so, setting up a company was risky. "If we are able to break even this year we can be extremely proud of ourselves," he says.

Widler had been thinking for years about starting a company. When Roche offered him an early-retirement package in 2011, he took the plunge, setting up Widler & Schiemann with former Roche colleague Peter Schiemann this year.

Widler says that the shifts in the industry are making it easier for former pharma employees to set up shop, as big companies and small biotechs turn to an outsourcing model with low overhead costs. And cost pressures are leading companies to rely on experts to help them trim the fat from their clinical trials, while keeping standards high.

Widler's network includes connections at professional organizations such as the European Forum for Good Clinical Practice in Brussels and the Drug Information Association, based in Horsham, Pennsylvania, where he has served on committees and given talks. That experience, he says, helped him to build his reputation and meet clients.

Without the infrastructure of a large organization, Widler has had to adapt. For example, he spent hours creating the template for a form for auditing a client. "You do everything from scratch. It's pretty intense, but it's pretty fun," he says.

He has no regrets and remains optimistic, but is mindful of how long his personal funds can last while he builds up his business. "Be very realistic about finances," he says. "It is critical to do your homework." **C.S.**

TURNING POINT

Jim Hoch

In April, Jim Hoch, a molecular biologist at the Scripps Research Institute in San Diego, California, celebrated the ninth renewal of the grant supporting his study of bacterial signalling proteins. Here, he reflects on how his efforts to unravel sporulation led to a three-decade US National Institutes of Health (NIH) grant — one of the longest-running at Scripps.

How did your research get started?

I came to Scripps after an NIH-funded postdoc at the Molecular Genetics Centre in Gif-sur-Yvette, France, where I learned about mapping genetics in bacteria. Once here, I applied the technique to begin to sort out the mechanisms that trigger sporulation, the process by which bacteria or fungi suspend their growth to form tough, seed-like spores. Since we started, my team and I have learned about the genes and proteins involved, but we are still piecing together how it works. The signalling mechanisms are a mess to unravel.

Was your first grant, to study the bacterium *Bacillus subtilis*, a turning point in your career?

I owe my career to this grant from the US National Institute of General Medical Science. I've been told that you should have several grants, but I had just one that I bundled everything into. If I had lost that grant at any renewal, I would have been dead. The renewal process is fairly traumatic, but it has motivated me to work hard each grant cycle. Because Scripps started hosting graduate students only recently, I have employed technicians, various undergraduates and some postdocs. And we managed to do pretty amazing things.

How have modern technologies influenced your research?

The evolution of technology has driven the experiments. I started with genetics, but molecular cloning and DNA sequencing changed everything — letting us find out about the proteins encoded by the genes. Using biochemistry, we could work out their functions. From there we used crystallography and nuclear magnetic resonance to establish the structure of the proteins. Most recently, we have been working with statistical physicists to determine how these proteins interact. Every year is a complete learning process — a quantum leap from one technology to the next. It has been a hell of a journey.

How have NIH requirements changed?

Proposals used to be more than 20 pages long, and the study sections that review grants lasted for three days. Now, proposals are 12 pages,



study sections last one day and half of the applications, the less-impressive ones, are not even discussed. There is a lesson here. Applications of 12 pages need to be clear and concise to make them understandable outside the field. Most importantly, they need to be exciting to read. A proposal needs to have clearly articulated goals that transmit your excitement.

Have you ever thought that your grant wouldn't get renewed?

It has become more difficult over the years; there is more competition. I was worried in the latest round. I broke my leg and was recovering for a year. Normally, I have five or six publications a year, so that every four years, when it is time for renewal, I have 20–25 papers showing my progress. I didn't have that this time, but I squeaked by with a few good papers in good journals.

Your career has been mostly in basic research. Have there been any interesting applications?

There have been some spin-offs. When I first came to Scripps, I was working on genes involved in the hyperproduction of proteolytic enzymes. One of my postdocs ended up as an executive at the biotechnology company Genentech, based in South San Francisco, California. He recognized that proteases could be important in the production of detergent. The proteases in most US soaps come from different species of *Bacillus*, and from some hyperproduction genes that we discovered. A company was spun off: Genencor, which is now owned by Dupont. It has produced more than US\$1 billion's worth of enzymes. ■

INTERVIEW BY VIRGINIA GEWIN