CONSULTANCY: THE TWO-WAY STREET

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One definition of consulting is "the exchange of views". Consulting in the pharmaceutical industry is a learning experience for both the statistician and the scientific client on the receiving end of the consult. For clients, there are opportunities to learn statistical principles and procedures to broaden their understanding of the interplay between the statistical method and the scientific method. For the statistician, there is the obvious scientific learning experience about the subject matter that is involved at the center of the consultancy. However, the statistical learning experience for the statistician is to find the balance between purity of mathematical statistics versus the flexibility required to achieve practical goals. Striking this balance is the quintessential dilemma of statistical consultancy.

The other element of statistical consulting that distinguishes industry practice versus academic pursuits is the need for the industrial consultant to be more of a generalist than a specialist. The diversity of problems and situations that present themselves to the pharmaceutical statistical consultant requires a breadth of exposure to statistical methodology and on-the-job training that may not be typical of other settings. This is both the challenge and the reward of statistical consulting in industry.

At Hoechst Marion Roussel, Inc., we are looking for candidates that possess the following skills:

a) an advanced degree - M.S. or Ph.D.;

b) good communication skills - both oral and written;

c) a general interest in science; and

d) a genuine willingness to work with others in a team environment.

We feel these characteristics are essential for a good consultant. In the ensuing sections of this paper, I will illustrate how we train statisticians along these lines and how such training impacts other scientists with whom the statistician interacts.

NEW STATISTICIANS

To start, I will discuss the assimilation of new graduates in to the Biometrics Department at Hoechst Marion Roussel. A question that is asked often is, "Do you want or require a candidate to have a degree in Biostatistics?" The answer is emphatically, "No!" There are as many associates in our Department with degrees in Statistics as there

are with degrees in Biostatistics or Biometrics. Furthermore, while most of the associates have degrees in these areas, we have recruited and interviewed candidates with degrees in Psychometrics, Mathematics and other technical disciplines. Our philosophy is to attract the best talent possible and let them become experts through on the job experience and training.

When new associates arrive on the job, we emphasize a training philosophy of "learn by doing." Immediately, new statisticians are given a project on which to work, most often under the guidance of a more senior project statistician, who then serves as a mentor to the new associate. The Department has collected a series of papers that we call "seminal papers", which are treatises or position papers on topics of importance to clinical trials for new chemical entities. A new statistician is expected to read these papers in the first six months on the job. Discussions may be held with the mentor or other experts in the Department. Other documents included with the seminal papers are the Food and Drug Administration "Guideline for the Format and Content of a New Drug Application" and the emerging International Conference on Harmonization - Efficacy Topic 9 Guideline entitled "Statistical Principles for Clinical Trials."

We do not have a formal program for initiating new hires on concepts related to consulting. We do make available a course based on the *book The Seven Habits of Highly Effective People* by Stephen Covey, in which concepts about goal setting, initiative, negotiation and teamwork are emphasized.

As stated in the Abstract, the primary challenge of the consulting statistician is to strike the appropriate balance between the purity of mathematical statistics and the constraints of practical applications or limited resources - both time and money. This lesson is best learned by observing directly the senior statisticians as they interact with all members on the project team. Projects involve scientists from many disciplines as well as regulatory personnel due to the complex and highly regulated environment that exists in the US and other developed nations of the world. Because the process of new drug development is complex and prolonged, it often takes several years for the new statisticians to mature into a role where they can take the lead on a project.

ONGOING DEVELOPMENT AND TRAINING

Since research and development are the heart of innovative drug development companies, it is widely recognized that all scientists in the company must stay abreast of their technical areas of expertise. At Hoechst Marion Roussel we are no different than most companies in that we have several approaches.

We bring in outside speakers, usually experts from academia, to teach short courses on specific technical topics. Such courses may last one to three days and generally involve everyone in the Department. Since Hoechst Marion Roussel is a global company, access to universities and professors spans the globe as does the attendance of Hoechst Marion Roussel associates at these courses. Some companies are now large enough to hold their own statistics conferences within the company as a forum to discuss technical topics as well as give the opportunity for the company statisticians around the world to present their ideas to a familiar audience. This is a particularly good training ground for newer statisticians to develop presentation skills as well as develop collaborative research efforts with colleagues.

We are also very interested in sending statisticians to various conferences and meetings throughout the world. We are deeply involved in the American Statistical Association, the Biometric Society and the Drug Information Association. This too is an opportunity for statisticians to attend short courses offered in conjunction with these annual conferences. As part of our ongoing effort to stay connected to academia, we also send Department members on campus visits to give technical talks, inform students about jobs in industry and to advise faculty on the training needs as we see them from an industrial perspective. Our company is also exploring a sabbatical program for scientist to spend time at an academic institution of their choice in order to refresh their technical skills. I believe such programs already exist at some companies. We are also very interested in having academicians spend a sabbatical in industry to understand better how to provide practical experiences and perspective in their courses.

THE EXCHANGE OF VIEWS

For those who have interests that span a variety of scientific fields, the consulting process in the pharmaceutical industry is both challenging and fascinating. For the statistician to be effective as a contributor to the project team, the statistician must gain an in-depth knowledge of the therapeutic areas or disease state under study by the project team. Much of this learning comes from one-on-one interactions with a clinical scientist

or within the project team. There are a wealth of other opportunities for statisticians to become fluent in the vernacular of the disease or therapeutic area related to their project team, including clinical conferences, investigator meetings or investigator site visits. Most find such opportunities challenging and enriching to their professional careers and make them valuable associates to Hoechst Marion Roussel.

It is less likely that clinical scientists or regulatory staff take an interest in biometrics such that they attend biometrics courses or conferences. However, on occasion a statistician may provide an internal course in basic statistics to a general audience. Where most of the statistical training is done, however, is in the routine interaction between statistician and clinical scientist on clinical trial design, the collaborative review of study results and the preparation of reports for company purposes or for Food and Drug Administration presentation. Most clinicians have a firm grasp of concepts dealing with power and sample size in a hypothesis testing framework, intent-to-treat analysis and issues surrounding multiplicity adjustments. Those who are more interested may gain an understanding of subtleties in trial design relating to factorial or crossover designs. Perhaps the greatest credit to statisticians as a whole in the pharmaceutical industry is that there is no question about the integral role that statisticians play in the clinical development of a new drug, especially in larger scale or confirmatory clinical trials.

Statisticians are also making headway in a variety of other areas in the pharmaceutical industry by consulting/training scientists in a variety of scientific fields. Certainly, some statisticians are well-known for their involvement in pharmacokinetics and pharmacodynamics. These fields involve substantial use of non-linear and physiologic models and are typically done early in the clinical development of a new drug. At the other end of the spectrum, some statisticians are exhibiting value by their contributions to the study of health economics, quality of life and epidemiology. These issues tend to arise later in the drug development process or even after the marketing of a new drug. Here there is interest beyond the activity of the new compound in a controlled setting. The interest is in how the drug makes a difference in the patient's life - economically or socially.

Beyond the scope of the individual controlled clinical trial to address specific scientific questions, many statisticians are now deeply involved in design of clinical development programs; that is, not only how to do a single study well, but how to design a sequence of studies and decision rules for how (or if) to proceed with a new chemical

entity in further development. Even now, there are more and more examples of statisticians leading multi-functional project teams through the drug development process. Such leadership requires skills that go far beyond statistical analysis, but certainly that leadership is derived in part from the logical and quantitative analysis training that is inherent in any advanced statistical program. Even beyond this arena, some pharmaceutical companies are supporting statisticians who are involved in the selection or decision-making process for what drugs to study in the whole portfolio of chemical entities that are produced in the research labs.

CONCLUSIONS

There are three general themes that I hope emerge from this paper - orientation, training and, most importantly, expanding the role of statistics in the pharmaceutical industry.

Orientation is the process by which we try to align our associates in terms of the baseline knowledge that they have regarding issues in the pharmaceutical industry. It is also the process we use to help new associates focus on the most important matters in those early months on the new job, which can be quite confusing and overwhelming.

Training is the way in which we protect our human investment. It is in the best interest of the associate, the Department and the Company to keep our associates well-trained to meet the challenges of the rapidly changing scientific arena. I heard an interesting exchange of comments between two managers regarding the costly investment of training associates. One manager said, “What if we spend all this time and money to train our people and they leave?” To which the other manager replied, “What if we do not train them and they stay?!”

Finally, I want to point out perhaps the greatest contribution of the consulting statistician in the pharmaceutical industry - that is the “evangelization” of other disciplines with regard to the utility of the statistical method. The process of integrating statistical principles from the preclinical laboratory to the marketplace through health economics has been a gradual and hard-fought battle. It did not come by saying that we as statisticians need better public relations. It did not come by claiming that statisticians inherently belong in these areas because of their skill in analyzing data or making decisions in the face of uncertainty. It came by working side-by-side with scientists and demonstrating the utility of the statistical method through success stories. I believe what

statisticians face within a pharmaceutical company is a microcosm of the marketplace - innovation and good products get rewarded. If consulting statisticians are unable to “sell” their methodologies or ideas to the scientists, then some self-examination may be warranted. Are the statisticians sufficiently flexible to meet the customer needs? Are the statisticians sufficiently involved enough to understand the science? In the end, did the statistical design or analysis lead to better decisions?

Clearly, there are many examples in today’s pharmaceutical companies where statisticians are playing key roles in a wide range of endeavors. It may be that through the successful consulting of many industrial statisticians, more education of scientific and business personnel is occurring than in all the classrooms of the universities that span the world. That’s a bold statement. In this regard, perhaps the two-way street of consulting could be viewed as the ultimate information highway.