Pharma Navigators Business Rationale

I have been frequently asked to discuss my adventures in the pharmaceutical industry with graduate and post doctoral students that are interested in a career in drug discovery and development. I tell them that a career in pharma is “not for the feint of heart” but that it can be a tremendously rewarding experience. I started as a non-degreed laboratory technician at Sterling Winthrop in 1972. Life has not been dull since. I now consult for various pharma and contract research organizations (CROs) on DMPK/bioanalytical and business development issues. A snap shot of the current state of the pharmaceutical industry, a seminal experience I had on a team developing a NSAID, and what I can provide to the new pharmaceutical industry is shown below.

The pharmaceutical environment:

The business model followed by the majority of companies developing pharmaceutical products has radically changed in the past 40 years. The model followed in the 1970’s was that of a monolithic “pharmaceutical house” that provided all the services needed to develop a new product or support an existing one. A company’s support needs were quite different then. But Federal regulations such as the GLP, the Waxman Hatch Act in 1984 (which established the modern system of generic drugs), and the globalization of pharmaceutical services radically altered the landscape of drug discovery and development. The model now is driven more by short term financial issues than long term scientific and production concerns. With the appearance of CROs that can offer quality services, many pharmaceutical managers consider maintaining an internal physical plant a financial liability. Acquisitions, RIFs (so-called “Reductions in Force”), and laboratory closings have been the norm.

The need for new pharmaceutical products has never been greater. The extent of global poverty is decreasing, increasing the demand for these products. Members of the OECD, a global community of rich nations, and the US, the largest pharmaceutical market in the world, have aging populations. Aging populations need more and newer drugs. Alzheimer’s, SARS like infections, and cancers of all kinds are still with us and preferentially attack the old among us.

Financial and medical success in this environment requires the discovery and development of robust products at a rapid rate. This will require bold but reasoned activity. The need for intelligent, well educated people and processes has radically increased. Speed is life.

The Celebrex Story

Celebrex and celebra were introduced in 1999 and rapidly became the most frequently prescribed new drugs in the United States. Sales in 2001 were $3.1B. Celebrex (celecoxib) inhibits the enzyme COX-2. Prostaglandins whose

synthesis involves the cyclooxygenase-I enzyme, or COX-1, are responsible for maintenance and protection of the gastrointestinal tract, while prostaglandins whose synthesis involves the cyclooxygenase-II enzyme, or COX-2, are responsible for inflammation and pain. Traditional COX inhibitors such as aspirin and ibuprofen inhibit both COX 1 and COX 2 enzymes. Prolonged administration of these agents frequently causes severe GI irritation.

The mouse COX-2 gene was cloned by UCLA scientist Dr. Harvey Herschman. The enzyme was discovered in 1988 by Daniel Simmons, a Brigham Young University researcher. The pharmaceutical company G.D. Searle patented celecoxib in 1995, received regulatory approval to market in December 31, 1998, and has a patent expiration (barring extensions) on May 30, 2014. The company, long since taken over by Pfizer, had 2009 sales of $1.4B.

The remarkable aspect of the development of this product was the amount of time from patent approval to marketing: 4 years. Although a 4 to 6 year development time and 2-4 major approvals per year were the major goals of the senior pharmaceutical managers of the time, celecoxib was one of the very few success stories. These goals are still elusive.

Bioanalytical Development Lessons from the Celebrex Program

Drug development in the 1990's required a broad range of disciplines. The range has only increased since then. At the heart of the development, a small team of cross trained scientists worked with internal resources and decided what work could be outsourced to CROs. Studies that could be run in parallel were so conducted. Turnaround times for projects were drastically reduced with stringent quality control. This was with the solid backing of the President of Searle Research and Development, Dr. Philip Needleman, himself a scientist. He and his team realized that every day that regulatory approval was delayed could mean a revenue loss of $3M for a $1B/year product.

The bioanalytical work needed for the pharmacokinetic study of celebrex was risky, expensive but effective. Samples were received (from another CRO), analyzed, and approved by the analytical CRO QAU. Data was sent to the client within 24 hours. Sometimes it was faster. The bioanalytical team leader was the scientist responsible for the project and served as the primary contact to Searle, eliminating most communication transfer issues. The team leader was also responsible for leading efforts of assay research, sample analysis production, business development, sample handling, report coordination and QAU connections. Research processes were refined and personnel from the research team made part of the sample analysis "production" team. Unique production processes were developed.

The primary lesson was that even with a relatively specialized activity such as bioanalysis, it is critical that staff have extensive scientific training and have a strong appreciation for production processes. A wide a range of cross training should be a requirement. This is also true for senior management, including business development. This allows “central points of control” that are small in number but are empowered and accountable, with full access to necessary resources and a full understanding of the drug development process.

What can I provide?

Some of the central issues the celebrex program illustrates are the need for investigator honesty, intelligence, experience, and broad training in the multiple disciplines of drug discovery and development. Communication is key. It is essential to be able to describe the needs of a drug development program not only to knowledgeable participants but also to well meaning but un-informed managers, administrators, business development personnel, and the public.

I have spent over 30 years in the drug development industry, roughly half in DMPK/bioanalytical laboratories and half in business development. I’ve been able to make bridges between the two for both pharmaceutical companies and for CROs. . I am looking for opportunities, large and small, to provide or aid a pivot point (the central point of control mentioned above) in drug development. A list of the services I can provide is below. Basically, I can

train scientific and business personnel,
design and coordinate discovery and development projects, and
represent CROs and Pharma in scientific, production, and regulatory discussions.

My goal is to provide a “win-win” environment for all the stakeholders in the drug development process.

Primary services:

1. consulting pharma and CRO companies on how to integrate disparate resources in non-clinical drug development and providing a pivot point between pharma and CRO operations, business development and the drug sponsor
    - identification and evaluation of service providers and consultants
    - coordination of resources
    - development team support
        - meeting attendance
            - in person
            - teleconference
            - internet chat
        - minutes and action plans
        - facilitate data base interpretation
            - research for relevant/missing information
    - study recommendations
2. providing strategic and tactical approaches in
    - discovery PK,
    - bioanalytical analysis,
    - in vivo and in vitro models
    - constraint based management (TOC)
3. documentation review
    - evaluation and interpretation of data
    - Bioanalytical and DMPK reports bound for regulatory submission
    - IND and NDA submissions
4. Presentations on DMPK, bioanalytical, and laboratory operation topics