What's Your Opinion?

2005 — A LOOK AHEAD

What are the most significant business challenges you believe the industry will face in 2005?

Tighter FDA scrutiny of new products in development

Regulatory guidelines for approved products are being confused with preapproval nonregulation of scientific information by major pharmaceutical MLR review committees. Big pharma purchasing departments are sacrificing the innovation and quality provided by boutique-service providers for low price and one-stop shopping provided by advertising conglomerates.

Bill Hahn
VP, Marketing and Business Development
Shaw Science Partners Inc.

ing of potential issues so that adverse events can be identified, characterized, and diagnosed sooner. In the next year, we will notice a greater emphasis on three key areas: better visibility of trial data; better electronic enablement, which allows for faster processing, analysis, and sharing of data; and more qualitative patient feedback. Statistics are great indicators of many things, but they are not a substitute for a patient's experience.

KOVAC. There are many challenges, such as privacy and confidentiality of genetic and other patient information, ethical issues surrounding the use of genetic information, and information overload because of the need to manage increasing volumes of research data and apply them to the clinical-development process effectively. With only one-third of clinical-trial data stored electronically, it is difficult, if not impossible, to share data during a trial. This scenario leads to duplicate data entry and errors. Scientists and clinicians are then unable to easily review data in areas such as patient safety (for example by data safety monitoring boards). By using EDC and breaking from the tradition of using paper documentation, technology will play a significant role in bringing about the organizational and process changes needed to create and maintain a more streamlined, automated, secure, and integrated clinical process. With technology in place, drugs also will be safer because of a revolutionized supply process, which will result in less counterfeit drugs and problems with expired drugs.

WILSON. The process we use to protect patients in clinical trials already is good and effective. The issue is, what happens to patients after the trials are complete and the product is brought to market? Product safety is an industry issue, and recent product withdrawals are bringing increased scrutiny on the industry from all quarters. And the greatest scrutiny is on the regulatory process before and after product approval. In 2005, I predict that we'll experience increasing pressure to improve postmarketing insights and to enhance our ability to ensure patient safety in the real-world setting. Our current challenge is that the very thing that increases internal validity of a clinical trial may jeopardize the ability to predict its impact postlaunch. We establish very tight inclusion/exclusion criteria to measure efficacy, but those criteria also limit our knowledge of the impact of comorbid conditions and concomitant medications. We need to evaluate products in broad-based, real-world settings where we can measure safety and product value and provide rapid feedback of this information to the manufacturer for improved decision-making and product positioning. I predict we'll see more such research taking place in the coming year.

W. THOMPSON. Patients are well-protected in trials. Problems occur upon initial marketing, when population information is sparse. Physicians and patients don't perceive that they are part of an extended clinical trial without the protections of the protocol safety features. There should be a three-light regulatory approval: red (not safe for anyone outside a formal trial); green (we know enough for general use); and yellow (patients can get but only with reporting of events and prescribed monitoring). Whether all physicians should be able to prescribe all drugs is another key safety issue.

▶ REGULATORY

HAMELIN. The departure of Dr. Mark McClellan as commissioner of the FDA is creating a leadership void for the time being. The last time we saw such a void at the FDA, before Dr. McClellan took the position, it took many months to fill the commissioner role and in that time the different divisions within the FDA became very introspective, requiring more clinical trials with significantly more patients in trials thus yielding slower product approvals. We now face the prospect of a slowing down of the FDA again, which has devastating effects on smaller pharmaceutical and biotech companies that are trying to get their first products to market. In addition to the leadership gap at the FDA, there is also the issue of uncertainty about who the next commissioner will be. Dr. McClellan worked aggressively to speed up product review timelines and set clear, strong leadership guidelines for reviewing products as quickly as possible within the bounds of guidelines and safety. If a new commissioner who is not as protechnology were to head up the FDA it would have huge long-term ramifications for the industry.

ASTRUE. Right now, we see the regulatory uncertainties created by the already long wait for a successor to FDA Commissioner Dr. McClellan as the biggest challenge. For example, the initiative to establish standards for follow-on biologics faltered after his departure, and the agency has been exceptionally cautious about guidelines for innovative technologies. We need a FDA commissioner who will push advisory committees to set standards for approval before companies invest years and tens of millions of dollars in clinical trials, not afterward. At TKT, we believe regulators need to work with industry and consumers to create clear standards for follow-on

biologics. We also believe that there is a reasonable middle ground between a mere showing of bioequivalence and the current practice of raising the bar for approval on second and third entrants to the market. Patients and taxpayers are losing billions as well as therapeutic choices because of inaction on this issue.

ZELDIS. The FDA has moved to a greater degree of working in partnership with industry. This is a very good trend and should be encouraged. By having a partnership and open

FDA ACTS TO STRENGTHEN THE SAFETY PROGRAM FOR MARKETED DRUGS

On Nov. 5, 2004, Acting FDA Commissioner Dr. Lester M. Crawford issued the following statement: Modern drugs provide unmistakable and significant health benefits, but experience has shown that the full magnitude of some potential risks have not always emerged during the mandatory clinical trials conducted before approval that evaluate these products for safety and effectiveness.

Occasionally, serious adverse effects are identified after approval either in postmarketing clinical trials or through spontaneous reporting of adverse events. FDA has a drug-safety program designed to assess adverse events identified after approval for all of the medical products it regulates.

"In this program, our clinical reviewers work with our epidemiologists to evaluate and respond to identified concerns," he says. "This is what occurred recently with antidepressants and Vioxx. Detecting, assessing, managing, and communicating the risks and benefits of prescription and over-the-counter drugs is a highly complex and demanding task. The FDA is determined to meet this challenge by employing cutting-edge science, transparent policy, and sound decisions based on the advice of the best experts in and out of the agency."

To this end, Dr. Lester authorized the Center for Drug Evaluation and Research (CDER) to take the following measures:

1 SPONSOR AN INSTITUTE OF MEDICINE (IOM) STUDY OF THE DRUG-SAFETY SYSTEM:

An IOM committee, under a FDA contract, will study the effectiveness of the U.S. drug safety system with emphasis on the postmarket phase and assess what additional steps could be taken to learn more about the side effects of drugs as they are actually used. The committee will examine the FDA's role within the healthcare delivery system and recommend measures to enhance the confidence of Americans in the safety and effectiveness of their drugs.

2 IMPLEMENT A PROGRAM FOR ADJUDICATING DIFFERENCES OF PROFESSIONAL OPINION:

CDER will formalize a program to provide an improved process to ensure that the opinions of scientific reviewers are incorporated into its decision-making process. In most cases, free and open discussion of scientific issues among review teams, and with supervisors, managers, and external advisors, leads to an agreed course of action. Sometimes, however, a consensus decision cannot be reached, and an employee may feel that his or her opinion was not adequately considered.

Such disagreements can have a potentially significant public-health impact, so CDER's program provides for a review of the involved differing professional opinions by the FDA and outside experts. An ad hoc panel, whose members were not directly involved in disputed decisions, will have 30 days to review all relevant materials and recommend to the center director an appropriate course of action.

3 APPOINT DIRECTOR, OFFICE OF DRUG SAFETY:

CDER will conduct a national search to fill the currently vacant position of Director of the Office of Drug Safety, which is responsible for overseeing the postmarketing safety program for all drugs. The center is seeking a candidate who is a nationally recognized drug-safety expert with knowledge of the basic science of drug development and surveillance and has a strong commitment to the protection of public health.

4 CONDUCT DRUG SAFETY/RISK MANAGEMENT CONSULTATIONS

In the coming year, CDER will conduct workshops and advisory committee meetings to discuss complex drug-safety and risk-management issues. These may include emerging concerns for products that are investigational or already marketed. Examples of input that might be sought include whether a particular safety concern alters the risk-to-benefit balance of a drug; whether the FDA should request a sponsor to conduct a particular type of study to further address an issue; what types of studies would best answer the question; whether a finding is unique to one product or seems to be a drug class effect; and whether a labeling change is warranted and, if so, what type, and how to otherwise facilitate careful and informed use of a drug.

These consultations will include experts from FDA, other federal agencies, academia, the pharmaceutical industry, and the healthcare community.

5 PUBLISH RISK-MANAGEMENT GUIDANCES

The FDA intends to publish final versions of three guidances that have been developed by the agency to help pharmaceutical firms manage risks involving drugs and biological products. These documents are premarketing guidances, covering risk assessment of pharmaceuticals before their marketing; RiskMAP Guidance, which deals with the development and use of risk-minimization action plans; and pharmacovigilance guidance, which discusses postmarketing risk assessment, good pharmacovigilance practices, and pharmacoepidemiologic assessment.

Note: These guidances, which were first issued as draft guidances in May 2004, are designed to assist manufacturers in the management and minimization of risks of pharmaceutical products throughout their life cycle.

Source: The Food and Drug Administration, Rockville, Md. For more information, visit fda.gov.

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What are the most significant business challenges you believe the industry will face in 2005?

Rising tide of negative perception

The biggest challenge I see the pharmaceutical industry facing in the next year is dealing with the rising tide of negative public perception. Healthcare and healthcare marketing, and more specifically, pharmaceuticals and pharmaceutical marketing, lay square in the center of the public ire. There will be less and less that we do over the next year, and in coming years, that won't somehow be influenced by this issue.

The influence it has on the way our clients will do business will be powerful, but it probably will be unspoken and will manifest itself in a new conservatism: more conservative claims, more conservative DTC campaigns, and more conservative spending. It appears that, in general, there will be a "hunkering down" while the public storm swirls around us.

On a personal and practical level, as an agency head concerned with staffing a growing company with the most talented people, it will become even harder to lure talent to an industry that already finds it difficult to attract and cultivate the best talent.

Pot shots at the pharmaceutical industry, companies, and the agencies that represent them, are now fair game at cocktail parties, within our children's school curriculum (as I learned one weekend over dinner), and in our places of worship. The issue has reached a cultural tipping point and will change the way we do business. This storm won't pass without leaving some trees uprooted. It will be a test to see how well we all handle these issues. It seems the best course would be to confront and address the real issues that do exist, while working to change the misperceptions, rather than just accepting them without a fight and allowing them to become cultural truths.

Ed Wise
President and CEO
Cline, Davis & Mann

communication, the public is benefitting, and will continue to benefit, from the development of new drugs. This is especially true in the pharmacogenomic arena where new ground is being explored. I would encourage the expansion of FDA staff via increased congressional funding to make sure that the agency has the resources to do its job. I would also encourage industry to prioritize its search for new products for serious disease states and for new first-in-class products.

BIAGGI. As a by-product of the Vioxx recall, the approval of new drugs is likely to become increasingly stringent, further delaying the introduction of NCEs. Industry's biggest challenge will be how to cope with a drying well and still maintain double-digit growth. The best we can expect is further streamlining of the generics approval process to respond to political pressures and provide lower-priced pharmaceuticals faster. Another important issue for the FDA is to create an approval pathway for biogenerics.

SCOZZIE. Some of the biggest regulatory hurdles companies face are the emergence of biotech generics and the lack of defined regulatory pathways for some new therapies, for example, cell therapies.

BONNEY. A big challenge is adapting to the ever-changing regulatory rules affecting how we operate. A more fundamental, and exciting, challenge is the identification of interesting compounds from both internal and external sources to build the pipeline.

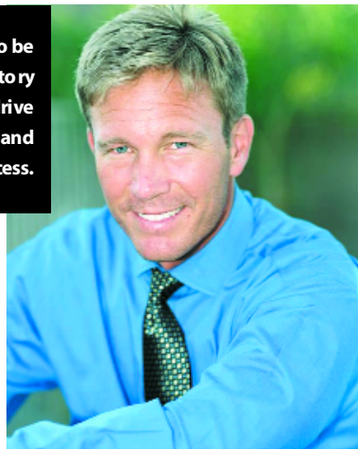
SAUNDERS. I believe that in 2005 we will start to see prosecutors shift their focus toward research and begin to look at the disclosure of clinical-trial information. In 2006 and 2007, research-related areas will be more in the cross hairs than the commercial areas. Safety reporting also will be an issue. GCP will become a hotter issue particularly as the clinical-trial directive in Europe matures. The key message is that CEOs have to be true believers in the importance of compliance, and business integrity is the key ingredient to a successful program.

SAVELLO. Both the European and the U.S. regulatory agencies are under scrutiny from their constituents and governments to do more in the area of drug surveillance and to do more to prevent unsafe medications from reaching the market. Even with the level of Western sophistication in monitoring adverse drug events, the population is becoming more and more risk averse. Therefore, it is extremely difficult to predict serious adverse events during drug development if there are rare events. But these very rare events are what much of the West is concerned about. There will be increasing pressure on regulatory agencies to better study serious adverse events thus slowing drug development and slowing the drug-review process and approval time.

FREIMAN. I believe that the subject of biogeneric drugs will be one of the larger tempests that regulatory authorities will face in the next few years.

ERICKSON. Despite FDA reform initiatives and efforts to "harmonize" regulatory processes, overall it seems that things do not get better for the industry. With tremendous innovation going on in areas such as target-specific therapies and multifactorial diagnostic technologies, including genomics and proteomics, old regulatory frameworks and guidelines will not work. A common problem in the diagnostics industry, for example, is that it is very hard

It is up to industry leaders to be aware of all the changing regulatory requirements. This will help drive efforts for a more uniform and transparent review process.



MICHAEL WILHELM
ImmuneRegen BioSciences Inc.

MICHAEL ASTRUE
Transkaryotic Therapies Inc.

We need a FDA commissioner who will push advisory committees to set standards for approval before companies invest years and tens of millions of dollars in clinical trials, not afterward.

The FDA is effectively increasing the hurdles companies must face to reach product approval by adding steps in the development process. While the information might prove useful, it will add years and significant costs to the development of new products.

DR. BRAD THOMPSON
Oncolytics Biotech Inc.

Companies need to avoid interference from certain authorities in the actual strategic positioning of a new drug through excessive control on protocol design.

to justify the cost of really innovative and large controlled clinical studies.

KOVAC. The requirements issued by the FDA for pharmaceutical and biotechnology companies to maintain formal records of specific transactions throughout the value chain will certainly become a sizable challenge in 2005 and years following. The FDA's plans to apply the doctrine of strict liability, under the Federal Food, Drugs and Cosmetics Act, as well as personal liability for CEOs and CFOs for compliance failure under the Sarbanes-Oxley Act are driving the transition to digital records management to better manage risk. Increasingly stringent regulatory requirements, patent infringement or patent interference suits, and product liability suits will stimulate the development and governance of digital record management systems that help companies comply with the regulations, protect their intellectual property, and limit their financial exposure.

W. LEVY. Harmonization of regulatory requirements should continue to be a top priority. Consistent requirements on a global basis will lower the cost of drug development. A rational policy must be developed for testing and approving products that are identical to existing products except that they are made using biotechnological processes. For too long, biotech products have been treated differently from products made by any other technology (the ANDA route is not available) and a policy must be established to deal with this issue. Also, continuing to streamline the approval process bears further attention.

REPUTATION ENHANCEMENT

AHN. The biopharmaceutical industry has blindly relied on the argument that high prices are needed because of increasing research and development costs. Focusing on innovation without discussing access is disingenuous. We risk alienating ourselves precisely when we have so much to contribute to the political and social debate. It is no coincidence that many polls rank the pharmaceutical industry as less trusted than the tobacco industry. We need to change the debate about biopharmaceutical innovation from a political football to a reasoned dialogue about two driving truths: one, as a society we possess an incessant drive for innovation leading to novel treatments based on emerging biological insights; and, two, we possess a deep desire for expanding access to medical treatments to all who need them. We need to separate the innovation issue from the access issue. By way of an example, as a society we don't ask our legislature to control the price of food; but as a society we ensure that anyone whose income is below the poverty line receives access through food stamps or other welfare services. It is time to seize the initiative and to be part of the solution on biopharmaceuticals. History shows that high-risk innovation is best conducted in the private sector and that the government is not good at choosing winners and losers in any industry. The biopharmaceutical industry should be leading the debate on the hard choices needed to ensure access to medicines in the developed and developing world.