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EXHIBIT 1, PART 3A

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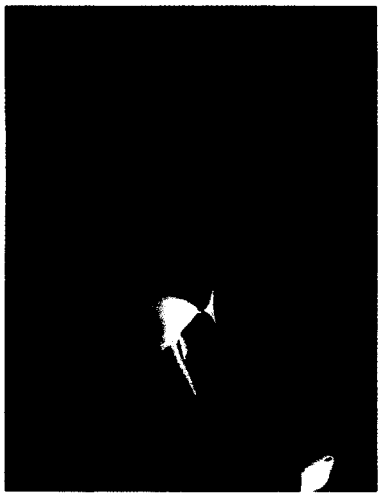

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Chairman:

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Keynote Presentation:

Metaworks, Inc

Elite Faculty:

Actelion Pharmaceuticals

Actelion Pharmaceuticals

Aris Global

Chesapeake Research Review, Inc.

Endo Pharmaceuticals

Endocrine & Metabolism Clinical Safety Director Global Clinical Safety and Pharmacovigilance GlaxoSmithKline Pharmaceuticals

Hogan and Hartson

Senior Scientist i3

Senior Scientist i3

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Pfizer Inc

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Co-Founder Sentrx

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Choose from Two Pre-Conference Workshops — Thursday, January 26, 2006

A. Establish and Sustain a Proactive Adverse Event Report Monitoring System

B. Assess Drug Safety and Performance with Enhanced Pharmaceutical Drug Registry Tools

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MANAGE ADVERSE EVENTS

Maintain FDA Compliance through Effective Collection, Reporting and Analysis of Pre and Post Marketing Drug Safety Information

January 26-27, 2006 • Doubletree Philadelphia • Philadelphia, PA

- Understand new documentation requirements for suspected adverse drug reactions (SADR)
- Establish systems to facilitate the collection and compilation of clinical safety data
- Streamline adverse event reporting (AER) by implementing data monitoring committees (DMCs)
- Value the responsibilities and powers of the drug safety monitoring board overseeing clinical trials
- Utilize dedicated review teams to analyze safety data related to individual products
- Recognize procedural approaches for submission to reduce confusion and complications
- Comply with the correct process of reporting to the Institutional Review Board (IRB) to streamline results
- Teach clinical trial investigators to properly use MedWatch and other regulatory submission systems
- Appreciate how evidence-based methods can improve the efficiency of the drug safety process from clinical development through pharmacovigilant activities
- Employ drug safety process improvements and enabling technologies to ensure safe clinical trials
- Develop practical methods for organizing the selection and evaluation processes for AER technologies
- Use MedDRA to promote consistency for encoding safety data

A. Establish and Sustain a Proactive Adverse Event Report Monitoring System

Understanding the importance of reporting related adverse events, pre- and post market, is imperative for the success of a drug and the company that supports it. A critical component of adverse event reporting (AER) is the system and or systems that manage all the information. Collecting, importing and retrieving adverse event data has to be a quick, efficient process since the number of adverse events reported to companies and authorities is growing simultaneously with the increasing number of drugs that are approved. Dependence on "spontaneous" reporting of adverse events in the post marketing period has been considered a deficient way of detecting potential signals of true adverse reactions that may affect the benefit/risk profile of a drug. There have also been many changes that may affect regulatory reporting found in the FDA's Proposed Rule of Safety Requirements for Human Drug and Biological Products (dubbed "TOME"). Due to these major issues, and many other areas of concern, companies have found it beneficial to implement a proactive adverse event report monitoring system to assist the adverse event reporting process and to have an efficient way of maintaining the data internally. This workshop reviews the history of the licensing of an orphan drug (**Tracleer®**) (**bosentan**) in Europe under exceptional circumstances and in the United States under Sub Part H, explaining the development of two very different post marketing surveillance programs, **TRAX PMS™** in the European Union and **T.A.P.** (Tracleer Access Program) in the United States. Different methods are contrasted for development time, efficiency, ease of administering, challenges and successes. Communication and cooperation with the health authorities while developing a pharmacovigilance program in a small biopharmaceutical company are highlighted, along with practical advice regarding development of Standard Operating Procedures (SOPs), working instructions and forms to meet all regulatory reporting requirements and internal risk management guidelines.

7:30 *Workshop Registration and Continental Breakfast*

8:30 *Workshop Leaders' Welcome and Opening Remarks*

I. Understand Necessary Components to Establish an Efficient, Proactive Adverse Event Monitoring System
- Define your company's need for a proactive adverse event monitoring system
- Positives and negatives of running an internal monitoring system – Is outsourcing possible?
- Decide which method or system is best for your company

II. Execute the Most Productive Monitoring Strategies for Proactive Reporting
- Educate clinical trial participants on suspected adverse event reactions (SADR) to ensure data quality
- Use the phone call method to monitor participants reactions
- Follow up with an organized written system
- Collect the data in person
- Explore monitoring technologies that can assist the proactive process

III. Ensure that Your System is Global
- Understand European Union (EU) reporting requirements, including the Clinical Trial Directive
- Learn how a web-based post marketing surveillance program can be utilized to answer clinical and regulatory questions in preparation for label expansion in a global market

12:00 *Close of Workshop A*

There will be a 30-minute networking and refreshment break at 10:00 am

— About Your Workshop Leaders —

Saundra Beacham is Director of Drug Safety Operations at **Actelion Pharmaceuticals**. Ms. Beacham started the Drug Safety Department in the South San Francisco office in 2001. Her responsibilities currently include managing operations of the collection of safety data, reporting and analysis for primarily post marketing products for the U.S., Canada and Asia Pacific region and creation and review of forms and templates used globally. She previously developed the Drug Safety department at **Chiron Corporation**, where she held a similar position and began her Drug Safety career at **Syntex Laboratories**. She has contributed to the development and design of several drug safety databases and was recently co-chair of the international user's group of a commercial safety database.

Eleanor S. Segal, M.D., is Vice President and Head of Global Drug Safety at **Actelion Pharmaceuticals**. Dr. Segal is a family physician and geriatrician who was a clinician/teacher for over 20 years before joining the pharmaceutical industry (**Syntex**) in 1991. A graduate of the University of Michigan Medical School, she is board-certified in family medicine, a Fellow of the American Academy of Family Practice, holds a Certificate of Added Qualifications in Geriatric Medicine and is a Clinical Professor at **Stanford University School of Medicine**. Before moving to Switzerland to join **Actelion** as Vice President and Head of Global Drug Safety, she was Senior Director of the joint departments of Drug Safety and Pharmacovigilance and Clinical Quality Assurance at **Chiron USA**, a consultant in pharmacovigilance for **Hoffman-La Roche** and head of Drug Safety and Quality Management for **Sequus Pharmaceuticals**. She has written a chapter on common medical problems of geriatric patients for the third edition of "Practical Gerontology" (Carstensen et al, 1996) and is particularly interested in the safety of pharmaceutical agents in the aging population.

B. Assess Drug Safety and Performance with Enhanced Pharmaceutical Drug Registry Tools

Drug safety is a highly visible issue for pharmaceutical companies, managed care organizations and other key stakeholders including the Food and Drug Administration (FDA), other government entities, physicians and consumers. During the last decade, the prescription drug approval period in the United States has been shortened and the number of drugs receiving approval has risen. Since 1986, twenty two drugs have been withdrawn from the market, yet only an estimated ten percent of all adverse drug reactions are reported to MedWatch. The U.S. market needs more robust public safety assessments of post-launch prescribed drug experiences. Claims-based drug registries can provide real-world information about new molecular entities (NMEs). The i3 Aperio drug registry leverages a proprietary database of de-identified health experiences from more than eleven million individuals and can help researchers identify signals that could indicate a drug's potential safety issues at a speed closer to real-time than previously available. This workshop helps attendees understand how to use drug registry tools to assess drug safety and performance. In addition, workshop attendees discover methods to ensure post market drug success and optimal drug development performance.

7:30 *Workshop Registration and Continental Breakfast*

8:30 *Workshop Leaders' Welcome and Opening Remark*

I. Drug Registry User Education
- Understand how drug experience registries work – What they can and cannot do
- Learn why drug registry tools can help identify safety signals sooner than before
- Realize the value of working with very large data cohorts that reflect real-world drug experiences in diverse patient populations
- Appreciate the value of comparator drugs for parallel analysis

II. Identify Other Potential Uses for Drug Registry Tools
- Hear how pharmaceutical companies can mine the data to seek safety signals in their own products
- Attribute post market performance success to drug registry tools

III. Derive Maximum Value from Registry Information
- Leverage faster access to drug safety information
- Perform meaningful analysis of drug safety information to optimize future drug performance

12:00 *Close of Workshop B*

There will be a 30-minute networking and refreshment break at 10:00 am.

— About Your Workshop Leaders —

K. Arnold Chan, M.D., Sc.D. is Senior Scientist at i3. Dr. Chan directs i3 Aperio™, which tracks newly approved prescription drugs in real-world use to provide stakeholders information on potential safety issues. In that role, he provides medical oversight and insight and oversees i3's research and the reports generated. Dr. Chan is a pharmacoepidemiologist whose research has focused on drug, device and vaccine safety, utilization and efficacy — in particular, studying them through large, linked automated health care databases. Prior to joining i3, he was director of the pharmacoepidemiology program at the **Harvard School of Public Health** and an associate professor in the Department of Epidemiology. He served as assistant director of epidemiology and statistics at **Ciba-Geigy Corporation** and on several committees, at the National Institutes of Health, the International Society for Pharmacoepidemiology and the Bureau of Pharmaceutical Affairs in Taiwan's Department of Health. Dr. Chan was elected Fellow of the International Society of Pharmacoepidemiology in 2003 and has received numerous international honors for his work; more than 40 of his articles have been published in peer reviewed journals.

John Seegar, Pharm.D., Dr.PH. is a Senior Scientist at i3. Dr. Seeger is one of the architects of i3 Aperio™, which tracks newly approved prescription drugs in real-world use to provide stakeholders information about potential safety issues. A pharmacoepidemiologist whose research has focused on predicting which drug therapies physicians will prescribe to specific patients, Dr. Seeger has worked extensively with propensity scoring, a mathematical method used to create models that aid those predications. He teaches a course on propensity scores at **Harvard School of Public Health** and has applied this method to longitudinal research involving rheumatologic, cardiovascular, neurologic, and gastrointestinal disorders. Dr. Seeger also serves on the faculty of the **Massachusetts College of Pharmacy and Health Science** and was a clinical assistant professor at the **University of Illinois at Chicago College of Pharmacy**. He has presented extensively at national and international conferences, and has numerous publications in peer reviewed journals.

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MAIN CONFERENCE

Day One — Thursday, January 26, 2006

12:00 *Main Conference Registration*

1:15 *Chairman's Welcome and Opening Remarks*
Ronald S. Waife, President, **Waife & Associates, Inc.**

Explore Processes to Ensure Clinical Trial Safety

1:30 **Understand the New Documentation Requirements for Suspected Adverse Drug Reactions (SADR)**
Current FDA adverse event reporting requirements mandate a monitoring system. With the amount of recent product recalls, the mandatory product guidelines set for product success must be closely followed. Recent changes to the regulations and guidances of AER require a clear understanding and increased diligence to ensure the guidelines are met. Both, pre and post market clinical employees need to understand the importance of the new documentation requirements and be able to prepare for FDA requests for compliance which can equal optimal clinical trial performance. This session outlines key changes to AER and teaches how to effectively manage SADR.
- Understand new requirements and comply effectively
- Learn the possible effects your clinical trial could encounter due to new FDA regulations
- Explore innovative and integrated approaches to communicate and prepare for the newest FDA regulations
- Ensure success and compliance simultaneously to enhance clinical trial performance

Jane Bultena, Partner, **Hogan and Hartson**

2:15 **Streamline Adverse Event Reporting with Data Monitoring Committees (DMCs)**
According to the FDA, the critical point in data safety monitoring is the level and type of risk that the participants could potentially be subject to. All studies need some type of safety monitoring as part of their good clinical practice (GCP) such as a DMC. DMC size (commonly three to eight people) and origin is an important decision, which reflects on clinical performance and outcome. This session provides benefits for each type of DMC and helps attendees decide which best fits their company's needs.

Case Study
- Recognize the work involved with independent DMCs and how they can help with AER
- Learn the advantages and disadvantages of AER and industry sponsored DMCs
- Explore investigator sponsored DMCs

John C. Campbell, Associate Director of Medical Affairs,
Endo Pharmaceuticals

3:00 *Networking and Refreshment Break*

3:30 **Comply with the Institutional Review Board (IRB) When Reporting Adverse Events to Streamline Results**
Submitting AERs to an IRB is a necessary function of the current human subject protection oversight system. The vagueness of Federal Regulations and Guidance about the IRB's role in reviewing AERs has led to confusion for pharmaceutical companies and their investigators. IRBs set their own policies and procedures to handle AERs, compounding the confusion and possibly introducing inconsistencies between individual IRBs. This session is designed to provide a foundation of current best practices regarding AER review by IRBs, to explain the variability in the present system and education about initiatives to institute reforms.
- Understand procedural approaches for submission to reduce confusion and complications
- Explore initiatives to streamline submissions, review and feedback
- Delineate investigator responsibilities and sponsor responsibilities
- Implement strategies to control the volume of meaningless reports, by defining AERs at study initiation

Jeff Trunzo, Vice President of Business Development,
Chesapeake Research Review, Inc.

4:15 **Drug Safety Process Improvement for Clinical Investigators**
Investigators have been known to report related and unrelated events due to the lack of education and potential pressures from the media. Clinical trial investigators are responsible for reporting adverse events, however, pharmaceutical companies are responsible for their drug's post marketed adverse events and must be proactive in educating their clinical trial investigators to ensure accurate safety reporting. In this session, learn the steps needed to protect your company, while educating clinical trial investigators to properly and efficiently report adverse events.
- Educate investigators of the need to determine seriousness, expectedness and causality
- Inform investigators of their continuing responsibilities
- Teach clinical trial investigators to properly use MedWatch and other regulatory submissions
- Use effective active inquiry methods to facilitate capture of critical information

Stanely Garbus, Chief Medical Officer and Co-Founder, **Sentrx**

5:00 **Discuss FDA's Update on Reporting Pre and Post Market Adverse Events and Drug Safety**
PANEL
This panel updates attendees on the upcoming FDA's advances and their effects on reporting drug safety information and adverse events. Clinical trials involve an immense amount of work that must comply with FDA standards and regulations, which are always changing and difficult to keep track of. This panel allows members from different areas of the industry to talk about the impact of the FDAs new guidances and the requirements that are going to be implemented on the clinical trial industry.
- Understand the drug safety monitoring board responsibilities and powers
- Recognize the changes to "Tome," the substance of FDA's risk management guidance and their effects on drug development
- Hear updated findings from the Institute of Medicine (IOM) committee on drug safety
- Learn about the new Drug Watch Website
- Reap the benefits of MedDRA
- Explore the MedWatch system and the progress it can make with drug development
- Discover information about federal and state clinical trial registry obligations

Moderator: Christina M. Markus, Partner, **King & Spalding LLP**
Panelists: Mark Lowdon, Director of Regulatory Affairs, **Aris Global**
Jane Bultena, Partner, **Hogan and Hartson**
Neha Sheth, Director of Risk Management Safety, **Pfizer Inc**
David Lilienfeld, Senior Director of Health and Drug Safety,
Protein Design Labs, Inc.
Stanely Garbus, Chief Medical Officer and Co-Founder, **Sentrx**
Sheryl F. Kelsey, Ph.D., Professor of Epidemiology,
University of Pittsburgh

5:45 *Close of Day One*

5:45-6:45 ***Networking, Wine & Cheese Reception***
Join colleagues and friends in a relaxed setting

Day Two — Friday, January 27, 2006

7:30 *Continental Breakfast*

8:00 *Chairman's Review of Day One*
Ronald S. Waife, President, **Waife & Associates, Inc.**

Understand Post-Market Adverse Event Reporting Systems

KEYNOTE PRESENTATION

8:15 **Use Evidence-Based Methods for Successful Post Marketing Drug Safety**
Risk management has become an integral part of clinical drug development and post-launch activities and as a result companies, consumers, regulatory and others have become increasingly aware of drugs and their safety issues. Drug safety "signals" appear throughout drug development. The earlier potential safety issues are identified and the more they are examined in an epidemiological manner, the higher the likelihood that real safety issues can be addressed and false signals can be understood. Evidence-based approaches to drug safety can help to optimize drug safety identification, categorization and response during development and post-launch.
- Understand how evidence-based methods can improve the efficiency of the entire drug safety process
- Learn how pharmacoepidemiology practices can help identify, educate and respond to safety signals
- Explore the factors that are important in understanding and clarifying "true" safety issues from "false signals"

Matthew W. Reynolds, Ph.D., Senior Director of Risk Management and Safety Services, **Metaworks, Inc**

9:00 **Safety Data Analysis and Reporting — Data-Mining and Next Generation Methodology for Drug Risk Assessment and Safety Research**
In its efforts to continue to serve the public health and protect public safety, the pharmaceutical industry is now challenged to set up sound pharmacovigilance plans that carefully analyze and report on pre-marketing clinical study data, minimize risk and monitor post-marketing safety. These plans include the statistical analysis and reporting of adverse events in clinical studies and the analysis of adverse event data such as FDA AERS for signal detection and risk management. This presentation includes a review of statistical analysis, reporting and data mining of clinical/safety data by way of several case studies involving clinical trial and AERS data. The case studies include statistical modeling methods such as hierarchical Bayesian models, neural nets, tree ensembles and logistic regression. The data analyses and reporting examples feature the use of S-PLUS, a highly flexible statistical workbench environment that enables advanced statistical analysis and reporting including interactive patient/subject profiling and standardized reporting.

Case Studies
- Create a post marketing plan for drug safety
- Understand the importance of using MedWatch to report adverse events
- Learn new statistical modeling, data analysis and reporting methods

Michael O'Connell, Ph.D., Director of Life Science Solutions,
Insightful Corporation

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Exhibit 1, Part 3B

9:45 *Networking and Refreshment Break*

Automate and Manage Drug Safety Reporting through Technology and Management Processes

10:15 **Employ Drug Safety Process Improvement and Enabling Technologies**

Pharmaceutical companies are facing an increasing multitude of demands on drug safety functions from many different aspects commercial, political and medical. While technology has always assisted in drug safety, even this component is changing significantly, as all vendors move from client server to web-based applications. All of this places enormous pressure on the efficiency and effectiveness of drug safety operations in pharmaceutical companies. This presentation reviews the strategic and tactical operational implications of the rapid changes in the clinical drug safety and pharmacovigilance profession along with its enabling technical tools.

- Examine and improve pharmacovigilance workflows, dataflows, roles and responsibilities, staffing resource efficiencies and departmental governance
- Identify inefficiencies and root causes common to pharmacovigilance operations
- Understand why companies are under-utilizing the tools they already have in place that could help them be more productive
- Explore new technologies that create a myriad of business rule decisions that can and must be considered for maximum investment value
- Learn practical methods for organizing the selection and evaluation process for technologies which assist in adverse event tracking and reporting, signal detection and trend analysis

Ronald S. Waife, President **Waife & Associates, Inc.**

11:00 **Interface Between Automated Systems and Humans in Signal Detection and Management**

Safety databases are growing tremendously with the accumulation of both pre and post market safety information. Organizing the information using one of the many new outstanding technologies seems the easiest method. However, there is also a need to analyze the data in a proactive way in order to optimize the way in which the benefit-risk profile of the product can be assessed. This session explores some of the methods of collecting and analyzing safety data with the view to enhancing signal detection and risk management during the life cycle of drugs in a user friendly manner for easier adoption.

- Learn how to use dedicated review teams to analyze safety data related to individual products
- Establish systems to facilitate the collection and compilation of safety data at different stages of the drug cycle (for both pre marketing and post marketing stages of drug development)

Suzette Y. Oxer, M.D., Ph.D., Endocrine & Metabolism Clinical Safety Director, Global Clinical Safety and Pharmacovigilance. **GlaxoSmithKline Pharmaceuticals**

11:45 **Explore the Benefits of AER Clinical Trial Data Management Technologies**

Pharmaceutical companies are trying to expand the number of clinical trials per each drug to streamline the production process, especially since the high number of adverse events has been slowing down the time to market. The amount of data is growing at a fast pace and it is important for pharmaceutical companies to properly house this data. When pharmaceutical companies can easily access the data needed, clinical trial timelines can accelerate and products are created to be efficient for the market. This session educates attendees on the importance of adverse event data and innovative ways for storage and access.

- Learn how data warehousing can accelerate decision making in clinical trials
- Explore the benefits and opportunities associated with data mining
- Evaluate and enhance safety data quality
- Understand the differences between all methods and which is the best fit for you

Alan Hochburg, Vice President of Research, **ProSanos Corporation**

12:30 *Networking Luncheon*

1:45 **Adopt Electronic Administration for AER to Support Standardized Administration**

Each day a new type of technology is introduced to the world and there is the choice to adopt or not. Members of the pharmaceutical industry are always leveraging their technologies to keep up and hopefully get ahead in creating the next high quality drug. As pharmaceutical companies adopt these technologies and start using them for adverse event reporting processes it can also increase the speed of standardized administration.

- Understand the importance of standardized administration with AER
- Explore projected results of standardized administration
- AER technologies that can speed up the revolution

Mark Lowdon, Director of Regulatory Affairs, **Aris Global**

2:30 **Use MedDRA® as Your Drug Development Assistant Pre and Post Market**

MedDRA® (the Medical Dictionary for Regulatory Activities) is an International Conference of Harmonization (ICH) standard for medical terminology used for pre and post marketing safety data reporting analysis. Major global regulatory authorities have adopted MedDRA, including the U.S. The FDA has already implemented MedDRA within its AERS database. MedDRA is a useful tool for safety data coding and analysis since it has many features that were lacking in some of the previously used technologies, such as specificity of terms, a broad scope, a medically logical hierarchy to group related concepts and data retrieval options such as Standardized MedDRA Queries (SMQs). This session shows prospective and current users how to leverage MedDRA in the assessment of safety data collected during pre and post marketing phases.

- Use MedDRA to support clinical studies and harmonize coding across the enterprise
- Understand how MedDRA promotes consistency for encoding safety data when used with proper coding conventions
- Learn approaches for using MedDRA in an assessment of coded safety data

Patricia Mozzicato, M.D., Medical Officer USA. **MedDRA Maintenance and Support Services Organization (MSSO)/Northrop Grumman Corporation**

3:15 *Close of Conference*

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MANAGE ADVERSE EVENTS

Maintain FDA Compliance through Effective Collection, Reporting and Analysis of Pre and Post Marketing Drug Safety Information

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Critical Take-Aways of this Event

- Understand the Importance of the Unified Education on Pre and Post Market Drug Safety Information
- Learn About New FDA Documentations and Regulations (such as Tome) from Top Compliant Organizations
- Know How to Leverage AER Technologies and Management Processes within Your Company for Optimal Clinical Outcomes

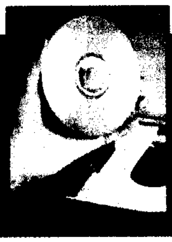
Features of this Event Include

- Case studies and Presentations from Leading Organizations in the Pharmaceutical Industry on Data Monitoring Committees, Signal Detection, Collection of Safety Data and more!
- A Presentation Directly from the MedDRA Organization about their Role in the Safety of Drugs

Choose from Two Pre-Conference Workshops — Thursday, January 26, 2006

A Establish and Sustain a Proactive Adverse Event Report Monitoring System
B Assessing Drug Safety and Performance with Enhanced Pharmaceutical Drug Registry Tools

CD-Rom Compendiums



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The firm also announced that it has established an "internal high-level team...that is dedicated to assessing the ability of other companies and partners to either produce or provide capabilities in Tamiflu production."

The Administration's plan also includes efforts to "develop new technologies that will allow us to produce new vaccines rapidly."

To that end, the plan would earmark $2.8 bil. for development of cell culture-based vaccines, which HHS has said could allow for faster vaccine manufacturing ("The Pink Sheet" April 4, 2005, p. 29).

Another aspect of the plan would be to provide liability protections for vaccine manufacturers. The request is noteworthy because the existing Vaccine Injury Compensation Program is often held up by industry as a good model for how to handle other kinds of medical liability cases ("The Pink Sheet" May 30, 2005, p. 10).

Also under the HHS plan, FDA would assume additional activities beyond its current regulatory scope.

For instance, the agency would evaluate "long-term stability of stockpiled antiviral drugs for purposes of shelf life extension."

The plan also highlights some mandates that FDA currently performs that would be more important during a pandemic, such as monitoring "to protect against the distribution of counterfeit antiviral drugs and pandemic vaccines."

The National Institutes of Health, meanwhile, would develop and evaluate "novel influenza vaccines and vaccination strategies (e.g., adjuvants, delivery systems)" and evaluate "the molecular and/or environmental factors that influence the transmission of influenza viruses, including drug-resistant strains."

NIH is also tasked with maintaining "close communication with drug and vaccine manufacturers."

The Centers for Disease Control & Prevention will coordinate antiviral delivery from the National Strategic Stockpile and monitor "antiviral drug use, effectiveness, safety and resistance" as well as vaccine effectiveness. ♦♦

Complex Indications For Drugs Have Lengthened Development Time – Tufts

Increased complexity of therapeutic indications is one factor contributing to longer clinical development times for drugs, according to Tufts Center for the Study of Drug Development Director Kenneth Kaitin.

In a study appearing in the November/December issue of the center's *Impact Report*, Tufts found that the average clinical development time for drugs increased from a low of 5.8 years in 1999-2001 to 7.0 years over the 2002-2004 time period.

Companies are seeking "indications where a patient gets their medications over longer periods of time and the indications are more complex," Kaitin said in an interview with *"The Pink Sheet."*

Kaitin said that clinical development time is also being affected by the requirement of many third party payors, including European health agencies, that manufacturers perform cost-effectiveness studies.

In addition, regulatory burden, increased trial sizes and recruitment difficulties have led to longer clinical development times, Kaitin said.

The Tufts report breaks out standard new chemical entities versus priority NCEs and concludes that clinical development time for priority NCEs are the longest they have been since the enactment of the Prescription Drug User Fee Act in 1992.

Tufts also found that the average approval time for priority drugs increased from 0.9 years in 1999-2001 to 1.2 years in 2002-2004.

Increased review times for priority NCEs may be due to the recent focus on drug safety problems, despite FDA denials that the agency has become more risk averse, Kaitin said.

"It's hard to imagine that...the individual reviewers within the agency aren't more concerned about safety issues and as a result are being more cautious in their drug reviews, which is tending towards requesting more data and extension of the overall approval time," Kaitin said.

Clinical development and review times vary by therapeutic area, Tufts found. For the 2002-2004 time period, the average total clinical and approval time for neuropharmacologic drugs (12.6 years) was double that for cardiovascular drugs (6.3 years). ♦♦

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Schering Seeks Salvation In External Deals; Hassan Outlines Licensing Plan

The solution to the "innovation threat" facing big pharma lies in making deals outside the company, Schering-Plough CEO Fred Hassan said during an R&D update Nov. 1.

"Our philosophy is that about half of our pipeline and portfolio should come from other people's labs," the exec stated. "I can tell you today we are in deal mode."

"Our industry faces a serious innovation threat," Hassan asserted, "what I would call the post-*Vioxx* innovation threat."

Merck's withdrawal of its COX-2 inhibitor due to cardiovascular risk more than five years after its approval and the ensuing liability issues have raised concerns that companies may take a more cautious approach towards development, avoiding newer products that have unknown safety profiles.

"Our industry faces a serious innovation threat...what I would call the post-Vioxx innovation threat," Hassan says.

"One critical impact is in the regulatory arena," Hassan maintained. "FDA drug safety advisories are on the rise, FDA black box warnings are multiplying, average approval times are lengthening," he cautioned.

"In the meantime, there are indications that our industry is in an R&D productivity slump. The low-hanging fruit has been harvested. Development hurdles and costs are increasing," Hassan stated. "We see escalating later date attrition rates. This later stage attrition is hugely costly."

In addition to the dwindling flow in big pharma R&D, pipelines have been clogged by increasing late-stage failures in recent years. The *Phase III* failure rate has reached about 50%, up from 20% 10 years ago.

Hassan acknowledged that Schering-Plough has "a reality of a late-stage pipeline gap."

As a result, he said, the company has adopted the approach of striving for a "balance between internal and external innovation – because we realize that no single team has a monopoly on innovation."

Schering is thus attempting to bolster its pipeline and portfolio through both internal development and acquisition of innovative products.

On the internal side, Schering has underway a "development excellence" program that emphasizes "cycle time reduction in all phases of clinical development," Exec VP-Global Development Thomas Koestler said.

"Our discovery engine has been very productive," he noted. "We have 14 new molecular entities rapidly approaching proof-of-concept, another eight that are in *Phase II* and four more that are [in]*Phase III* and registration" *(see following story)*.

"The number of compounds in full development we expect may grow by almost 40%," Koestler added.

In terms of in-house development, "we are now on the upswing and we project a significant increase as a result of new product candidates entering full development over the next few years," Koestler said.

Schering has bolstered its development team with several appointments and promotions this year. The company named an Aventis researcher, Susan Arbuck, as VP-global clinical development for oncology and a former Novartis exec, James McLeod, to the post of global VP-clinical development, early clinical research & experimental medicine.

The company also announced the promotion of two management execs to development posts: Koestler to the post of exec VP-global development and James MacDonald to exec VP-preclinical development.

Hassan detailed Schering's external efforts to build its portfolio during the R&D presentation – the company's first in two years – by outlining a series of licensing plans.

Schering's first focus is on technology alliances, then early-stage acquisitions and alliances and late-stage deals. The firm is also open to full product acquisitions and complete company buyouts, particularly if they offer access to late-stage projects.

Schering has already begun to step up its partnerships, putting into practice the licensing strategy outlined by Hassan. The company announced the signing of several technology alliances over the past year.

In August, Schering said it exercised its rights to develop and commercialize a fully human monoclonal antibody with Centocor; golimumab (CNTO 148) is in *Phase II* for the treatment of rheumatoid arthritis and other inflammatory diseases.

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