



## **Executive Summary of Proceedings: Inaugural DSEC Member Retreat (Summit)**

### ***“Confronting Major Safety Issues of the 21<sup>st</sup> Century.”***

#### **Program Overview**

On June 10-11, 2008 the Drug Safety Executive Council (DSEC) brought together leading safety experts from across the biopharmaceutical industry at the inaugural DSEC Member Retreat, “Confronting Major Safety Issues of the 21<sup>st</sup> Century.” The meeting was held at the Hyatt Regency at Penn’s Landing in Philadelphia, PA.

Summit participants included senior safety executives from a broad range of large biopharmaceutical companies, including Amgen, Astellas, AstraZeneca, Bayer Healthcare, Biogen Idec, Boehringer-Ingelheim, Genzyme, GlaxoSmithKline, Pfizer, Procter & Gamble, Roche, Shire, Takeda, UCB, and Wyeth. Also participating were numerous senior executives from other industry organizations with a vested interest in drug safety, including Baxter Healthcare, Cellumen, iCardiac, the National Institutes of Health (NIH), and the Critical Path Institute. The Summit agenda was crafted in close cooperation with the DSEC Advisory Board, led by Chairman Dr. Jack Reynolds, and including representatives from several of the large biopharmaceutical companies listed above, as well as Eli Lilly, F. Hoffman-La Roche, Johnson & Johnson, Sanofi-Aventis, and Schering-Plough.

The primary goal of the Summit was to explore strategies for evolving the drug safety assessment paradigm to enable improved and more confident decision-making and increased R&D productivity, within the context of the industry working collaboratively to overcome challenges too great for any single organization to address.

Over the course of the Summit, participants viewed presentations by their drug safety colleagues in which were shared perspectives and experiences in addressing drug safety challenges. After each pair of presentations the participants then rotated through a series of roundtable discussions in which they identified drug safety challenges of shared concern, prioritized those which if solved would most greatly contribute to improved R&D productivity, and debated collaborative strategies for overcoming those challenges.

#### **Key Themes Discussed During the Summit**

- ***A Call to Collective Action:*** Achieving the gains in drug safety assessment needed to realize this promise, however, is far beyond the means of any individual biopharmaceutical company working alone. Instead, the industry must work collaboratively to evaluate innovative safety assessment technologies, validate their optimal application, and obtain regulatory consent for their use. In this way each biopharmaceutical company can benefit from the collective experience—positive and negative—of the industry as a whole, leading more quickly to safer and more effective drugs and improved patient outcomes.
- ***Declining R&D Productivity:*** The biopharmaceutical industry’s productivity has declined over the last two decades despite a seven-fold increase in R&D spending. Many compounds are being lost in costly late-stage development and are directly linked to inadequate drug safety. Safety issues have also driven a number of highly successful drugs from the market, costing the industry billions of dollars in lost revenue and profoundly damaging public and regulatory goodwill.
- ***Evidence-Based Toxicology:*** Drug safety thought leaders are increasingly looking towards an evidence-based toxicology (EBT) approach to safety assessment. EBT is conceived as being substantially more quantitative than traditional drug safety assessment techniques, primarily through the validation and adoption of innovative safety assessment tools and methods. In addition, EBT seeks to optimize the interface between safety assessment and risk mitigation, comprehensively managing drug safety from early in the discovery process through the end of the drug’s life cycle.

- **Definitions of “Safe” Medicines:** Because no medically useful drug can be entirely free of risk, the industry needs to move away from its current unrealistic goal of *giving patients only absolutely safe drugs* to a more realistic paradigm in which the goal is to provide patients with only those *drugs that can be given with absolute safety*—in other words, drugs for which the risks are well characterized.
- **Better Learning from Late-stage Failures:** The biopharmaceutical industry has been reluctant to invest resources to understand why a prospective drug evidenced safety problems in late discovery or clinical development. Instead it has preferred to shift resources to projects perceived to have greater prospects for success. As a result, the industry does not “learn from its mistakes”, and squanders the opportunity to build an institutional knowledgebase of the causes of safety failures.
- **Need for Collaboration on Safety Issues:** Traditionally, the companies within the biopharmaceutical industry have been unwilling to work together, particularly because of the sensitivity of compound pipelines. From a practical standpoint, biopharmaceutical companies can no longer afford to work in isolation on safety concerns. A sharp decrease in productivity means that it is in the industry’s best interest to explore a collaborative approach. Patients have the right to expect that the industry will do all that is reasonably within its power to assure the safety of the drugs brought to market. In addition, the identification of a safety risk in a marketed drug harms not only that company that produces the drug but also the industry as a whole.
- **Successful Collaborative Models:** By working collaboratively, the biopharmaceutical industry can substantially improve R&D productivity. In recent months, the Predictive Safety Testing Consortium (PSTC)—a collaboration of several biopharmaceutical companies, academic research institutions, and both US and EU regulatory authorities—led a successful effort to identify, validate, and obtain regulatory approval of novel molecular biomarkers for kidney toxicity. A similar effort would have cost more and taken longer to complete without a collaborative strategy and may not have achieved regulatory acceptance.
- **Building the Case for Safety Assessment Investments:** Despite the economic cost to biopharmaceutical companies, many senior industry executives remain unconvinced that increasing the investment in safety assessment will improve productivity, patient welfare, or profitability. To overcome these objections industry’s drug safety leadership must clearly demonstrate that increased drug safety resources will lead to measurable “return-on-investment” (ROI). Industry leaders must present a robust business case for why moving towards a new drug safety assessment paradigm will lead to more productive pharmaceutical R&D, safer and more effective drugs, and greater revenues.
- **The Potential Impact of Better Safety Assessment:** The biopharmaceutical industry’s current growth rate in R&D spending is unsustainable, and even if the industry managed to freeze current R&D spending at its current level of \$1.35 billion per new compound brought to market, the results would be catastrophic. Given the current realities of competitive drug pricing and reimbursement, the industry must halve the resources required to bring a drug to market, to a level below \$700 million. Improved and innovative drug safety assessment can make a substantial contribution to this essential milestone, decreasing costly attrition both in clinical development and in drugs already on the market.

### **Recommendations and Next Steps**

The issues that emerged from the discussions and then were prioritized as most important for DSEC to take leadership on were:

1. DSEC leading objective evaluations of novel toxicology screens that have practical utility
2. DSEC leading participating member companies in the development of a blueprint that will enable eventual data sharing.
3. DSEC leading virtual roundtables between DSEC members and FDA representatives to discuss important and pressing issues facing industry and the agency
4. Building business case models demonstrating the ROI of investing in robust and innovative safety assessment capabilities

These priorities will shape the programming and initiatives for DSEC for the balance of 2008 and 2009. We hope to be able to discuss progress on each of these fronts at the 2009 Summit.

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