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PRESCRIPTION FOR THE FUTURE OF THE PHARMACEUTICAL INDUSTRY

TECHNOLOGY DRIVING CHANGE I N THE PHARMACEUTICAL INDUSTRY

Summary by Charles L.Cooney

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Technology Driving Change In Drug Discovery - Sinskey

- Changing drug discovery paradigm
  - New targets made available through genomics
  - New sources of chemical diversity
  - New technology for HTS (arrays, miniaturization, etc.)
- One must learn to integrate the genome-proteome-metabolome with new ways to management of knowledge and information

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Systematic Analysis of Cell Physiology - Sorger

- Data quality is critical to analysis of gene expression and protein response
- Metabolic Control Analysis provides a framework for data interpretation
  - Use genes as descriptors of physiology
  - Limitation in the quantity & quality of reagents - e.g. MCAs
  - Limitation in bioinformatics

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Systematic Analysis (cont.)

- Miniaturization of solid phase sensors
  - Cellular response
  - Immobilized highly specific reagents
  - Rapid analysis with mass spec
    - Metabolite release
    - Protein reagent interaction
    - Protein-protein interaction
  - Flexible format for reagent array and response detection

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Gene Expression Resolution, and Metrics for Microarrays - Goodwin

- Microarray spot analysis
  - Non-uniform
  - Expression can occur over >1000 fold
- Well defined and appropriate metrics enable improving the quantity and quality of data
- With sophisticated data analysis one can shorten cycle time in the discovery process
- Reduction in number of measurements enabling increased research productivity

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Measurements Techniques for Neurobiology, Memory and Learning - Wilson

- Analytical methods in neurobiology are complex
- Knock-out animals provide means to test specific molecular targets
- There is a need to understand integrated signaling
- Opportunity to probe rat dreams
- Model opens up means to evaluate therapeutic intervention

INNOVATION IN ANALYTICAL METHODS WITH ANIMAL MODELS OPENS UP NEW STRATEGIES FOR TARGET VALIDATION

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Diagnostics and Delivery in the 21st Century - Hunter

- **Microfabrication technology is enables the miniaturization of drug discovery**
  - **Cost per target falls with miniaturization**
  - **Can interface with many sensors**
  - **Microarrays for cell cultivation**
- **NanoWalker - a path to micromanufacturing and drug delivery**
  - **Enables observation and delivery at microscopic scale**
  - **Measure properties in one million compound array with NanoWalker**
  - **Allows one to bring the scientific instrument to the specimen with flexibility is task implementation**

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New Measurement Technologies in Human Trials - Rubin

- New paradigms needed for clinical evaluation
- There are strategic times for go/no go decisions
- Quality decisions require quality information
- One needs to measure where the action is
  - Link PK and PD & Establish dosimetry
- Clinical phenotyping is required - does patient fit profile?
- Future use of diagnostics enhance efficacy of disease management
- Genomics will be applied to define risk, plot a therapeutic path and avoid adverse reaction

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Profiting from Innovation in Pharmaceutical Manufacturing - Raju

- Manufacturing is central to making profits
- There are major opportunity for improvement
  - An analysis of cycle time in manufacturing illustrates that value time to total time is low
  - Process time drives expense
  - On-line analytical technology reduces development cycle time and process variability
- Application of simulation to evaluate change

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Profiting from Innovation (cont.)

- Current methods of learning are inefficient
- Product life cycle analysis
- Use performance measurements to assess both product and process development

Manufacturing offers an underutilized opportunity to enhance profitability

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Microreactioin Technology for Pharmaceutical Manufacturing - Jensen

- Microchemical systems for analysis and synthesis
- One can gain flexibility and speed in development
- Microsystems can be simulated easily
  - Scale-up - by parallel processing
  - Modular system, make standard reaction cards
  - Ease of integration of reaction, separation, analysis
- Personal chemistry devices
  - Diagnostics
  - Drug delivery
  - Environmental testing

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Microreaction Technology (cont.)

- Opportunities
  - Facilitate use of electrochemistry
  - Remove diffusion limitations
  - Application to multiphase reactions
  - Integration of reaction and separation
  - Synthesis of hazardous materials (Phosgene)
  - Can do reactions under high pressure
  - Interface with wide range of analytical techniques (UV, IR, fluorescent, etc)
  - Excellent control, scale by parallel processing
  - Can microfabricate with many materials

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Evaluation of Alternatives R&D Portfolio Management Strategies - Pindyck

- **As uncertainty increases, do more exploration and create options**
- **With uncertainty delay exercising the options**
- **Pharmaceutical company value is created by options**
  - **Their ability to invest in research opportunities that may meet future needs and make profitable drugs,**
  - **Their infrastructure to capture value from a discovery**
  - **Their IP associated with the options**

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Evaluation of Alternatives in R&D (cont.)

- **R&D is valued through the creation of option**
- **Most options will expire worthless, there is uncertainty and risk, but one invests since some will succeed**
- **Drug development is a compound option**
  - **Need means to evaluate optimal abandonment**
  - **There is additional value in sequential options**
- **How does one evaluate network externalities?**
  - **Should you be first in an area?**

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Quantitative Techniques for Evaluating Product Success in the Marketplace - Azoulay

- Advertising is important and science enhances advertising
- Trend to move from academic to commercial centers for clinical investigation
- Enhance learning from clinical trials
- What are the optimal ways to conduct clinical trials and learn?

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New Approaches to Evaluating Effectiveness of Pharmaceuticals - Cockburn

- Assess the impact of disease and treatment on patients in the workplace
- Metrics and data analysis are major challenge
- Methodology provides insight into assessing the benefit to cost ratio
- One can measure the impact of therapeutic intervention on patients in the workplace

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Meeting the 2010 Challenge

- Technology is a driver of change
- Analytical methods are central to enabling change
  - Discovery, development, clinic, manufacturing, R&D
- Miniaturization enhances exploration and creation of options
- New paradigms are essential for
  - Drug discovery and development
  - Clinical evaluation
  - manufacturing
  - Valuation of your options
- The industry needs to prepare and manage for change

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THANKS TO EVERYONE FOR THEIR PARTICIPATION IN THIS CONFERENCE

A COPY OF THIS SUMMARY WILL BE AVAILABLE ON THE WEB SITE FOR THE PROGRAM ON THE PHARMACEUTICAL INDUSTRY

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HAVE A SAVE JOURNEY HOME

THE JOY OF SUCCESS AS WE MEET THE 2010 CHALLENGE

McKinley, 20,300 ft
June 28, 1998