- This presentation should NOT be interpreted to imply or encourage inference that it reflects Guidance, Regulation or Statutes or the intent to develop such.
- The presentation and views expressed are not to be used as support for scientific, clinical or regulatory actions before FDA or any other regulatory agency.

"The Fantastic Voyage"



http://www.google.com/images



I was born in 1961.

I am at the age where I realize I need safe and effective medical products on the market soon. Policy Issues in Nanotechnology & Oncology: A View of Regulatory Science from CDRH

Jonathan Sackner-Bernstein, MD, FACC Associate Center Director, Post Market Operations Center for Devices and Radiological Health U.S. Food and Drug Administration

July 2010

The FDA's Mission Includes Advancing Public Health By Helping Speed Innovations

Potential Approaches for New Science

- Analytic Methods
- Collaboration Models
- Novel Technologies
- Education for Innovation

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Analytic Methods

- Bayesian Statistics
 - Decision Sciences

- Topologic Data Analysis
 - Seeing relationships

Topologic Data Analysis

- Patterns in data are encoded in geometry
- Exploit the natural geometry of complex data using priors such as density estimators, entropy, etc.
 - Allows discovery of patterns without formulating queries
 - Relationships can be evident visually
 - Large data sets can be managed readily

Understanding Relationships in Gene Expression

OPEN a ACCESS Freely available online

PLOS BIOLOGY

Mapping the Genetic Architecture of Gene Expression in Human Liver

Eric E. Schadt¹[®], Cliona Molony¹[®], Eugene Chudin¹[®], Ke Hao¹, Xia Yang¹, Pek Y. Lum¹, Andrew Kasarskis¹, Bin Zhang¹, Susanna Wang¹, Christine Suver¹, Jun Zhu¹, Joshua Millstein¹, Solveig Sieberts¹, John Lamb¹, Debraj GuhaThakurta¹, Jonathan Derry¹, John D. Storey^{1,2,3}, Iliana Avila-Campillo¹, Mark J. Kruger¹, Jason M. Johnson¹, Carol A. Rohl¹, Atila van Nas⁶, Margarete Mehrabian^{4,5}, Thomas A. Drake⁷, Aldons J. Lusis^{4,5,6}, Ryan C. Smith¹, F. Peter Guengerich^{8,9}, Stephen C. Strom¹⁰, Erin Schuetz¹¹, Thomas H. Rushmore¹², Roger Ulrich¹

Research

Systematic genetic and genomic analysis of cytochrome P450 enzyme activities in human liver

Xia Yang, ^{1,9,10,13} Bin Zhang, ^{1,9,10} Cliona Molony, ¹ Eugene Chudin, ¹ Ke Hao, ¹ Jun Zhu, ^{1,10} Andrea Gaedigk, ² Christine Suver, ^{1,10} Hua Zhong, ^{1,10} J. Steven Leeder, ² F. Peter Guengerich, ³ Stephen C. Strom, ⁴ Erin Schuetz, ⁵ Thomas H. Rushmore, ⁶ Roger G. Ulrich, ⁷ J. Greg Slatter, ⁸ Eric E. Schadt, ^{1,11} Andrew Kasarskis, ^{1,10,13} and Pek Yee Lum^{1,12,13}

Understanding Relationships in Gene Expression

- 466 Caucasians with liver gene expression profiling on an Agilent 44K human microarray
- . Age: 0-93, mean 50
- . Gender: 213 Females, 253 Males
- . All candidates for organ donation





Oxidoreductase activity Steroid Metabolism Metabolism of xenobiotics by cytochrome P450





Male gonad development Menstrual cycle Female gonad development Female sex differentiation DMRT1 LHCGR CA12 KCNIP4 OR5AR1

OR5AR1 INSL5 SI ACSS1 SLC36A2 CYP51A1







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Collaboration Models

- Blood Pharming
 - DARPA & CBER

- Council for Medical Device Innovation
 - CMS, NIH, AHRQ, CDC, VA, DoD, DARPA
 - Identifying Unmet Public Health Needs
 - Aligning barriers with needs

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How Can the FDA Prepare for New Science?

Evolutionary and Revolutionary Developments

High Profile Platforms That May Lead to Revolutionary Products

- Nanotechnology
- Synthetic Biology
- Tissue Engineering
- Stem Cells
- Robotics

What is Nanotechnology?



Properties

 If it's small or may behave differently, let's talk about it.

A Potential Risk-Based Model for Nano-product Oversight

Lower Risk

First Generation

No nano-properties (predictable behavior)

Second Generation

Nano-properties (unpredicted behavior)

Third Generation

 Mechanism of action via chemistry and physics (unpredictable behavior?)

Fourth Generation

Nano-factories

Higher Risk

Should Medical Product Assessment Be Risk or Risk-Benefit Based?

Should Medical Product Assessment Be Risk or Risk-Benefit Based?

 Should the willingness to accept risk be affected by the potential benefit of the product?

 Should the presence/absence of alternatives or the severity of clinical target affect the threshold for acceptable risk/benefit for a product?

Carbon Nanotube Based Artificial Muscle



Baughman, et al, UT Dallas

Robotics and Upper Extremity Prosthetics



www.google.com/images

Robotics and Upper Extremity Prosthetics



www.google.com/images

The Combination: A Miracle Ready to Happen?



www.google.com/images

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Bloom's Taxonomy of Education

Affective

Psychomotor

Cognitive

Bloom, 1956

Bloom's Taxonomy: Affective



- Characterize
- Organize
- Value
- Respond
- Receive

Bloom, 1956

Bloom's Taxonomy: Cognitive



- Analyze
- Evaluate
- Synthesize
- Apply
- Comprehend

Recall

Bloom, 1956

Bloom's Taxonomy: Cognitive



Apply Comprehend Recall

What Kind of Skills Are We Teaching?

Innovative Skills

Analyze

Evaluate

Synthesize

Apply

Comprehend Recall

Technical Skills

Bloom 1956, Sackner-Bernstein 2010

Are We Ready for the Pace of Change?

Semmelweiss' Observations





http://www.absoluteastronomy.com/topics/Ignaz_Semmelweis

From Tool to Impact

- 1675: Leeuwenhoek
- 1847: Semmelweiss
- 1862: Pasteur
- 1929: Fleming
- 1940: Florey

The Microscope

Observations

Pasteurization

Penicillin discovered

Penicillin isolated

From Practice to Impact

- 1716: Lady Montagu
- 1770s: Farmers
- 1796: Jenner
- 1840: British Government 1979: WHO

- Variolation observed
- **Cowpox inoculation**
- **Smallpox vaccination**
- Free vaccines for all
- Smallpox eradicated

Impact Realized

 ~ 100 years for Semmelweiss' observations to evolve into cures for bacterial infections

 ~ 200 years for vaccinations to become routine with global impact

Treatment of End Stage Heart Disease

- 1964: NIH starts Artificial Heart Program
- 1966: Methodist Hospital reports LVAD success
- 1982: Barney Clark implanted with artificial heart
- 1994: First LVAD approved for use
- 2001: LVAD shown to prolong survival
- 2004: First artificial heart approved for use

Treatment of Sudden Cardiac Death

- 1947: First human use of defibrillator (open chest)
- 1950s: Development of external defibrillator
- 1969: Johns Hopkins initiates research program
- 1980: Johns Hopkins implants defibrillator
- 1996: Implanted defibrillator shown to prolong life (there would be several more trials thereafter)



~ 30 years for NIH program to complete its goal

 ~ 40 years for defibrillators to go from use during surgery to common ambulatory procedure

Impact Realized

~ 30 years for NIH program to complete its goal

 ~ 40 years for defibrillators to go from use during surgery to implants as common ambulatory procedure

• Even if technology is successful, that's not enough.

In Parallel, Increasing Pace of Technology Advances

- From flight on a beach to landing on the moon took 70 years.
- From the first electronic computer to the internet took 30 years, then to the web another 20 years.
- From establishing itself as a corporate entity to becoming a verb in less than a decade (Google)
- And mapping the human genome in a decade.

Watson: A Computer that Reasons

	YOU'VE GOT BAGGAGE	HISTORIC FASHION	WHO'S YOUR DADDY COMPANY?	BEFORE AND AFTER	WHAT, ME WORRY7	A MUSICA PASTICHE
	1	1	1	1	Î	1
	2	2	2	2	2	2
Choose a question from the board at the right. Questions with higher point values are more difficult.	3	3	3	3	3	3
	4	4	4	4	4	4
	5	5	5	5	5	5

http://www.nytimes.com

