• 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 Have a Conflict

I was born in 1961.

I am at the age where I realize
I need safe and effective medical products
on the market soon.
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
Potential Approaches for New Science

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

Courtesy Gunnar Carlsson, PhD, Stanford University
Mapping the Genetic Architecture of Gene Expression in Human Liver


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


Courtesy Gunnar Carlsson, PhD, Stanford University
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

Courtesy Gunnar Carlsson, PhD, Stanford University
Acute phase response
Defense/immunity protein
Inflammatory response

SPINK1
SAA1
PLA2G2A
SAA3P
SAA2
LOC283483
NM_000331

Courtesy Gunnar Carlsson, PhD, Stanford University
Oxidoreductase activity
Steroid Metabolism
Metabolism of xenobiotics
by cytochrome P450

Courtesy Gunnar Carlsson, PhD, Stanford University
Male gonad development
Menstrual cycle
Female gonad development
Female sex differentiation

DMRT1
LHCGR
CA12
KCNIP4
OR5AR1
INSL5
SI
ACSS1
SLC36A2
CYP51A1

Courtesy Gunnar Carlsson, PhD, Stanford University
Interactively explore subset of 20,000 genes

Courtesy Gunnar Carlsson, PhD, Stanford University
Potential Approaches for New Science

- Analytic Methods
- Collaboration Models
- Novel Technologies
- Education for Innovation
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
Potential Approaches for New Science

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

• Size

• Properties

• If it’s small or may behave differently, let’s talk about it.
A Potential Risk-Based Model for Nano-product Oversight

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
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
Robotics and Upper Extremity Prosthetics

www.google.com/images
The Combination: A Miracle Ready to Happen?
Potential Approaches for New Science

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

Analyze        Evaluate        Synthesize

Apply          Comprehend      Recall

Bloom, 1956
What Kind of Skills Are We Teaching?

Innovative Skills

Analyze      Evaluate      Synthesize

Technical Skills

Apply       Comprehend       Recall

Bloom 1956, Sackner-Bernstein 2010
Are We Ready for the Pace of Change?
Semmelweiss’ Observations

http://www.absoluteastronomy.com/topics/Ignaz_Semmelweis
1675: Leeuwenhoek  The Microscope
1847: Semmelweiss  Observations
1862: Pasteur  Pasteurization
1929: Fleming  Penicillin discovered
1940: Florey  Penicillin isolated
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1716</td>
<td>Lady Montagu</td>
<td>Variolation observed</td>
</tr>
<tr>
<td>1770s</td>
<td>Farmers</td>
<td>Cowpox inoculation</td>
</tr>
<tr>
<td>1796</td>
<td>Jenner</td>
<td>Smallpox vaccination</td>
</tr>
<tr>
<td>1840</td>
<td>British Government</td>
<td>Free vaccines for all</td>
</tr>
<tr>
<td>1979</td>
<td>WHO</td>
<td>Smallpox eradicated</td>
</tr>
</tbody>
</table>
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)
Impact Realized

- ~ 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.
Choose a question from the board at the right. Questions with higher point values are more difficult.

http://www.nytimes.com
Improved Public Health

Information → Improved Public Health → Innovation