Maximizing FDA-CTSA Interactions

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Deputy Commissioner for Medical Products and Tobacco
US Food and Drug Administration
Maximizing FDA-CTSA Interactions

• Why are we interested at FDA?
• What do we need from you?
• What can we offer that you need?
• How do we make a deal?
FDA’s Regulatory Scope: 25 cents of every GDP dollar
FDA Mission

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation.
FDA Mission

- FDA is also responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health. FDA also has responsibility for regulating the manufacturing, marketing and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.
Finally, FDA plays a **significant role in the Nation’s counterterrorism capability**. FDA fulfills this responsibility by ensuring the security of the food supply and by fostering development of medical products to respond to deliberate and naturally emerging public health threats.
Why are we Interested?

- FDA makes decisions
- Our decisions need good evidence
  - They are better decisions
  - They can be better defended when questions arise
Why are we Interested?

• You oversee critical people and assets that we need
  - Almost all providers are trained/educated at your institutions
  - You get the vast majority of our nation’s public investment in biomedical research
    • You have fortresses of concentrated technology
  - Your integrated health systems are the delivery system we depend on to
    • Get the research done to evaluate benefit and risk of medical
    • Teach clinicians how to use medical products appropriately
How can you help us?

- **More effective T1 translation**
  - Appropriate use of the continuum of measures from studies (biomarkers/surrogates; clinical outcome assessments)
  - Reproducible science

- **Better job with clinical trials and clinical epi studies**
  - Human phenotyping
  - Precision Medicine Initiative
  - Mechanistic
  - Pragmatic

- **Overcome obstacles to learning health system**

- **Incorporate up to date knowledge about scientific underpinning of regulation in translational science**
  - curriculum and practical experience
Evidence Generation-Human Phenotyping

- Systems biology now on “launching pad”
- The “healthy human state”, risk of disease and disease will be characterized in multiple dimensions:
  - Genetics and genomics
  - Integrated biomarkers and biological pathways
  - Integrated measures of functionality form wearable devices
  - Measures of environment and social interaction
  - Measures of preferences and beliefs using personal, interactive devices
  - The “time dimension” will be transformed
- This has major implications for technology development
  - “off target effects”
  - Estimates or risk and benefit from multiple simultaneous measures
  - Integration of real time information into device and pharmacological therapy
Big Challenges in Biomedicine

- **Lack of significant information over the time dimension** — Measurements made to assess biology and human health are made periodically in visits to healthcare or research.

- **Missing systems biology** — When developing concepts of human biology or drug development we make limited measurements focused on specific mechanisms—we’re looking “under the lamppost”.

- **Missing the ability to measure the interactions of biology, sociology, environment and decision-making that could enable optimization of individualized and population health** — Although we know that health and disease are the product of the interactions of genes, multiple derivative biological systems, environment, social context and personal decisions, we tend to look at one part of the time.
Our national clinical research system is well-intentioned but flawed

• High percentage of decisions not supported by evidence*

• Health outcomes and disparities are not improving

• Current system is great except:
  – Too slow, too expensive, and not reliable
  – Doesn’t answer questions that matter most to patients
  – Unattractive to clinicians & administrators

We are not generating the evidence we need to support the healthcare decisions that patients and their doctors have to make every day.

Generating Evidence to Inform Decisions

1. FDA Critical Path
2. NIH Roadmap
3. Data Standards
4. Network Information
5. Empirical Ethics
6. Priorities and Processes
7. Inclusiveness
8. Use for Feedback on Priorities
9. Conflict of Interest Management
10. Evaluation of Speed and Fluency
11. Pay for Performance
12. Transparency to Consumers

Discovery Science

Outcomes

Early Translational Steps

Clinical Trials

Clinical Practice Guidelines

Measurement and Education

Performance Measures
## Re-engineering the Clinical Research Enterprise

<table>
<thead>
<tr>
<th>Demonstration networks</th>
<th>Funding mechanism to sustain national system through consensus of all constituents (&quot;1% solution&quot;)</th>
<th>National Clinical Research System creates effectiveness data that moves rapidly into the community AND data on outcomes and quality of care; sustained efficient infrastructure to rapidly initiate clinical trials; scientific information for patients, families, advocacy groups</th>
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<tbody>
<tr>
<td>Simplify complex regulatory systems</td>
<td>Simplified regulatory system in place for networks</td>
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<td>Networks in place for all institutes</td>
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<tr>
<td>Establish repositories of biological specimens and standards for collection</td>
<td>Data standards shared across NIH institutes</td>
<td>ONE medical nomenclature with national data standards (agreed to by NIH, CMS, FDA, DOD, CDC)</td>
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<tr>
<td>Standardize nomenclature, data standards, core data, forms</td>
<td>Funding mechanisms evaluated to determine which are most efficient</td>
<td>Data standards updated ‘in real time” through networks</td>
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<td>Library of elements shared between institutes and NLM</td>
<td></td>
<td>National repository of images and samples</td>
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<td>Efficient network administration infrastructure at NIH</td>
<td></td>
<td>Critical national “problem list”</td>
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<tr>
<td>Standards for capturing images for research</td>
<td></td>
<td>Most efficient network funding mechanisms in place across NIH</td>
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<tr>
<td>Create NIH standards to provide “safe haven” for clinical research</td>
<td>Standards for safe haven in place</td>
<td>Participation in research is a professional standard</td>
</tr>
<tr>
<td>Inventory and evaluate existing public-private partnerships, networks, CR institutions, and regulatory systems</td>
<td>Regulations and ethics harmonized with FDA, CMS</td>
<td>Study, evaluation and training regarding clinical research a part of every medical, nursing, pharmacy school</td>
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<tr>
<td>Establish FORUM(S) of all stakeholders</td>
<td>Public private partnership mechanisms in place</td>
<td>Clinical research practices documented and updated regularly to maintain safe haven</td>
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<td>Standards and pilot creation of a National Clinical Research Corps</td>
<td>100,000 members of certified “Clinical Research Corps”</td>
<td>Networks provide detailed training about network specific issues</td>
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<tr>
<td>Demonstration/planning grants to enhance/evaluate/develop model networks</td>
<td>Standards shared across NIH</td>
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**Increasing Level of Difficulty**

- **1-3 years**
  - 1% solution
  - Simplified regulatory system in place for networks
  - National Clinical Research System creates effectiveness data that moves rapidly into the community AND data on outcomes and quality of care; sustained efficient infrastructure to rapidly initiate clinical trials; scientific information for patients, families, advocacy groups
- **4-7 years**
  - Data standards shared across NIH institutes
  - Funding mechanisms evaluated to determine which are most efficient
  - ONE medical nomenclature with national data standards (agreed to by NIH, CMS, FDA, DOD, CDC)
  - Data standards updated ‘in real time” through networks
  - National repository of images and samples
  - Critical national “problem list”
  - Most efficient network funding mechanisms in place across NIH
- **8-10 years**
  - Participation in research is a professional standard
  - Study, evaluation and training regarding clinical research a part of every medical, nursing, pharmacy school
  - Clinical research practices documented and updated regularly to maintain safe haven
  - Networks provide detailed training about network specific issues
Learning health care systems

In a learning health care system, research influences practice and practice influences research.

**EVALUATE**
Collect data and analyze results to show what works and what doesn’t.

**IMPLEMENT**
Apply plan in pilot and control settings.

**DESIGN**
Design care and evaluation based on evidence generated here and elsewhere.

**ADJUST**
Use evidence to influence continual improvement.

**INTERNAL AND EXTERNAL SCAN**
Identify problems and potentially innovative solutions.

**DISSEMINATE**
Share results to improve care for everyone.
Sentinel: Distributed Data Networks
(Over 150,000,000 people included)
FDA Safety and Innovation Act

- Section 1136 of FDASIA (Jul 9, 2012) amended the FD&C Act by adding new section which addresses electronic submissions.
- Starting 24 months after final guidance for a specific submission type, Sponsors must use the standards defined in the data standards catalog (for submissions for NDAs, ANDAs, and BLAs)

Guidance document for Submissions Under Section 745A(a):
- Draft published February 2014
- Final publication December 17, 2014
PCORnetwork

Working together to find answers

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TWEETS 444  FOLLOWING 180  FOLLOWERS 539

Learn more about @joevselby's views on #healthdata in research: buff.ly/1Q3KeR5 via @Health_Affairs #hdpalooza

Rethinking Healthcare Delivery with 21st Century Data

“The key is linking data in electronic health records, insurance claims, patient registries, mobile devices, and other sources for research and care while protecting privacy and other interests.”

Joe V. Selby, MD, MPH
Executive Director
Patient-Centered Outcomes Research Institute
10 Demonstration Projects spanning 12 NIH institutes and centers

1-year planning phase (UH2)

Implementation phase (UH3)
The U.S. Precision Medicine Initiative
“And that’s why we’re here today. Because something called precision medicine … gives us one of the greatest opportunities for new medical breakthroughs that we have ever seen.”

President Barack Obama
January 30, 2015
Patient Partnerships

EHRs

Technologies

Genomics

Data Science
Historical model of clinical research: Many recruitment sites and a coordinating center

- Hub & spoke model
- Top-down decision-making
- Sites operated independently
Interoperable Networks
Share Sites and Data
Researchers and sponsors now recognize the value in integrating clinical research networks

- Linking existing networks means clinical studies and trials can be conducted more effectively
- Ensures that patients, physicians, and scientists form true “communities of research”
- Creates “interoperability” – networks can share sites and data
Medical Product Safety Surveillance

Sponsor(s)
Medical Product Safety

Sentinel Coordinating Center

FDA

Quality of Care

Sponsor(s)

Coordination Center(s)

Public Health Surveillance

Sponsor(s)

Coordination Center(s)

Comparative Effectiveness Research

Sponsor(s)

Coordination Center(s)

Randomized Clinical Trials

Sponsor(s)

Coordination Center(s)
**Patient**

- Participant in Research
- Activated Patient
- Reviewer of Research
- Designer of Research
- Creator of Disease Specific Infrastructure
- Driver of National Research Infrastructure
Major Ethics and Regulatory Issues for Pragmatic Clinical Trials

Informed consent
Defining minimal risk
Research/quality improvement distinction
Data monitoring
Vulnerable subjects
Identifying direct and indirect subjects
Gatekeepers
FDA-regulated products
Nature of intervention
Privacy
EXPLORING THE ETHICAL AND REGULATORY ISSUES IN PRAGMATIC CLINICAL TRIALS
LEADING A SERIES OF 12 ARTICLES ON DIFFERENT ASPECTS OF THIS TOPIC

COLUMN
Clinician Trials Rounds 2B: When RCT Participants are Lost to Follow-Up.
Part I: Why Even a Few Can Matter
M. Mathi, M. Sinha and S. Jacob

TRIBUTE
An Interview with David Sackett
RB Heywood and PN Goodman

Full contents are listed on the back cover
Planet of the Phones

Cost of data per mb, $

Mobile-broadband connections, bn
- Developing
- Developed

Mobile data transmitted
Exabytes* per month
- N America
- W Europe
- Asia Pacific
- Rest of world

Forecast

Jon Berkeley

The Economist. Feb 2015
For Big-Data Scientists, ‘Janitor Work’ Is Key Hurdle to Insights

By STEVE LOHR  AUG. 17, 2014
Advertising

• “The science of arresting human intelligence long enough to get money from it” — Stephen Leacock

• Hippocampus—”prescription-writing center of the brain”…”processes information by connecting new concepts with the parts of the brain where gut instincts are formed, areas that influence emotional behavior and form memories”

— Advertisements that go directly to the hippocampus. Lancet 1996
I DON'T GET IT.
Training, Education and Scientific Exchange

• **Training**
  – the action of teaching a person or animal a particular skill or type of behavior

• **Education**
  – the act or process of imparting or acquiring general knowledge, developing the powers of reasoning and judgment, and generally of preparing oneself or others intellectually for mature life

• **Scientific Exchange**
  – We can learn from each other

• **We need all 3 of these to produce the pipeline of talent now and for the future!**
Examples in which Educated Workforce is Critical

“Training is a good start, but its not enough”

- Next generation sequencing
- Wearable devices that monitor and provide decision support for serious conditions
- Targeted precision therapies in combinations
- Organ replacement, stem and cell therapy
- The pregnant woman and fetal pair in therapeutics
- E Cigarettes
- The Animal Rule
- Monitoring the safety of the food supply
- Determining when advertising is false and/or misleading
Key Formats for Training and Education

• “Regulatory Science” curricula
  – We need to work together to develop core knowledge base and approach to creative education
  – FDA speakers and seminars
  – We want to be more proactive in arranging these events

• More outgoing FDA to let the world know what we are thinking
  – We will be using multiple formats (journals, blogs, guidances, workshops)
Considerations on Education and Training Logistics

• Centers for Excellence in Regulatory Science (CERSI)
• CTSA’s
• Academic Health Systems in General
• Individual student experiences
• Individual fellowships
Special Issues for FDA

- **Issues with commercial confidential and trade secrets that require extreme security measures**
  - Disclosures have criminal penalties

- **Production metrics for almost everything we do**
  - Costs of making selections, orienting and assimilating trainees and fellows must be covered to create the bandwidth

- **Substantial societal concern about conflict of interest in FDA decision making**
  - The AMC has become the academic health and science system; big not-for-profit businesses with major clout, financial stake in medical products and technologies and many COI issues
The New Einsteins Will Be Scientists Who Share

From cancer to cosmology, researchers could race ahead by working together—online and in the open

By MICHAEL NIELSEN

In January 2009, a mathematician at Cambridge University named Tim Gowers decided to use his blog to run an unusual social experiment. He picked out a difficult mathematical problem and tried to solve it completely in the open, using his blog to post ideas and partial progress. He issued an open invitation for others to contribute their own ideas, hoping that many minds would be more powerful than one. He dubbed the experiment the Polymath Project.

Several hours after Mr. Gowers opened up his blog for discussion, a Canadian-Hungarian mathematician posted a comment. Fifteen minutes later, an Arizona high-school math teacher chimed in. Three minutes after that, the UCLA mathematician Terence Tao commented. The discussion ignited, and in just six weeks, the mathematical problem had been solved.
We Want to Work with you to Improve Translation and Develop the Workforce of the Future!