The Regulatory Landscape for Precision Medicine

Robert M Califf MD
Vice Chancellor for Health Data Science
Duke University
Advisor, Verily Life Sciences
Roundtable on Science and Welfare in Laboratory Animal Use
October 5th, 2017
An approach for disease treatment and prevention that takes into account the individual differences in lifestyle, environment, and biology
FDA and Precision Medicine: the Bottom Line

• Since the Kefauver Harris Act in 1962, precision medicine has been a goal of the FDA
  – The right treatment at the right dose at the right time for the right patient—this is basically the goal of a medical product label (and a nutritional label)
  – Predictive, preventive, personalized, participatory
• FDA needs the research community to develop an ecosystem for non-human studies that accounts for the complexity of biology, develops reproducible, predictive models and responds rapidly to the need for “co-clinical” mechanistic studies
• The complexity makes “gum shoe” regulation impossible—must move to development of quality systems
FDA Regulates a Spectrum of Health Products:
20-25 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 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.
FDA Mission

• FDA is also responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products 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.
FDA Mission

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.
Labeling

...FDA (also) regulates the labeling of products under its jurisdiction. This information, which must be rigorously truthful, well documented, and not misleading, plays a major role in protecting consumers and the public health. The FDA-regulated food label is helping shoppers eat a healthy diet; the labeling of drugs and medical devices gives prescribers and patients reliable guidance about the safety and effectiveness of health care products.
Which Treatment is Best for Whom?
High-Quality Evidence is Scarce
< 15% of Guideline Recommendations Supported by High Quality Evidence

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.
Precision Medicine Initiative: Modernizing FDA Regulation of Genomic Laboratory Tests

Traditional testing

Next generation sequencing
CRISPR/Cas9 Gene Editing

- Cas9 nuclease can be directed to cut at specific locations designated by guide RNAs
- Though there is some concern for off-target effects, CRISPR/Cas9 is a powerful technique for altering genes
WE’VE MAPPED THE WORLD. NOW LET’S MAP HUMAN HEALTH.

www.projectbaseline.com
WHAT IS THE PROJECT BASELINE STUDY?

A coalition to develop **gold standard data, tools and technologies** to provide a holistic view of human health and more efficiently and effectively conduct clinical research.
COMPREHENSIVE ONSITE ASSESSMENTS

“Omits”
- Genomics
- Proteomics
- Transcriptomics
- Metabolomics
- Microbiome
- Etc.

Eye exam, audiometry, PFT, etc.

Personal, family history surveys, etc.

Imaging
- Chest x-ray
- Coronary CT
- Echocardiography
- Etc.

Cognitive tests, physical performance tests, etc.

Blood, urine, stool, saliva, microbiome

Continuous monitoring study watch, sleep sensor, app
CONTINUOUS MONITORING THROUGH PASSIVE SENSORS

Study watch
Investigational wrist-worn sensor for continuous recording of physiological and environmental data

Sleep sensor
Commercially available, placed under mattress to passively monitor multiple physiologic data parameters

App
Mobile interface for self-reported and passive data acquisitions

Study hub
Safely sends device data to secure, encrypted Baseline database
MOBILE APP

Project Baseline

Sleep Poll
14-day poll • 1 minute per day

How you slept yesterday may help us predict how you function today.

LEARN MORE START

On site visit
Wed June 24th • 9:00am - 9:28pm

How you slept yesterday may help us predict how you function today.

LEARN MORE START

How many times did you wake up?

Select a number

1
2
3
4
5
6
7

NEXT
The Process of Digital Phenotyping
Digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.
DEEP MOLECULAR PROFILING

SAMPLES
- SERUM
- WHOLE BLOOD
- PBMCS
- PLASMA
- STOOL
- SALIVA
- URINE

CORE PLATFORMS
- CLINICAL LABS
- GENOMICS (WGS, DNA arrays)
- EPIGENOMICS (Methyl arrays)
- TRANSCRIPTOMICS (RNA-seq)
- IMMUNOPHENOTYPING (CyTOF)
- MICROBIOME (16S rRNA)
- PROTEOMICS
- METABOLOMICS

AUTOMATION
~6TB data per subject

Project Baseline
# DATA ANALYTICS PLATFORM

<table>
<thead>
<tr>
<th>Disease Management</th>
<th>Computer-Aided Diagnostics</th>
<th>Research Informatics</th>
<th>Clinical Study Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensors</td>
<td>Imaging</td>
<td>Molecular</td>
<td>Clinical</td>
</tr>
<tr>
<td>Collaborative Data</td>
<td>Public Datasets</td>
<td>Private Data</td>
<td>Self-Reported</td>
</tr>
</tbody>
</table>

Data Management, Security, Compliance, Quality
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.

ADJUST
Use evidence to influence continual improvement.

IMPLEMENT
Apply plan in pilot and control settings.

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

DISSEMINATE
Share results to improve care for everyone.

INTERNAL AND EXTERNAL SCAN
Identify problems and potentially innovative solutions.
Drug Surveillance and Trials
Post Market Studies, including comparative effectiveness
An innovative initiative funded by the Patient-Centered Outcomes Research Institute (PCORI), PCORnet is a large, highly representative, national patient-centered clinical research network.

Our **vision** is to support a learning U.S. healthcare system and to enable **large-scale clinical research** conducted with **enhanced quality and efficiency**.

Our **mission** is to enable people to make informed healthcare decisions by efficiently conducting clinical research relevant to their needs.
PCORnet® embodies a "network of networks" that harnesses the power of partnerships
Resulting in a national evidence system with “research readiness”

PCORnet represents:

~122 million patients who have had a medical encounter in the past 5 years

*some individuals may have visited more than one Network Partner and would be counted more than once
Regulatory Science

• Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.

• FDA definition—can be expanded to other regulatory agencies
The Regulatory Dream

• Integrative non-clinical models that provide reliably probabilistic estimates of translation into human biology
  – Realistic pronouncements about “traslatability”
• Quality management systems that enable assurance about data provenance, analytical appropriateness and reproducibility
• Rapid, less expensive and scalable models to test mechanisms when surprises occur
• Ecosystem engagement in rapid learning given the new capacity to acquire, store and analyze digital information
• Deliberate risk-taking to advance beyond “regulatory inertia” to move the field forward