Transatlantic Workshop on Drug-Related Progressive Multifocal Leukoencephalopathy (PML)

Building Collaboration for Research

Janice Soreth, M.D.
FDA Liaison to EMA
Who has a stake in further collaborations?

- Patients, families
- Healthcare professionals
- Researchers
- Industry
- Regulators
Building Collaboration: Regulator and Patient

FDA involves the public/patients in several ways

- **Advisory Committee** meetings are typically public
  - Committee membership includes consumer and patient representatives; members cannot have conflicts of interest
  - Open Public Hearing is part of every meeting

- We convene open public or ‘**Part 15’ hearings**
  - FDA announces the topic in Federal Register
  - Members of the public sign up, speak, and FDA listens

- **Public Workshops**
  - Formal panels convened, including consumers, academia, industry reps
  - Allows for wide-variety of participants; no COI process.

- **Comments to the docket**: FDA invites comments from the public when publishing draft rules and guidances
Building Collaboration: Regulator and Patient

- EMA involves patients in its core work:
  - Patients are members of Management Board and scientific committees (COMP, CAT, PDCO and PRAC)
  - Participate in benefit/risk discussions (e.g. scientific advisory groups –SAGs-)
  - Review information prepared by EMA (Package Leaflets, safety communication, EPAR summaries)
  - Observers in PhVWP
  - EMA Patients & Consumers Working Party (PCWP)
Building Collaboration: Regulator and Regulator

- FDA can exchange non-public information with international counterparts [21CFR20.89]

- FDA shares information through confidentiality agreements with other agencies
  - Commercial confidential data, investigative, pre-decisional information
  - Preliminary thinking as we develop guidances, policies, enforcement actions, internal analyses
FDA Confidentiality Arrangements

- Austria
- Belgium
- Denmark
- France
- Germany
- Ireland
- Italy
- Netherlands
- Sweden
- Switzerland
- United Kingdom

- EMA
- EC- DG Enterprise
- EC- DG SANCO
- EDQM
- WHO

- Australia
- Canada
- Israel
- Japan
- Mexico
- New Zealand
- Singapore
- South Africa
FDA International Agreements

- Confidentiality Commitments
  http://www.fda.gov/InternationalPrograms/Agreements/ConfidentialityCommitments/default.htm

- Memoranda of Understanding and Other Cooperative Arrangements
  http://www.fda.gov/InternationalPrograms/Agreements/MemorandaofUnderstanding/default.htm
Building Collaboration:
Patient-Regulator-Researcher-Industry

Learning from experience
Learning from experience

- HIV in the 1980s—one of the most frightening medical challenges in recent times
- Advocacy groups and protests
- Drug developers, diagnostic companies, academia and FDA collaborated
- Pooling of data allowed the development of viral load testing as the centerpiece for our strategy to control HIV
Lessons learned

• It became the surrogate marker on which all HIV drugs have been approved reducing the time of follow-up from decades to weeks
• It has become the most important tool in clinical management of HIV
• All this would have been impossible without new areas of science, new biomarkers, and collaborations
Lessons learned

• It served as a model to expedite medical product development
• One of the themes was developing the tools for product development
• Another was collaboration - the idea that FDA, academia, and industry should be working together
• The initiative was inclusive - it involved all FDA Centers - CDRH, CDER, CBER, CFSAN CVM & NCTR
History of the Critical Path Initiative

- Created in 2004
- Office of cross-cutting programs
- Pipeline problem-Increasing R&D with diminishing returns
- No funding initially, later appropriated by Congress
- Projects solicited from outside
Critical Path mission

- To focus on the part of regulatory science dealing with the “pipeline” piece, the rising cost of R&D and diminishing returns
- FDA, working together with greater scientific community, to facilitate development of important new products
- 6 project areas
### Tool buckets

- Biomarkers
- Modeling
- Trial design/strategy
- Bioinformatics
- Education and communication
- Manufacturing

### CPI Strategy

#### Public health goals

- Product safety
- Unmet needs: tuberculosis/neglected diseases
- Special populations: pediatrics, pregnancy
- Antimicrobial resistance
- Other urgent public health needs
- Personalized medicine

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**CPI Strategy**
CPI Strategy

Discovery
Preclinical testing
Phase 1 and 2
New science
Phase 3
Information management
Training
Post marketing

Collaborations
Regulations and guidance
Infrastructure

Public health goal e.g. product quality, safety and efficacy
OCPP portfolio

• Portfolio of projects using
  – the tool sets
  – the information we have on challenges facing medical product development
  – Priority areas identified by FDA and Congress
TB a targeted public health need

- Congressional language:
- $2m appropriated for TB and neglected diseases
- Report requested on neglected and rare diseases
Several activities

- Cross center TB working group to identify priority areas
- TB diagnostic workshop together with CDC & NIH
- RFA for projects related to TB and tropical diseases
- 30 applications, many from premier institutions
- Reviewed by ad hoc committee of internal (FDA) and external (CDC, NIH) experts
Selected projects

Of 30 applications 6 were selected by a broad review panel for funding

- Five biomarker projects
- One modeling project
- Animal models
- Latency marker
- Urinary small molecule signatures
- Ultrasensitive detection platform
- Biomarkers of vaccine efficacy
- Frozen trial initiative- a specimen bank of samples and corresponding patient data obtained during clinical trials
Other Critical Path Key Projects

- Biomarker consortium
- Manufacturing
- DAPT
- Clinical Trial Transformation Initiative (CTTI)
- CPath
  - CAMD
  - Nephrotoxicity
  - PRO
- Sentinel
- Medwatch
- Registration and listing
- Bioinformatics board
Update on CPI Key Projects

• CPath institute- using 2010 grant from OCPP
  – PRO-developing patient reported outcome tools for irritable bowel syndrome and others
  – Nephrotoxicity- multiple biomarkers of early renal injury have been approved using biomarker qualification process
  – CDER is very active in this program and have take over management during 20
Update on CPI Key Projects

On reducing cardiac toxicity:

- **ECG Warehouse**: A repository of digital electrocardiograms (ECGs) used to study the cardiac toxicity of drugs
  - Allows FDA to electronically search abnormal ECG’s and determine if they were linked to a drug
Update on CPI Key Projects

Safer Use of Targeted Drugs

- Clopidogrel (discovery of genetic variations that may render the drug ineffective)

- Warfarin (funding to develop genetically-based instructions for dosing and to develop dosing algorithms for patients new to drug)
Update on CPI Key Projects

Clinical Trials Transformation Initiative

- Began by FDA and Duke University to improve the quality and efficiency of clinical trials

- Comprised of over 50 organizations, including government agencies, industry representatives, patient and consumer representatives, professional societies, investigator groups, academic institutions, and other interested parties

https://www.trialstransformation.org/
Clinical Investigator Training Course

- Annual 3-day course targeted at medical professionals to help develop a cadre of well-trained investigators
- Includes lectures given by senior FDA experts and guest lecturers from industry and academia

November 2010 materials:

http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/SpotlightonCPIProjects/ucm236523.htm
Update on CPI Key Projects

Sentinel System

- Enables FDA to actively query diverse automated electronic health record systems, administrative and insurance claims databases, and registries to evaluative possible medical produce safety issues quickly and securely.
- Pilot with Harvard Pilgrim Health
- Has expanded to include additional federal partners
Update on CPI Key Projects

SafeRX

- Provides close to real-time, electronic vaccine safety monitoring of seasonal and H1N1 influenza vaccines.
- Enhances FDA’s existing safety surveillance capacity
- Collaboration with Centers for Medicare and Medicaid Services (CMS), Assistant Secretary for Planning and Evaluation, VA, DoD and other federal agencies
DAPT Collaboration to Improve Patient Safety

• Launched in September 2009 under the management of Harvard Clinical Research Institute, FDA spearheaded an unprecedented collaboration, bringing together 4 device and 4 drug manufacturers to participate with regulators, clinical investigators, and academia in a four-year, 20,000-patient study in 220 clinical trial centers in North America and Europe.
CPI: FDA-NIH Collaboration

- Announced in February, 2010
- A key goal is to identify ways that FDA and NIH can work together to support common goals.
- Will help focus additional funding ($6.5 million in 2010) on many of the areas CPI has identified to support the development and evaluation of human medical products and ensure their safety and effectiveness.
In Conclusion

• Emerging areas of science, evolving technologies, and globalization require us to modernize our tools and processes
  – *But this cannot be done by one entity alone*

• Regulators must continue to forge partnerships and collaborations, to continue to leverage resources for research and lay the groundwork for transforming medical treatment, in the best interests of patients