



# Science at the FDA: Update for the Science Board



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# Overview

- Welcome to our new members: Dr. Mark McLellan, Dr. Barbara Kowalcyk, and Dr. Lisa Nolan
- Brief Updates
  - Regulatory Science and Innovation, including NCTR
  - Scientific Professional Development
  - Medical Countermeasures Initiative (MCMi)
  - Women's Health & Minority Health
- Comments at transition and my personal appreciation
  - Returning to academia as Professor of Medicine and Attending at Georgetown and the DC VA, starting new Center on Medical Product Access, Safety and Stewardship (COMPASS)
  - Pleased to be working closely with Dr. Steve Ostroff and Dr. Luciana Borio, who will serve as Acting Deputy, to help ensure a smooth transition, and as OCS is in excellent hands!



# Regulatory Science, Innovation, and Critical Path Updates

- Broad Agency Announcement (BAA)
- Targeted extramural and collaborative regulatory science
  - May 2013 renewal: expanded scope to include Social and Behavioral Sciences and Global Product Safety Net
  - FY13: 95 white paper applications reviewed and 14 awarded
  - Examples of funded projects:
    - Wyss: Organ-on-Chip Tools for Radiation Countermeasures
    - University of Auckland: Musculoskeletal Atlas Project (MAP): anatomical/functional model to facilitate virtual clinical trials

# Progress on FY12 BAA Projects: Example: Social Media Data Mining

- Currently in 2nd year (FY14) of 3-year option
- OCS/CDER/CBER/CDRH/CFSAN/CTP
- Successful 1st year mining Twitter, Facebook, and web information – documented ability to identify Aes
- Second year plans:
  - Rigorous analysis of products from all centers
  - Triage of events by severity, label status, refine filters and analytics
  - Create notifications and incorporate into reviewer workflow
  - Improve visualization platform to allow in-depth analysis





# *CERSI's: selected highlights*

- Training
  - Online MS in Regulatory Science – UMD Baltimore
  - Masters in Regulatory Science and Engineering – UMD College Park
  - Masters in Regulatory Science – GU
- Research
  - Collaborations to support new standards for transporter proteins and for tissue scaffolding - UMD
  - Collaborations on health disparities including clinical trial participation and triple neg breast Ca - UMD & GU
  - Pathways modeling and visualization including new review tools - GU

# ***CERSI's: selected highlights (cont.)***

- Workshops, Lectures and Events
  - 2<sup>nd</sup> CERSI Day at UMB
  - Mesenchymal Stem Cells for Clinical Trials,
  - Outcomes Research Utilizing Imaging;
  - Validation & Qualification of *In Vitro* Tools and Models,
  - Clinical rounds
  - UMD monthly lectures (>1000 FDA participants)
  - "America's Got Regulatory Science Talent" Competition – UMD
- Currently reviewing applications for potential added site(s)



# NCTR: Collaboration and Outreach

- FDA/NIEHS
  - Bisphenol A: 90d toxicology and internal dosimetry studies completed. No evidence for altering existing safety assessment (*in press*); chronic study data available 2016; human pK studies with NIEHS clinical unit ongoing.
  - Bioassay/Mechanism/PBPK studies conclude acrylamide carcinogenicity mediated through glycidamide.
  - Whole leaf extracts of *Aloe vera* induce large intestine tumors in rats.
  - Quantitative hazard assessments continue with furan, triclosan, nanoscale silver, retinyl palmitate, oxybenzone, and melamine + cyanuric acid.
- Partnership Intermediary Agreement (PIA) fostered with Arkansas Research Alliance to facilitate IP transfer and development
- Global Coalition for Regulatory Science Research inaugurated with signatories from 9 countries including U.S.
- NexGen Sequencing Project (SECQ) -7 collaborative manuscripts



# NCTR Update *(cont)*

## Advancing Regulatory Science 1

- Selected innovative R and D
  - Algorithms to mine AERS for subsets of adverse events- across drug classes to develop predictive interaction profiles.
  - E-notebook systems developed to support data dense imaging modalities in the NanoCore facility; FDA hands-on-techniques methods training.
  - *In vitro* human airway model demonstrating complex tissue structure developed and being used to assess toxicity and inflammation.
  - *In vitro* organotypic models for 3D skin models undergoing basic genetic toxicology profiling.
  - *In vitro* stem cell models from rodents established to identify developmental toxicants; human cell model systems in development.

# Scientific Professional Development Highlights

- 4<sup>th</sup> Cadre of 30 Commissioner's Fellows graduated - 63% retained
- 6<sup>th</sup> Cadre of 13 Commissioner's Fellows and 10 FDA-NCI/NIH Interagency Oncology Taskforce (IOTF) Fellows recruited and recently started
- Created FDA 101 course for Agency, planning for public access
- New Frontiers in Science Lectureship Initiated - Cosponsored by HRA
  - Dr. Lee Hood, Institute for Systems Biology: “Systems Medicine, the Emergence of Transformational Technologies and Proactive P4 Medicine”
    - Dr. Irving Weissman, Stanford; “Stem Cells and Cancer Stem Cells: From Discovery to Clinic”
- Chief Scientist Distinguished Lecture Series
  - Dr. Todd Golde, Center for Translational Research in Neurodegenerative Disease, “Novel Therapies for Neurodegenerative Disease: Lost in Translation”
  - Dr. Jerome Cantor, St. John's University, “Animal Models: What They can (and cannot) Tell us about Human Lung Disease”
- 1305 staff attended MCM related conferences, workshops, lectures, courses
- Public Workshop, Microphysiological Systems for Use as Regulatory Tools, co-sponsored with NIEHS, EPA, NCATS, JHU, ICIQPD, > 200 attendees

# Medical Countermeasures initiative (MCMi)

## Recent Accomplishments

- Selected Approvals:
  - Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)
  - New sample purification kit -- Joint Biological Agent Identification and Diagnostic System for detection of anthrax, plague, and tularemia DNA
  - Organophosphate test system -- quantitation of organophosphate metabolites in human urine from individuals with possible cholinesterase poisoning
  - Burn Resuscitation Decision Support System (BRDSS), a fluid resuscitation calculator for care of adult patients with >20% total body surface area burns
  - Modified diagnostics to improve performance with influenza H7N9 & H3N2
- EUAs:
  - CDC Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7
  - CDC Novel Coronavirus Real-Time RT-PCR for detection of MERS-CoV



## MCMi Recent Accomplishments *(cont)*

- Sustained Public Health and Security Action Teams
  - ARS/biodosimetry, multiplex diagnostics, warfighter trauma, MCM surveillance, pediatric and maternal populations
- Expanded MCM Professional Development Program
  - MCM Lecture Series, Foundations for Pre-Clinical Review Lecture Series, conference support, Georgetown University Certificate Program on Biohazardous Threat Agents and Emerging Infectious Diseases, Training Course on Emergency Management of Radiation Victims
- Enhancing Studies Performed in BSL3/4 Laboratories –
  - Launched pilot training program with UTMB Galveston National Laboratory to identify and share best practices for feasibly ensuring data quality and integrity for studies being conducted to support MCM development using Animal Rule

## MCMi Recent Accomplishments *(cont)*

- Guidances
  - Qualification Process for Drug Development Tools
  - Preclinical Assessment of Investigational Cellular and Gene Therapy Products
  - Distribution of In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only
  - Medical Device Development Tools
  - Design Considerations for Pivotal Clinical Investigations for Medical Devices
  - Expanded Access to Investigational Drugs for Treatment Use – Qs & As
  - Expedited Programs for Serious Conditions – Drugs and Biologics



## MCMi Recent Accomplishments *(cont)*

- Workshops
  - Battery-Powered Medical Devices Workshop: Challenges and Opportunities
- Advisory Committee Meetings
  - BLA for Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G) (Equine) (BAT)
  - Effects of extreme weather and natural disasters on the production and supply of medical devices
  - safety and efficacy of currently approved leukocyte growth factors as potential treatments for radiation-induced myelosuppression associated with a radiological/nuclear incident
  - Reclassification of rapid influenza detection devices, currently regulated as Class I, to Class II
  - Ethical issues in pediatric product development, including MCMs



# Office of Women's Health and Office of Minority Health: Science Updates

- Section 1138: Ensuring Adequate Information Regarding Pharmaceuticals for All, particularly under-represented Subpopulations, Including Racial Subgroups (OMH); FDA Language Access Plan completed
- Finalizing MOUs with the NIH Office on Women's Health and the Karolinska Institute in Sweden to support FDA research activities and data-sharing (OMH)
- New FDA intramural research program addressing minority health and health disparities and graduate and postdoctoral fellowships to address health disparities in product safety, efficacy, and quality (OMH)
- Twenty year review of women's health research at FDA (OWH- to be discussed later)



# Transition: some thoughts





# Major Accomplishments & Directions

- Enhanced strategic leadership and advocacy for science & scientists at FDA
  - Chief Scientist and Center Science leadership positions
  - FDA-wide and Center Science Strategic Plans and emphasis on anticipating and using emerging technologies
- Increased visibility & support of FDA Science
  - Defining & championing regulatory science & its unique role
  - First dedicated appropriation for cross-cutting regulatory science



# Major Accomplishments & Directions: (cont.)

- Enhanced the breadth of support for FDA science to include critical but underrepresented dimensions
  - Inclusion of review science, non-lab based science, social and behavioral science and Women’s and Minority health-related science
  
- Supported opportunities for and culture of collaboration
  - CERSIS and other novel collaborations at both Agency and Center levels, multi-sectoral consortia and workshops, support for extramural engagement in regulatory science and training
  - Inter-center collaboration and cooperation through SSC, working groups, shared facilities, equipment and other resources



# Major Accomplishments & Directions: (cont.)

- Supporting a culture of and environment for excellence and integrity in science
  - New FDA-wide OSPD & cross-agency coordination, collaboration & expansion of training & development opportunities, peer review
  - New OSI and FDA policies for scientific integrity, dispute resolution and publications – ensuring all voices are heard and considered
  
- Reviewed PHEMCE, developed & implemented the MCMi
  - Model of proactive FDA engagement, and appropriated support, to meet public health and product development challenges, including targeted research and training , multi-sectoral and cross-Agency collaboration and innovative approaches to review and policy



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# Risks





# Risks

- The aforementioned gains and directions:
  - Need to serve as a foundation that: (1) illustrates the possibilities, (2) serves as a starting point for further building, innovation, and continuous improvement, and (3) must continue to be institutionalized
  - Have only very limited or no dedicated resources attached to them
  - Can be potentially fragile under burdens of day to day work, real or perceived crises *du jour*, and real and perceived resource constraints
  - Represent and require not only concrete actions, but also, as part of a science culture, continued leadership, advocacy, and staff level engagement, as well as outside interest, feedback, engagement and advocacy, to maintain and renew



## Other Risks

- Generational/workforce change, recruitment challenges
- Continuing acceleration of risk/opportunity factors like technical innovation, information overload product complexity, globalization
- Constantly increasing regulatory responsibilities
- Budget uncertainties and resultant challenges in areas often seen as “luxuries” but critical for long term organizational health and learning culture - investing in talent recruitment (e.g. CFP) and development, training, infrastructure, and needed core infrastructure and facilities
- Tendency, as a regulatory agency with requirement for many protections of information and data, toward isolation



## Selected Additional Opportunities

- Build on and institutionalize linkages to and scientific collaboration with other Agencies/sectors e.g. NIH/NCATS, DARPA, NIST, EPA, academia, and with global regulatory and public health partners
- Institutionalize horizon scanning & budget preparedness for new technologies and public health threats
- Develop new systematic approaches, involving FDA review staff/scientists, academia and product developers, to continue to identify & collaboratively solve major “precompetitive” regulatory science problems
- Identify & institutionalize best practices, new models in enhancing development of products where public health needs are unmet and, particularly, market forces diverge



*Such risks and challenges are clearly outweighed by both the excitement and rewards of what has been accomplished, and the future opportunities as FDA and its partners in the product development and public health ecosystems apply new science, technology and synergies....from gene and tissue engineering to empowering communities and patients with information...to addressing the public health challenges of the 21<sup>st</sup> century*



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# Clearly a Bright Future!





## Thanks so much!

- For your engagement, perspective, input and guidance.
- For your collegiality and support, past, present and future.
- For what you have done for FDA and our nation's health – the Science Board's engagement and advocacy have powerful impacts both within and outside FDA.
- I am excited by how much FDA has accomplished, and its future, have been privileged to work with our terrific staff of dedicated scientists and others, and am looking forward to working together and toward the same ends in my new role, from a new vantage point.
- *Bon voyage but not goodbye!*

