Global Summit on Regulatory Science Research: Modernizing Toxicology

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National Center for Toxicological Research, U.S. Food & Drug Administration

The views provided in this presentation may not reflect those of the FDA
Products Regulated By FDA

Foods
- All interstate domestic and imported; including produce, fish, shellfish, shell eggs, milk; except meat and poultry
- Bottled water
- Beverages (<7% alcohol)
- Infant formula

Food Additives
- Colors
- Food containers

Dietary Supplements
- Animal Feeds

Pharmaceuticals
- Human (safety, efficacy)
- Animal (safety, efficacy)

Medical Devices
- Radiation Producing Devices

Vaccines
- Blood Products

Tissues
- Sterilants

Tobacco
Regulatory Science: Challenges and Opportunities

• Product discovery and development: What are the issues?

• Regulatory Science – What is it? How is it changing assessment of safety and enhancing innovation?

• Supporting regulatory science through training

• Global issues and food safety – Impact on training needs
Decreased Translation of Basic Science Investment to Products


Innovative science to improve public health
As an example, focus on drug development:

What is the problem?

Main reasons for drug attrition and withdrawal:

- **Safety and efficacy related reasons of drug attrition, Adverse Drug Reactions (ADRs), drug withdrawal.**

- What is the evidence?

- What is the prevalence?

- When does this occur?
What is the problem?

**Drug discontinuation and withdrawal**

- Failure to manage attrition during development
- Enforced withdrawals from the market place
- Efficacy and safety still the main reason for drug discontinuation

From Tim Hammond, PhD, AstraZeneca
What is the problem?
Main reasons for drug attrition and withdrawal

PBF data 2003-7, Principal reasons cited for attrition at the various stages of drug development

From Tim Hammond, PhD, AstraZeneca
Safety related reasons of drug attrition, ADRs, drug withdrawal.

What is the evidence? What is the prevalence? When does this occur?

<table>
<thead>
<tr>
<th>Phase</th>
<th>Preclinical</th>
<th>Non-clinical</th>
<th>Phase I</th>
<th>Phase I-III</th>
<th>Phase I-III</th>
<th>Phase III/Approval</th>
<th>Post-Approval</th>
<th>Post-Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information:</td>
<td>Causes of attrition</td>
<td>Causes of attrition</td>
<td>Serious ADRs</td>
<td>Causes of attrition</td>
<td>Causes of attrition</td>
<td>ADRs on label</td>
<td>Serious ADRs</td>
<td>Withdrawal from sale</td>
</tr>
<tr>
<td>Sample size:</td>
<td>156 CDs stopped</td>
<td>88 CDs stopped</td>
<td>1,015 subjects</td>
<td>63 CDs stopped</td>
<td>82 CDs stopped</td>
<td>1,138 drugs</td>
<td>21,298 patients</td>
<td>47 drugs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity Domain</th>
<th>Cardiovascular</th>
<th>Hepatotoxicity</th>
<th>Haematology/BM</th>
<th>Nervous system</th>
<th>Immunotoxicity</th>
<th>Gastrointestinal</th>
<th>Reprotox</th>
<th>Musculoskeletal</th>
<th>Respiratory</th>
<th>Renal</th>
<th>Genetic tox</th>
<th>Carcinogenicity</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular:</td>
<td>24%</td>
<td>27%</td>
<td>9%</td>
<td>35%</td>
<td>21%</td>
<td>36%</td>
<td>15%</td>
<td>45%</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hepatotoxicity:</td>
<td>15%</td>
<td>8%</td>
<td>7%</td>
<td>29%</td>
<td>21%</td>
<td>13%</td>
<td>0%</td>
<td>32%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematology/BM:</td>
<td>3%</td>
<td>7%</td>
<td>2%</td>
<td>3%</td>
<td>4%</td>
<td>16%</td>
<td>10%</td>
<td>9%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system:</td>
<td>12%</td>
<td>14%</td>
<td>28%</td>
<td>2%</td>
<td>21%</td>
<td>67%</td>
<td>39%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunotoxicity:</td>
<td>7%</td>
<td>7%</td>
<td>16%</td>
<td>10%</td>
<td>11%</td>
<td>25%</td>
<td>34%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal:</td>
<td>5%</td>
<td>3%</td>
<td>23%</td>
<td>2%</td>
<td>5%</td>
<td>67%</td>
<td>14%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reprotox:</td>
<td>9%</td>
<td>13%</td>
<td>0%</td>
<td>5%</td>
<td>1%</td>
<td>10%</td>
<td>0%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal:</td>
<td>8%</td>
<td>4%</td>
<td>0%</td>
<td>5%</td>
<td>1%</td>
<td>28%</td>
<td>3%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory:</td>
<td>1%</td>
<td>2%</td>
<td>0%</td>
<td>2%</td>
<td>0%</td>
<td>32%</td>
<td>8%</td>
<td>2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal:</td>
<td>6%</td>
<td>2%</td>
<td>0%</td>
<td>5%</td>
<td>9%</td>
<td>19%</td>
<td>2%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic tox:</td>
<td>5%</td>
<td>5%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity:</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
<td>4%</td>
<td>16%</td>
<td>2%</td>
<td>2%</td>
<td></td>
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</tr>
</tbody>
</table>

The various toxicity domains have been ranked first by contribution to products withdrawn from sale, then by attrition during clinical development. Note general agreement between pairs of equivalent studies.

Adapted from Redfern WS et al. The Toxicologist 2010; 114 (S-1), 1081.
What is the problem? Impact of **functional** adverse effects on drug development – over a 2 months period!

<table>
<thead>
<tr>
<th>Date</th>
<th>Drug</th>
<th>Therapeutic target</th>
<th>Functional adverse effect</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 Oct</td>
<td>Qnexa</td>
<td>Obesity</td>
<td>Tachycardia [<em>and embryotox</em>]</td>
<td>Non-approval (US)</td>
</tr>
<tr>
<td>22 Oct</td>
<td>Saquinavir-ritonavir (in combination)</td>
<td>HIV</td>
<td>QT prolongation → TdP</td>
<td>Labelling (US)</td>
</tr>
<tr>
<td>21 Oct</td>
<td>GnRH agonists</td>
<td>Prostate cancer</td>
<td>Metabolic syndrome → MI; stroke</td>
<td>Labelling (US)</td>
</tr>
<tr>
<td>20 Oct</td>
<td>Bydureon</td>
<td>Type II diabetes</td>
<td>QT risk</td>
<td>FDA requested TQT study (after reviewing NDA)</td>
</tr>
<tr>
<td>12 Oct</td>
<td>Adusuve Staccato (inhalation)</td>
<td>Agitation during schizophrenia/bipolar disorder</td>
<td>Respiratory (reduced FEV)</td>
<td>Non-approval (US)</td>
</tr>
<tr>
<td>11 Oct</td>
<td>Meridia (sibutramine)</td>
<td>Obesity</td>
<td>Increased risk of heart attack &amp; stroke</td>
<td>Withdrawn from market (US)</td>
</tr>
<tr>
<td>11 Oct</td>
<td>Fibanserin</td>
<td>Female hypoactive sexual desire disorder</td>
<td>Depression, anxiety, fatigue</td>
<td>Development abandoned</td>
</tr>
<tr>
<td>24 Sep</td>
<td>Avandia</td>
<td>Type II diabetes</td>
<td>Increased risk of heart attack &amp; stroke</td>
<td>Withdrawn from market (EU); restricted use (US)</td>
</tr>
<tr>
<td>17 Sep</td>
<td>Lorcaserin (Lorgess)</td>
<td>Obesity</td>
<td>Increased risk of heart attack &amp; stroke</td>
<td>Non-approval (US)</td>
</tr>
<tr>
<td>16 Sep</td>
<td>Valganciclovir (Valcyte)</td>
<td>Paediatric transplantation</td>
<td>Abdominal pain, vomiting, diarrhoea, tremor, seizure.</td>
<td>Labelling (US)</td>
</tr>
<tr>
<td>13 Sep</td>
<td>Taspoglutide</td>
<td>Type II diabetes</td>
<td>Nausea and vomiting</td>
<td>Suspension of Phase III trial</td>
</tr>
<tr>
<td>02 Sep</td>
<td>Tigecycline</td>
<td>Infection</td>
<td>Death</td>
<td>Physicians advised to consider alternatives (US)</td>
</tr>
</tbody>
</table>

Source: DIA Daily
September / October 2010

From Tim Hammond, PhD, AstraZeneca
Regulatory Science

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

Innovative science to improve public health
Advancing Regulatory Science

ENSURING THE SAFETY AND QUALITY OF FOOD AND MEDICAL PRODUCTS HAS NEVER BEEN MORE complicated. Societies around the world face increasingly complex challenges that require harnessing the best available science and technology on behalf of patients and consumers. This effort requires a strong field of regulatory science to develop new tools, standards, and approaches that efficiently and consistently assess the safety, efficacy, quality, and performance of products. Yet, despite being a critical component of the scientific enterprise, regulatory science has long been underappreciated and underfunded.

Today, we are neither effectively translating scientific discoveries into therapies nor fully applying knowledge to ensure the safety of food and medical products. We must bring 21st-century approaches to 21st-century products and problems. Toxicology is a prime example. Most of the toxicology tools used for regulatory assessment rely on high-dose animal studies and default extrapolation procedures and have remained relatively unchanged for decades, despite the scientific revolutions of the past half-century. We need better predictive models to identify concerns earlier in the product development process to reduce time and costs. We also need to modernize the tools used to assess emerging concerns about potential risks from food and other product exposures.

The U.S. Food and Drug Administration (FDA) is prepared to lead the way in strengthening regulatory science and transforming toxicology. But this will require collaborations and partnerships with academia, industry, and other government agencies. Fortunately, this work has already begun. For example, the FDA and the European Medicines Agency have recently worked to characterize novel biomarkers that identify drug-induced kidney toxicity in preclinical animal models, and several of these biomarkers have now been qualified for regulatory use. And last year, the FDA and the U.S. National Institutes of Health (NIH) launched a new NIH-FDA Regulatory Science Initiative to encourage new research in the field; we recently awarded our first set of grants—$9.4 million over 3 years to support four research projects. The FDA will continue to make targeted investments in such collaborations, including, if resources are available, Centers of Excellence in Regulatory Science housed in academic settings and focused on collaborative, multidisciplinary, multisectoral regulatory science research.

With an advanced field of regulatory science, new tools, including functional genomics, proteomics, metabolomics, high-throughput screening, and systems biology, can replace current toxicology assays with tests that incorporate the mechanistic underpinnings of disease and of underlying toxic side effects. This should allow the development, validation, and qualification of preclinical and clinical models that accelerate the evaluation of toxicities during
NCTR - A Unique FDA Resource

Established in January 1971 by Executive Order as a non-regulatory national resource owned and managed within DHHS by FDA to conduct integrated, toxicological research and foster interagency, academic, and industrial collaboration in support of risk-assessment needs related to public health.

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I changed the NCTR logo to our 40th anniversary. Correct? Am not certain it is the one with the best graphics, though. May be the smaller one for emails.

dmendick, 8/8/2011
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NCTR Mission

• Conduct peer-reviewed and comprehensive toxicological research to assess safety of FDA-regulated products

• Develop new scientific approaches and methods to speed product development

• Provide multidisciplinary training in regulatory science

• Foster national and international collaborations with scientists from government, academia, and industry
The First Global Summit on Regulatory Science Research and Innovation held August 11, 2011 in Little Rock, Arkansas

**Overall Goal:** To establish a Global Coalition of Regulatory Research Scientists to work collaboratively to promote the development of regulatory science and improve public health.
Accomplishments of the Global Summit on Regulatory Science Research and Innovation held August 11, 2011 in Little Rock, Arkansas

**Outcomes:**

- Published summary (February 2012)
- Establishing systems that expand research agreements (Coalition vision and CRADAs)
- Institutionalizing international training opportunities by exploring mechanisms of support for training (ISEP)
- Building credentialing program in regulatory science and potential distance learning (MOU with Arkansas)
Innovative science to improve public health.

Workshop Report

Advancing global health through regulatory science research: Summary of the Global Summit on Regulatory Science Research and Innovation

William Slikker Jr.*, Margaret Ann Miller, Mary Lou Valdez, Margaret A. Hamburg

United States Food and Drug Administration, Silver Spring, MD 20993, United States

ABSTRACT

As a first step in the implementation of the Food and Drug Administration's (FDA) Pathway to Global Product Safety and Quality (Anonymous, 2011), FDA's Office of International Programs (OIP) and the National Center for Toxicological Research (NCTR) sponsored a Global Summit on Regulatory Science Research and Innovation. Through a series of presentations and panel discussions, the Global Summit participants explored how research could be used more effectively as a tool for advancing regulatory science, food safety, medical technologies, and public health. Speakers provided an overview of each of the components in the global regulatory-science research initiative, including scientific innovation and modernizing toxicology; and discussed how the integration of these components is needed to achieve the promise of regulatory science at the global level. All participants agreed with the formation of a Global Coalition of Regulatory Research Scientists who will work collaboratively to build knowledge, promote the development of regulatory science, discover novel ways to clearly define research needs, and improve public health.

Published by Elsevier Inc.
Global Summit on Regulatory Science (GSRS12) - Focus on Research, Innovation and Partnership

• To establish a coalition of regulatory science research partnerships;
• To explore the future of regulatory science research as a tool for advancing regulatory science, food safety, medical technologies, and public health;
• To discuss and describe the role of global research collaborations in advancing regulatory science and its impact on public health;
• To emphasize the importance of training scientists for the global regulatory science research enterprise;
• To determine the future direction for regulatory science research and innovation to promote global health.
Global Coalition for Regulatory Science Research
A Vision to Realize the GSRS Goals

Coalition for Regulatory Science Research
GSRS Board

- Kaohsiung Medical University
- Fudan University
- State Key Lab of Drug Delivery Tech and PK
- Tianjin Univ. of TCM
- KFDA NITR
- SFDA NIFDC
- US FDA NCTR
- Zhejiang University
Charge to the Board and Participants

• Establish a Global Coalition for Regulatory Science Research
  – Discuss approaches to achieving a coalition of universities, government institutions and others throughout the world to support regulatory science research
  – Evaluate instruments to actualize a functioning coalition

• Establish systems that allow expansion of research agreements
• Institutionalize international training opportunities
• Explore mechanisms to support training and regulatory science needs
• Receive nominations for the host and location for GSRS13
Global Coalition for Regulatory Science Research

Issues to be discussed:
1. How can we make progress on a common vocabulary for describing the regulatory science framework
2. How can we move toward comparable research standards on a global basis?
3. What are the criteria or credentials necessary to define a regulatory science expert?
4. Do we need global standards for the certification of laboratories to enhance global regulatory science comparability?
5. How do we train and retain regulatory scientists with desired regulatory science credentials?
6. How can this coalition efficiently serve to enhance regulatory science research on a global scale?
Regulatory Science at NCTR

- Leadership to strengthen and support science and promote innovation at FDA
- Mission critical applied research
- Scientific excellence and professional development
- Training and retention of outstanding scientists
- Collaboration and partnerships throughout the Agency and globally

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Regulatory Science

NCTR has engaged several next-generation regulatory science initiatives to increase the predictive capacity and cost-effectiveness of regulatory safety studies:

- Comprehensive whole animal studies including exposure and multiple organ system assessments,
- Development and evaluation of reliable technologies to improve or replace animal models,
- Evaluation of established, noninvasive-diagnostic clinical technologies for use in preclinical studies for hazard identification,
- Improving the efficiency of regulatory evaluation processes through use of bioinformatic technologies, and
- Exploration of new computational toxicology methods (toxicology in silico) for accurate hazard identification and development of new product leads.
Advancing FDA Regulatory Science
Science Strengths and Focus Areas at NCTR

- Safety assessment
- Bio-Imaging
- Biomarkers
- Bioinformatics
- Food safety
- Nanotoxicology
- Regulatory science training

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Interactions to Strengthen Regulatory Science and Innovation

- Arkansas: MOU on Regulatory Science
- Other agencies: NIEHS, NICHD, NCI, NIH, EPA, ATSDR, NIDA, NAS, NIH/FDA Council,
- Asia
- Europe
- South America
- Africa
- Others
Nanotoxicology

• Nanotechnology

  “Will eventually impact all Regulatory Centers and Regulated Products of the FDA”
  - Component of regulated products (e.g., drugs, sunscreens, cosmetics, food, food additives, packaging, devices)
  - Contaminant in regulated products
  - Challenge to current “safety paradigms”

• Nanotechnology Core Facility
  Supports FDA, NCTR, ARL/ORA, and NIEHS/NTP partner. Nanomaterial characterization and detection in biological matrices.

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Nanotechnology at NCTR, ORA/ARL

Research projects requested by FDA Centers (protocol-based studies)
- FDA resources
- Through NTP IAG
- Through CRADA, MOU (NCI/NCL) and MOU with Arkansas and FDA

Support/Resources
- NCTR/ORA Nanotechnology Core Facility
- UALR
- UAMS
- UA

Engage/Dialogue
- FDA
- NTP/NIEHS
- EPA
- SOT
- NNI
- OECD
- DOD

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Bio-Imaging at NCTR/FDA

MicroPET
23 cm bore

Biospec MRI
7 Tesla, 30 cm bore

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microPET images from a ketamine-treated rat using the specific tracer $[^{18}\text{F}]-\text{AnnexinV}$

$[^{18}\text{F}]-\text{AnnexinV}$

Apoptosis

Externalization of phosphatidylserine

Plasma membrane

Cytoplasm

Dendrites

Nucleus

Axon

Body
MicroPET Images of Rat Brain after $[^{18}F]$ AnnexinV administration

Control

Ketamine

5 min 10 min 15 min 20 min

25 min 30 min 35 min 40 min

Control

Ketamine
Dynamic Uptake of [18F]-AnnexinV

Innovative science to improve public health
RAPID-B™, a Flow Cytometry-Based System for the Rapid Detection of Bacterial Pathogens
Jon G. Wilkes, Dan Buzatu and Randall Tucker

Research Objectives
- Development and validation of a field-rugged, fast assay for detecting bacterial contamination of food or surfaces
- Working to develop the ability to identify viruses (food, biologics, etc.)

FDA Significance
- Interest shown by FDA regulatory centers (e.g., CBER, CVM) and commercial entities for food pathogen testing
- Results of validation testing for *E. coli* O157:H7 show 100% accuracy and the performance not affected by food matrix type
- Can detect 1 viable cell in 25 g food after 4-5 hours
RAPID-B™ Detection of Bacterial Pathogens

1. Sample (swabs, rinses, or extracts)

Time in Seconds

- Collection
- Swab Vortex
- Reagent Mix & Incubate
- Sample Loading & Run Time
- Display & Analysis

Innovative science to improve public health
Features of RAPID-B™

• The goal …”One compact, universal platform for all diagnostic testing that can be used for bacteria, viruses and toxins.”
• Limit of Detection (LOD) in the systems two operating modes:
  – Basic, Fast Mode, LOD 5 cells/mL, results in <15 minutes
  – Sensitive Mode, LOD $10^0$ (1 cell in 25 grams of food), after 4–8 hour enrichment
• Compatible with complex food matrices that are problematic to other detection platforms
• Cost is ~$15/assay
• *Salmonella* assay shows zero false positives.
• *Salmonella* assay detects almost all important serotypes, missing only those in the same serogroup as *S.* Newport. (Based on *Salmonella* infections the U.S., this represents a false negative rate of about 5-8%).
  – Work ongoing to eliminate most false negatives
MicroArray Quality Control (MAQC)

- Objective: Analyze the technical performance and practical utility of pharmacogenomics for clinical application and safety assessment

- An FDA-led community wide consortium
  - All FDA Centers have participated in the project
  - Broad participation from research community, industry, and government agencies

- Emphasized transparency
  - Results and conclusions published in peer-reviewed journals
  - Data is freely available to the public
  - Biological samples are available from commercial vendors (e.g., for MAQC-I)
MAQC-I: Are Microarrays Reliable?

Feb 2005

Six research manuscripts (2006)

1. Cross-platform consistency (e.g., one-color versus two-color arrays)

2. Microarray results versus three quantitative gene expression platforms

3. The effect of normalization methods

4. QC based on external RNA samples

5. How to obtain a reproducible results (i.e., DEGs); demonstrated in a toxicogenomics data set

6. **Main conclusion**: microarray technology is reliable if the SOP and proper analysis are followed

Nat. Biotechnol. 24(9) and 24(10s), 2006

137 participants
51 organizations

Sept 2006
MAQC-II Implementation and Findings

• Implementation
  – 6 datasets (3 preclinical and 3 clinical datasets) with 13 endpoints; 4 blind controls were embedded in the process
  – Each dataset was divided into the training set and validation set
    • A biomarker was developed on a training set and its performance was validation on the validation set
    • The validation set contains the population that is not (1) used in the training set; and (2) generated in a different date
  – 36 data analysis teams with freedom of choice of methods
  – >30,000 biomarkers were generated and statistically validated
  – Emphasized biomarker performance on the validation set

• Main findings:
  – Biomarker performance can be estimated from training
  – Endpoint is a major determining factor
  – Simple methods perform as good as complicated methods

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MAQC-II: Are Genomic Biomarker Reliable?

Sept 2006

202 participants
86 organizations

Aug 2010

www.nature.com/focus/maqc2/

Foundation for FDA Guidance …
FRIDAY, NOVEMBER 4, 2011

FDA In The News: FDA Officials Hail Increased Drug Approvals.

• The New York Times (11/4, A18, Harris, Subscription Publication) reports that officials at the Food and Drug Administration "on Thursday claimed credit for an increase in the approval of new drugs…

• CQ Health Beat (11/4, Bunis, Subscription Publication) reports that drug makers "have complained in the past that the approval process takes too long and puts the US at a competitive disadvantage with other countries." The FDA report "says that in the US, 24 of the 35 drugs approved were approvals that occurred in the United States before any other country in the world and also before the European Union." Among the successes highlighted in the report are approval of medicines for lung cancer and lymphoma that "are breakthroughs in personalized medicine," seven major improvements in cancer treatment and 10 for rare "orphan" diseases. Almost half the new approvals were viewed as significant therapeutic advances for heart attack, stroke and kidney transplant rejection, and two-thirds were completed in a single review cycle.

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FDA In The News: FDA Officials Hail Increased Drug Approvals.

- Reuters (11/4, Yukhananov, Selyukh) Janet Woodcock, the director of the FDA's Center for Drug Evaluation and Research, said that the higher number of approvals did not stem from the agency receiving significantly more applications, but from getting better-quality applications.

- Senator's Op-Ed Calls For Further Innovation, Adequate FDA Funding. In a Washington (DC) Examiner op-ed (11/3), Sen. Michael Bennet (D-CO) writes that a recent report from the National Venture Capital Association's MedIC Coalition... credits FDA Commissioner Hamburg for pushing to modernize the agency and improve its regulatory processes, citing as "initial successes" its "Advancing Regulatory Science" initiative...
November 28, 2011

FDA In The News: **Novartis CEO Says FDA Has Improved Under Hamburg.**

- **In a Smart Money interview (11/28, Prior),** Novartis CEO Joe Jimenez, asked whether it was frustrating to deal with the Food and Drug Administration when seeking to get a drug approved, replied, “There’s a new level of predictability since Peggy Hamburg came in as FDA commissioner [in 2009]. So we’re not frustrated, because we understand how to react now to discussions that we have with them, which wasn’t the case just a few years ago.” Asked to explain, Jimenez added that, “historically, the FDA hasn’t been as science-based as some of the other regulatory agencies around the world. The debate has been more political, but now it seems like there’s a very strong science base being brought to decision making. And to me, that’s a positive.”
Globalization: Impact on training needs

- Half of all medical devices used in the US are imported.

- 40% of finished drugs and 80% of APIs (Active Pharmaceutical Ingredients) are imported from more than a 150 countries.

- 35% of all fresh produce originate outside of the US.

- Imports of APIs grew from $2.8 billion in 2000 to nearly $4.6 billion in 2007.

- Imports of pharmaceutical products have grown at about 13% per year for the past seven years.

- China has tripled its annual R&D investment over the past 15 years and will likely have the largest R&D workforce in the world by 2015.

Source: Deb Autor, FDA WebView, 09/19/2011

Innovative science to improve public health

• Diverse research training portfolio at NCTR:
  – Postdoctoral training program through ORISE
  – FDA Commissioner’s Fellowship Program
  – Summer student training program
  – STEP program (Science Training and Exchange Professional Development Program)
International Scientist Exchange Program (ISEP) – A New Training Program With Focusing On Global Reaching

• Established in 2009 and cooperated with the FDA’s Office of International Programs
  – Provides funding for Foreign Regulatory Scientist to visit NCTR to learn core competencies of regulatory research by conducting state-of-the art research
  – Continued support of scientists in their home country to strengthen national regulatory systems

• Goals
  – Prepare international regulatory scientists for regulatory science
  – Generate opportunities for tomorrow’s leadership
>1000 Scientists from 47 Countries Have Been Trained at NCTR
Summary

• Regulatory Science promotes innovation and partnership
• NCTR advances Regulatory Science by promoting and conducting innovative research
• Research training is a key mechanism of advancing Regulatory Science
• NCTR has implemented diverse research training programs with emphasis on Regulatory Science
• Regulatory Science in the global context: Global training for global health and safety
• NCTR leadership of Regulatory Science research is needed and seems to be generating positive outcomes