Current Device & Biopharma Trends
Medical Countermeasures Trends

- Impacts of the Ebola Outbreak in West Africa include:
  - EUA granted to EZ-1 Assay; research jumpstarted.
  - Higher visibility of medical countermeasure (MCM) gaps for protection against chemical, biological, radiological, or nuclear attacks;
  - Consideration of Priority Review Vouchers for MCMs;
  - Reevaluating the impact of the Emergency Use Authorization (EUA) provisions of the FD&C Act
  - Reevaluating the utility of the animal rule as an effective pathway for the development of MCMs.
Medical Countermeasures Trends

- Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)
  - Increased coordination between BARDA, NIH, FDA, CDC, DoD, DHS

- Re-evaluation of some elements of Federal procurement law
  - TRLs
  - Advanced development vs. basic and applied
  - FAR and DFAR provisions
Medical Device Trends

- Vexation over Medical Technology Innovations that outpace FDA’s regulatory response:
  - Mobile Medical Apps
    - Transforms a mobile platform (e.g., smartphone) into a regulated medical device or
    - Is used as an accessory a regulated medical device
  - Medical Device Data Systems
    - Class 1 low-risk devices
    - Hardware and software products used with medical devices
    - Ensures reliability of data stored, transferred, or displayed
Medical Device Trends

- Clash over Regulation of Laboratory Developed Tests (LDTs)
  - type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory
  - While the uses of an LDT are often the same as the uses of FDA-cleared or approved in vitro-diagnostic tests, some labs may choose to offer their own test.
  - Range of complexity and risk related to the conditions being tested for.
  - FDA concerned about the high-risk LDTs and the pervasiveness of multiple-lab LDTs
Medical Device Trends

- Clash over Regulation of Laboratory Developed Tests (LDTs)
  - FDASIA required Congressional notice before FDA issued any guidance on LDTs
  - Several notice documents published explaining how FDA will exercise its risk-based enforcement discretion on LDTs
    - Draft Guidance for Industry, Food and Drug Administration Staff and Clinical Laboratories – FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs) (Oct. 3, 2014)
Clinical Trends

- Inconsistent application of advance informed consent procedures between HHS’ Common Rule and FDA’s informed consent procedures.
  - 21 CFR 50.24 provides for emergency research with an investigational device where there “is a direct benefit to the patient”
  - 32 CFR 219.116(d) “Common Rule” permits waiver where there is “no more than minimal risk” to the patient.
  - Distinctions are particularly onerous on medical device investigations where there is “no direct benefit to the patient” and no ability to obtain advanced informed consent due to emergency circumstances.
Regenerative Medicine Trends

- Stem Cell-Based Therapies
  - Regenerative medicine community frustrated with the pace of innovations and FDA’s restrictive regulation of autologous use of stem cells.
  - A §361 Tissue under 21 CFR §1271.10(a) is one that is:
    - No more than minimally manipulated;
    - Intended for homologous use (same function in recipient as in donor)
    - Not combined with another drug or device;
    - Not have a systematic effect or depend on the metabolic activity of living cells for its primary function.
  - 21 CFR §1271.15(b) Autologous Use (use in same individual it was harvested from vs. allogeneic) in same procedure excluded.
Regenerative Medicine Trends

- Stem Cell-Based Therapies (cont.)
  - Some parts of industry and academia argue that autologous use should be permissible without regard to whether it could cross the line into a §351 biologic because the risks are significantly reduced when introducing the tissue into the same patient.
  - R&D community argues that this is limiting the innovation that is needed in the regenerative medicine field.
  - Other international regulatory bodies have created exceptions.
  - Congressional intervention likely needed to resolve this.
Biosimilar Trends

- Biosimilar User Fee Act, or BsUFA, was enacted as part of the FDA Safety and Innovation Act (Public Law No. 112-144, enacted on July 9, 2012).
- On March 6, 2015, FDA approved the first biosimilar, Zarxio (filgrastim-sndz), a biosimilar to Neupogen (filgrastim), to help stimulate growth of white blood cells in patients with cancer and help them fight infection.

Upcoming Guidance are expected to include:
- Considerations in Demonstrating Interchangeability to a Reference Product
- Statistical Approaches to Evaluation of Analytical Similarity Data to Support a Demonstration of Biosimilarity
- Labeling for Biosimilar Biological Products
Biosimilar Trends

- As of July 31, 2015, 57 proposed Biosimilar products to 16 different reference products were enrolled in the Biosimilar Product Development (BPD) Program.
  - created as a part of BsUFA to provide a mechanism and structure for the collection of development-phase user fees to support FDA’s biosimilar review program activities
  - BsUFA program established five meeting types specific to biosimilar development programs
- Guidance describing the use of a non-U.S.-licensed comparator in certain studies based on an adequate scientific bridge between the U.S.-licensed reference product and a non-U.S.-licensed comparator product.
Biosimilar Trends

- **Tuffs Center for the Study of Drugs 2015 Forecast:**
  - 4th Quarter of 2014 several hundred companies were testing biosimilars, with 30 to 40 molecules in late-stage trials in the U.S. and the European Union
  - Drug companies and CROs together will make greater use of adaptive trial designs and mining big data for biosimilar approval.

- **Biosimilar “Patent Dance” Litigation Hotly Contested**
  - Dispute resolution mechanism, part of which was recently deemed optional. Sandoz did not disclose its manufacturing processes and FDA application to Amgen, the patent holder for Neupogen (filgrastim).

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Biosimilar Trends

- Biosimilar “Patent Dance” (cont.)
  - Amgen vs. Hospira concerning biosimilar version of EPOGEN (epoetin alfa) on patent dance and 180 commercial marketing notice provision of BPCI.
  - Each BPCI patent dance lawsuit has a chance to alter the future course of law related to biosimilars

- Biosimilar Litigation in General
  - When will FDA get challenged over its implementation of the statute? This is inevitable.
  - Heavyweight battle? Perhaps over Avastin (Amgen and Allergan facing off against Roche and Genentech)?
**21st Century Cures Act**

- H.R. 6, “The 21st Century Cures Act” passed the U.S. House of Representatives on 7/10/15 and awaits consideration in the U.S. Senate
  - Follows the pattern of omnibus healthcare legislation that, in part, amends the FD&C Act and augments FDA’s processes and authorities.
  - Reported out of the House Energy & Commerce Committee with considerable bi-partisan support.
  - Aims to fund increase in “hard appropriated dollars to NIH ($1.75 Billion) and FDA ($550 Million)
  - Goal: to deliver new medical interventions to patients.
21st Century Cures Act

FDA-Related Provisions:

  - Requires FDA to implement framework in new drug review process that considers patient experiences in risk-benefit determination.

- **Title II.B, §2021, “Qualification of Drug Development Tools”**
  - Would codify FDA’s framework for submission, review and qualification of biomarkers and other DDTs for specific contexts of use that, if qualified, can be relied on by others.
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II.B. §2022 – Accelerated Approval Development Plan
    - Enables Sponsor of a drug that FDA determines is eligible for accelerated approval to request voluntarily that FDA agree to an accelerated approval development plan.
    - Unclear if this is Accelerated Approval + Special Protocol Assessment like tool.
  - Title II.C. §2041 – Precision Medicine Guidance
    - Requires FDA to issue guidance defining the term “precision drug or biological product” and authorize the agency – in a situation where the product is for a life-threatening disease condition or is designated as such – to rely upon data submitted by the sponsor for a different drug or biological product that incorporates or utilizes the same or similar underlying approach.
21st Century Cures Act

FDA-Related Provisions (cont.):

- Title II.D. §2062-2063 – Clinical Data
  - Requires FDA to establish a program to evaluate the potential use of evidence from clinical experience to help support approval of
    - New indication for a previously approved drug or
    - Satisfy post-approval study requirements.
  - Streamlined data review whereby Sponsor may submit summary of clinical data for new indication for the treatment of cancer and other types of indications.
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II.E. §2983 – Finalizing Guidance on Expanded Access
    - Requires certain mfrs. of investigational products to publish their expanded access policy. Requires FDA to issue Guidance on how to deal w/ adverse events experienced through an expanded access program.
  - Title II.F §2102 – Responsible Communication of Scientific and Medical Developments
    - Requires FDA to issue Guidance (w/in 18 months) to clarify how drug and device mfrs. Can permissibly disseminate truthful and non-misleading scientific and medical information about a drug or device that is not included in the approved labeling for the product.
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II. G. §§2121-2123 Antibiotic Drug Development
    - Builds on FDASIA’s GAIN Act to facilitate the development of new antibacterial or antifungal drugs through a new FDA approval pathway (for “DISARM Drugs”) and creating economic incentives for new drug development.
    - Allows for “limited patient populations” where there is an “unmet medical need”
    - Label must bear “limited population”
    - ***conforming amendment makes it (and GAIN) applicable to biologics licensed under the PHSA.
    - Ability to expand new §505(z) to other life-threatening diseases or conditions.
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II. I, §2151 – Orphan Products Extensions
    - Incentivizes repurposing of major market drugs for rare diseases. Provides a one-time, six month extension of certain exclusivity periods and patent protection for an already-approved drug if the drug’s sponsor obtains approval of a new indication for the rare disease or condition.
  - Title II. I, §2152 – Reauthorization of Rare Pediatric Disease PRV Incentive Program
    - Reauthorizes the rare pediatric disease priority review voucher enacted under FDASIA through 12/31/18
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II.L, §2201 – Priority Review for Breakthrough Devices
    - Requires FDA to establish a program to provide priority review for qualifying medical devices. Allows FDA sufficient flexibility to efficiently review devices that represent breakthrough technologies.
  - Title II.N, §§2241-2243 – Exclusion from Definition of Device
    - Resolves the confusion around the current regulatory approach for health technologies, include health software and wireless platforms, by updated statutory texts to create clarify for developers and reviews. Excludes “health software”
21st Century Cures Act

- FDA-Related Provisions (cont.):
  - Title II.O, §§2261-2263 Streamlining Clinical Trials
    - Requires HHS to harmonize the difference between the Common Rule for human subject protections and the FD&C Act human subject protections. Streamlined IRB process and eliminates advanced information consent process for medical device tests that pose “no more than minimal risk” to the patients while include appropriate safeguards