FDA Update:
The Impact of FDASIA and The Elections

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What I Will Cover

• The Election and the Political Arena
• **FDASIA** – The Food & Drug Administration Safety & Innovation Act of 2012
  – User Fees (only briefly)
  – Drug Provisions
  – Device Provisions
  – General Provision
• Other Trends
The Election and Political Arena
FDA -- Future under Obama 2

• **FDA – Commissioner Hamburg will remain**
  – Has shown indicia of understanding industry impacts
  – But, will be under pressure due to New England Compounding Center scandal to aggressively protect the public health
  > Enforcement – look for it to be even more aggressive
  > “Park Doctrine” – keep an eye out for more use

• **Sequestration** –
  – if it occurs, will lop about $320,000,000 off FDA budget in FY 2013 (which started on 10/1/2012)
  – ± 1,000 FDA employees if bulk of cuts taken from staffing
  – will impact user fee programs as well
FDASIA
Pediatric Drugs

- **PREA (Pediatric Research Equity Act) and BPCA (Best Pharmaceuticals for Children Act) –** made permanent (they were subject to sunset).
  - still must have a written request to do pediatric studies to get the 6-month exclusivity
  - PREA studies are eligible to qualify for exclusivity if in a written request

- **Initial pediatric plan –** FDASIA requires the submission of the plan no later than 60 days after the End of Phase 2 (EOP2) Meeting – outline of studies and any request for waiver or deferral
Rare Pediatric Drug Voucher Program

• “Priority Review Voucher” – for approval of a product for a “rare pediatric disease” – i.e., one that is an orphan that primarily affects children up to age 18 \[\S\ 529(a)(3)\]

• Get voucher that can be used for a later NDA to get priority review (even if not entitled otherwise)

• Limits:
  – drug must be a new chemical entity
  – can’t seek approval in adults in the application
  – must request designation as a rare pediatric disease at same time as requesting orphan status or fast track designation
  – have to market within 365 days of approval or voucher may be revoked
Accelerated Drug/Biologic Approval

• “Serious or life-threatening *disease* or condition”
• Fast track = accelerated situation with an unmet need
• Based on:
  – determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.” § 506(c)(1)(A)
Accelerated Drug/Biologic Approval …

- Evidence to support that a drug has the effect required (see prior slide) – may come from:
  - epidemiological, pathophysiological, therapeutic, pharmacologic, or other evidence developed using biomarkers, for example, or other scientific methods or tools.” §506(c)(1)(B)

- Still have to do post-approval studies –
  - but, those studies no longer have to validate a surrogate endpoint or confirm effect on the clinical endpoint
  - rather, “verify and describe the predicted effect on the irreversible morbidity or mortality or other clinical benefit”
Breakthrough Therapies

- **FDA may accelerate approvals -- § 506(a)(1)**

- **Defined as a drug intended to treat, alone or in combination:**
  - a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development

- **Designation -- any time at or after submitting IND**
  - FDA – 60 days to decide if a breakthrough therapy
  - If designated, FDA must act to “expedite development and review of the application” via such measures as meetings and development advice
  - Guidance – no later than January 2014
Other Drug Provisions

• **Orphan Drugs**
  – Grants program –
    ➢ extended through 2017
    ➢ appropriates $30 million per year for grants
  – Eliminated need for qualifying testing costs to occur after the product is designated an orphan

• **Risk-Benefit Decisions** – amends § 505(d) to mandate that FDA:
  – “implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs.”
Drug Supply Chain

• **Unique Facility Identifier (UFI)** – to be created along with an electronic database

• **Drugs (or devices) imported from unregistered foreign facilities** – deemed misbranded (means they can be detained under § 801 of Act)

• **Drug will be deemed adulterated** -- if made, processed or packed at a facility where owner/operator delayed, denied, or limited an inspection or refused to permit entry or inspection

• **GMPs** – law amended to make clear that oversight of suppliers is a GMP duty for drug makers
Drug Supply Chain …

• **Inspection schedule** – is supposed to be risk-based; focusing on several factors in § 510(h)(4)

• **Foreign government inspections** – FDASIA authorizes FDA to make pacts to recognize foreign inspections – in § 809(b)

• **Demand for documents** – in advance or in lieu of an inspection, FDA may require a drug maker to provide records to FDA – amends § 704(a)

• **Extraterritorial jurisdiction** – granted to FDA over any violation of the Act for any article intended for import into the U.S. -- § 311 – broad inspection power
Drug Supply Chain …

- **Commercial drug importers** – must register with FDA; failure to do so will render the imported drug misbranded
  - “Good Importer Practices” to be established by regulation by July 2015 by which importers must be able to ensure that imported drugs comply with the Act and/or the Public Health Service Act (PHSA) for biologics

- **New “Admission Standards”** – to be implemented by regulation by FDA by January 9, 2014
  - allows FDA to take a risk-based approach to vetting drug imports
  - importers can be required to submit info electronically
Drug Supply Chain …

- Increased penalties for knowing adulteration of a drug that causes serious adverse health consequences or death in humans or animals
  - Prison – up to 20 years; and/or
  - Fine -- $ 1 million

- Trafficking in counterfeit drugs – now a federal criminal code violation – 18 USC § 2320(a)(4)
  - Prison – up to 20 years; and/or
  - Fine -- $ 5 million
Antibiotics – G.A.I.N.

• Generating Antibiotic Incentives Now (G.A.I.N.) – new § 505E of the Act
  – “Qualified Infectious Disease Product” (QIDP) – adds five years to existing Waxman-Hatch exclusivity (including extending, for NCE, period during which ANDA can’t be filed, from 4 to 9 years)
  – QIDP – “an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by …”
    ➢ an antibacterial or antifungal resistant pathogen; or
    ➢ certain “qualifying pathogens”
Antibiotics – G.A.I.N. …

• **“Qualifying Pathogens”** – to be included in a list to be maintained by FDA – includes those pathogens that:
  – have potential to pose a serious risk to public health (e.g., resistant gram positive; multi-drug resistant gram negative bacteria; multi-drug resistant TB; and *Clostridium difficile*)
  – list to be made not later than July 9, 2014

• **QIDP Designation** – may be requested any time before submitting an NDA
  – FDA must decide within 60 days

• **Implementing regulations** – due by July 9, 2014

• **Priority Review** – post-FDASIA QIDP NDAs – get
Medical Devices

- **Investigational Device Exemptions (IDE)** -- amended § 520(g) of the Federal Food, Drug, and Cosmetic Act (“the Act”) to make clear that an IDE study did *not* have to be likely to support a PMA or 510(k) –
  - a draft FDA guidance had suggested this was needed
  - allows for more developmental studies under IDE process

- **Least Burdensome Standard** – clarified what is “necessary” in the way of clinical studies to be those that are the “minimum required information” to support a PMA or 510(k)
Medical Devices …

- **Decision Making and Documentation – new § 517A**
  - FDA must document the scientific and regulatory rationale for “significant decisions” (not defined) on IDEs, 510(k)’s, & PMAs
  - **Documentation**
    - must note “significant controversies or differences of opinion” and how resolved
    - applicants are to be given documentation upon request
  - **Appeals**
    - have 30 days to appeal significant decisions
    - have right to a telephone or in-person meeting
    - FDA has 45 days to decide the appeal (30 days if a meeting held)
Medical Devices …

• **Modifications to 510(k)’d Devices – adds § 510(n)(2)**
  – Withdraws the 2011 draft guidance on 510(k) changes
  – Reverts back to the 1997 guidance
  – 18 months for FDA to report to Congress on how to properly handle changes to 510(k) clearances
  – No new guidance allowed during the 12 months after report goes to Congress

• **Recalls – new § 518A**
  – FDA must create a program to assess information on device recalls, removals and corrections
  – Use info to identify strategies to mitigate risk from devices
Medical Devices …

* IDE Clinical Holds
  
  - Amends § 520(g) to give FDA specific authority to issue a clinical hold if FDA finds that a device presents an unreasonable risk to subject’s safety or other reasons (to be established by regulation)
  
  - Determination of unreasonable risk must assess
    - qualifications of investigators
    - information about the device
    - study design
    - the condition for which the device is being studied; and
    - health status of subjects
  
  - FDA must provide written decision within 30 days of request by sponsor to lift hold
Medical Devices …

• **De Novo Petition Changes** – changes to § 513(f)(2)
  – eliminates need to submit a 510(k) first and have it declared non-substantially equivalent (NSE)
    ➢ can directly request
    ➢ can include draft of special controls that would apply
  – FDA has 120 days to decide
  – FDA can decline if:
    ➢ concludes device belongs in Class III;
    ➢ that appropriate special controls are not possible; or
    ➢ identifies an appropriate predicate
Medical Devices …

• **Reclassification** – amends § 513(e)(1)(A)(i) to allow for reclassification petitions to be done by administrative order, rather than regulation
  – obviates need for formal notice and comment rulemaking
  – can be initiated by FDA or upon petition

**BUT**

– still must:
  - be published in Federal Register
  - hold a classification panel meeting
  - consider comments in docket
Medical Devices …

• **Third-party review and inspection programs** – reauthorized until 2017

• **Humanitarian Device Exemption (HDE)** – now can make a limited profit. Previously, only pediatric devices qualified -- §520(m)(6)(A)

• **Unique Device Identifier (UDI)** –
  - required FDA to issue proposed rule by 12/31/2012; actually proposed in July (77 Fed. Reg. 40735; July 10, 2012)
  - FDA has 6 months from close of comment period to finalize rule – comment period expired November 7 – so final rule due on May 7, 2013
Medical Devices …

- **Postmarket Surveillance**
  - Authority to order now can be exercised at time of FDA clearance or approval
    - device maker has 30 days to submit a plan after getting order
    - FDA has 60 days to review plan
    - 36 months or longer (if FDA and maker agree)
    - Surveillance must start within 15 months of FDA order
  - Devices subject to postmarket surveillance:
    - failure would reasonably have serious adverse health consequences
    - significant use in pediatric populations
    - intended to be implanted for more than 1 year
    - life-sustaining or life-supporting (used outside a device user facility)
Medical Devices …

• **Mobile Apps** – FDA required to issue a report by January 9, 2014 on a proposed strategy and recommendations for a risk-based approach to health information technology
  – must consult with FCC and the National Coordinator for Health Information Technology (within HHS) in preparing report

• **Laboratory Developed Test (LDTs)** – FDA must notify Congress at least 60 days prior to issuing a draft or final guidance on LDTs
Electronic Submissions

- **Drugs** – to be required no earlier than 24 months after FDA issues a final guidance – applies to: INDs, NDAs, ANDAs, BLAs (including biosimilar apps.)

- **Devices** – applies to 510(k)’s, PMAs, IDEs, and a number of other device submissions
  - after a guidance document is finalized
  - language is “shall include” an electronic copy, which implies it can still be submitted in paper format
Miscellaneous Provisions

• **Internet & Social Media** – FDASIA § 1121 orders FDA to issue guidance on its policy on the use of the internet, including social media, in promoting medical products -- due by July 2014

• **Acceptance of Foreign Data** – new § 569B – FDA must accept if applicant shows that data are adequate to support approval, clearance or licensing; *or*
  – FDA must notify sponsor of rationale why data are not OK

• **Conflicts of Interests** – loosened § 712 to allow FDA advisory committees to have better access to experts
Other Trends
FDA Reorganizations

• Center for Drugs – FDA considering:
  – **Generics** – to be a “super” office reporting directly to Woodcock
  – **Office of Pharmaceutical Quality** – entire lifecycle view

• Office of Device Evaluation – 2 new review divisions:
  – Surgical Devices
  – Neurological and Physical Medicine Devices,
  – Existing five divisions are:
    ➢ Anesthesiology, General Hospital, Infection Control, and Dental
    ➢ Cardiovascular –
      ▪ is now handling 30-day notices on changes that were in CDRH Office of Compliance
    ➢ Surgical, Orthopedic, and Restorative
    ➢ Ophthalmic, Neurological, and ENT
    ➢ Reproductive, Gastro-Renal, and Urological
FDA Reorganizations …

• **OIVD – now OIR – Office of In Vitro Diagnostics and Radiological Health** -- covering radiological and mammography devices both for market clearance and post-marketing roles

• **CDRH Compliance Office** – going to 5 divisions
  – Adding International Compliance Operations Division
  – Adding Premarket and Labeling Compliance Division
  – Combining two enforcement divisions into a Division of Manufacturing Quality
  – Bioresearch Monitoring (BIMO)
  – Risk Management Operation
FDA Reorganizations …

• **Office of Regulatory Affairs – FDA “Top Cop”**
  
  – Dara Corrigan – current head – to Brussels to head FDA’s European office and be Senior Advisor for Global Operations
  
  – creating **Office of Operations** – with oversight over:

  ➢ folding 4 existing offices (Enforcement, Regional Ops, and Domestic Field Investigations, & Foreign Field Investigations) into 3 new ones:
    
    ▪ Office of Food and Feed Operations
    ▪ Office of Medical Products and Tobacco Operations
    ▪ Office of Enforcement and Import Operations (OEIO)
  
  – new **Office of Policy & Risk Management**

  – no impact on field structure
Hurricane Sandy and IRBs -- OHRP

- HHS Office of Human Research Protection – e-mail November 13 -- expressing flexibility on situations where IRBs cannot function due to Sandy. **Key issues:**
  - **Continuing review for expiring research:**
    - Ideally – refer research to another IRB for continuing review
    - But, what if not possible and prior IRB approval expires:
      - Refer to another IRB (if records accessible)
      - If not possible to refer, “expired” research can continue if in best interests of subject
  - **May subjects be treated elsewhere at a facility that lacks an FWA or IRB** – research can be done if in best interests of subject
Questions?

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About Your Speaker

*Michael A. Swit, Esq.*, is a Special Counsel in the San Diego office of the international law firm, Duane Morris, LLP, where he focuses his practice on solving FDA legal challenges faced by highly-regulated pharmaceutical, medical device and food companies. Before joining Duane Morris in March 2012, Swit served for seven years as a vice president at The Weinberg Group Inc., a preeminent scientific and regulatory consulting firm in the Life Sciences. His expertise includes product development, compliance and enforcement, recalls and crisis management, submissions and related traditional FDA regulatory activities, labeling and advertising, and clinical research efforts for all types of life sciences companies, with a particular emphasis on drugs, biologics and therapeutic biotech products. Mr. Swit has been addressing vital FDA legal and regulatory issues since 1984, both in private practice with McKenna & Cuneo and Heller Ehrman, and as vice president, general counsel and secretary of Par Pharmaceutical, a top public generic and specialty drug firm. He also was, from 1994 to 1998, CEO of FDAnews.com, a premier publisher of regulatory newsletters and other specialty information products for FDA-regulated firms. He has taught and written on many topics relating to FDA regulation and associated commercial activities and is a past member of the Food & Drug Law Journal Editorial Board. He earned his A.B., *magna cum laude*, with high honors in history, at Bowdoin College, and his law degree at Emory University.