The Role of FDA in regulating Diabetes Devices and Advancing Safe Innovation in the Management of Diabetes

Bay Area Diabetes Summit

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Agenda

- General introduction to FDA and In Vitro Diagnostic Devices (IVD) regulation
- How does FDA regulate IVDs?
  - Device Classification
  - Premarket Review
  - Postmarket Requirements
- Diabetes Diagnostic Devices: Where are we now?

Diabetes

- People with diabetes face many challenges:
  - Immediate risks everyday due to potential for severe hypo- and hyperglycemia
  - Long-term heath risks due to glycemic variability and hyperglycemia
- Quality of life challenges
  - The need for multiple devices (meters, pumps, insulin pens, lancets, etc…)
  - Pain at lancing and injection sites
  - Complicated drug dosing and nutrition decisions
  - Data overload can be frustrating (e.g., CGM data)
- Needs:
  - Devices that improve lives without adding complexity
  - Simple, easy to interpret device data outputs
  - Easy to use, safe, and effective medical products

U.S. Food and Drug Administration
Protecting and Promoting Public Health

www.fda.gov

Center for Food Safety and Applied Nutrition

Office of Regulatory Affairs

Center for Devices and Radiological Health

FDA

Center for Biologic Evaluation and Research

Center for Drug Evaluation and Research

Center for Tobacco

Center for Veterinary Medicine

Protect and Promote Public Health

Who Are We?

- Center for Devices and Radiological Health/ Office of In Vitro Diagnostics and Radiation (OIR)
- Division of Chemistry and Toxicology Devices: Courtney Lias, Ph.D., Director
- Diabetes Diagnostic Devices Branch: Katie Serrano, Branch Chief
- 44 staff and managers in the Division
- Approximately 40-45% of Division work is directly Diabetes-related
  - Blood Glucose Meters
  - Point-of-Care glucose analyzers
  - Central Laboratory analyzers
  - Blood gas analyzers
  - HbA1c tests
  - Continuous Glucose Monitoring Systems (CGMs)
  - Artificial Pancreas Systems
- Other Divisions – insulin pumps (not CGM-enabled), insulin pens, lancets, etc.

FDA Regulation of Medical Devices

1976 Device Amendments modified the Act to provide for the regulation of Medical Devices

- Medical Devices: "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent or similar related article. . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals" (FFDCA 201(h))

Medical Devices

- Glucose Meters
- Artificial Hearts
- Drug Eluting Stents
- Hospital Beds
- Thermometers
- Tongue depressors
- Insulin Pumps
- Artificial Pancreas
- In Vitro Diagnostic tests (IVDs)

What is an IVD?

- IVDs are a subset of medical devices which are "**reagents, instruments, and systems** intended for use in the **diagnosis of disease or other conditions**, including a determination of the state of health, in order to cure, **mitigate, treat, or prevent disease or its sequelae"** (21 CFR 809.3)

- Used in:
  - Clinical laboratories
  - Point-of-Care
  - Over-the-Counter


AmpliChip
CYP450 Array
Pregnant
Not Pregnant
A rapid test for early detection of influenza A and B in a point-of-care setting benefits doctor, patient, and the community at large

Risk-Based Classification of IVDs:

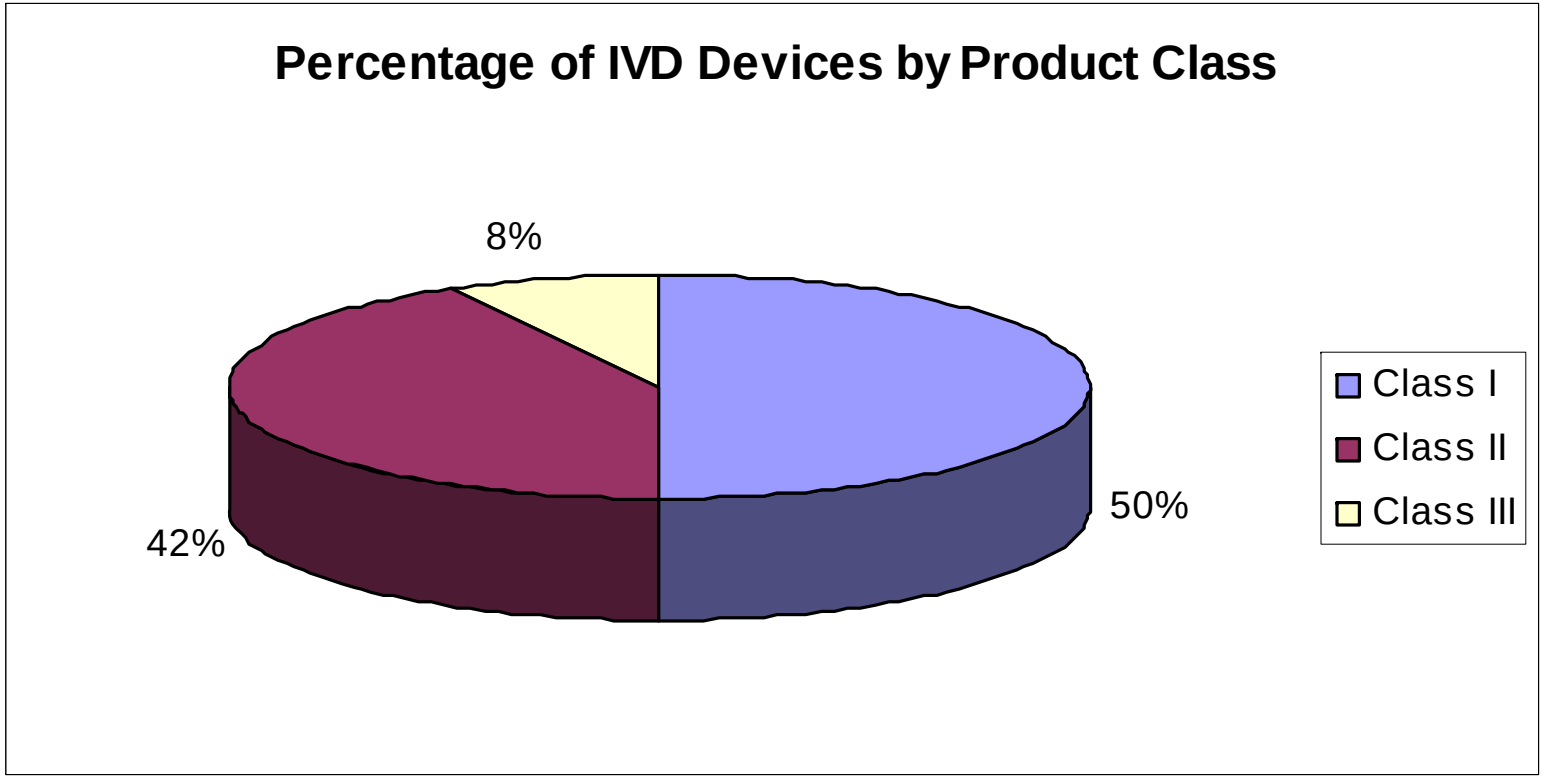
- The classification of an IVD is risk-based, and determined based upon the intended use of the device
- The risk of an IVD is based on the consequences of a false result
- Three Classification levels
  - Class I: **common, low risk devices**
  - Class II: **more complex, moderate risk**
  - Class III: **most complex, high risk and novel intended uses**

Intended Use

The Intended Use is the driving force of the review:

- Disease/condition
- Purpose, e.g., screening, diagnosis
- Population, e.g., men over 65 years of age
- Nature of result, e.g., quantitative
- Setting, e.g., point of care
- Instrument requirements

IVDs: Classification Breakdown



Class I IVDs

- Represent common, low-risk devices
  Example: OTC cholesterol Test
- Most exempt from premarket submission

Class II IVDs

- "Moderate risk" devices, tend to be more complex
- Examples:
  - Blood glucose meters
  - Insulin Pumps
- Usually require premarket review in the form of a premarket notification [510(k)] submission

Premarket Notification: 510(k)

- 510(k) submission required of most class II devices
- Submission has 90 day review clock
- FDA clearance based on “substantial equivalence” to legally marketed device (predicate device)
- What substantial equivalence to predicate device means:
  - Similar intended use
  - Similar performance characteristics
  - Similar fundamental scientific technology
- What substantial equivalence may not mean
  - Identical technology
- Submissions may require clinical data
- Summary of FDA’s review and basis for decision is posted on the FDA website

Class III IVDs

- Represent highest risk intended uses
  - Sometimes includes devices with new intended uses, technologies/methodologies, scientific questions
  - Examples:
    - Hepatitis B and C, HPV tests
    - Continuous Glucose Monitors
    - Artificial Pancreas Devices
- Premarket Application [PMA]
- Submissions often include clinical data

Premarket Application (PMA)

- 180 day review clock
- Demonstration of safety and effectiveness
- Does not use predicates
- Submissions often include clinical data
- Pre-approval inspection performed
- FDA may seek advisory panel decision prior to approval
- Summary of Safety and Effectiveness Data (SSED) posted publicly on web

Premarket Review

- Assessing Safety
  - Risk of misdiagnosis due to a false positive or false negative result
  - Assessing warnings against unsafe use
- Demonstrating Effectiveness
  - Assessing device performance characteristics
  - Directions and conditions for use

Analytical Validity

- Repeatability/Reproducibility
  - Will I get the same result in repeated tests over time?
  - Will I get the same result as someone else testing the same sample?
- Accuracy
  - Will I get results that are the same as “Truth”?
  - “Truth” – may be a reference method, clinical endpoint, predicate device, etc.

Example: Blood Glucose Meter

Blood Glucose Meter: Analytical Performance

- Precision SEB4
- Measurement Range
- Accuracy: Percent of Readings within 5, 10, 15 % of reference- example 95% w/in 15%, 100% w/in 20% SEB3
- Interference
  - Hematocrit
  - Altitude
  - Temperature

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SEB3 Add example table
Beck, Stayce E, 2/24/2014

SEB4 add examples of what would see
Beck, Stayce E, 2/24/2014

Clinical Performance

- Clinical Validity
  - Device must have a clinical indication
  - Device should add value to clinical management
- Clinical Validity claims may be based on:
  - Existing clinical data (i.e. no new clinical data needed)
  - New clinical trial data
  - Review of information in the literature SEB5
  - Current clinical knowledge

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SEB5 add example for CGM/artificial pancreas
Beck, Stayce E, 2/24/2014

Over the Counter

IVDs for consumer use (OTC) have additional requirements:

- Data submitted to demonstrate that the tests are accurate in the hands of lay users (including sample collection)
- Studies are performed to evaluate how well lay users can understand the instructions without prompting, perform a self-test (or collect a sample), and obtain an accurate result
- **Lay users' ability to understand the results of the test are also evaluated**
- Human factors are also considered in the review, where applicable

Post Market

Quality System Regulation (QS Reg)

As per 21 CFR Part 820

- Requires that manufacturers have an **appropriate** quality system and policies in place for their manufacturing operation
- Regulation designed to be flexible for both large and small manufacturers
- Appropriate trained personnel and facilities
- Correction and prevention system
- Complaint handling
- Documentation

Medical Device Reports (MDRs)

- Reports to FDA by user facility/manufacturer when a device:
  - Caused or contributed, or may have caused or may have contributed to a death
  - Caused or contributed, or may have caused or may have contributed to a serious injury
  - Malfunctioned or failed to meet specifications (manufacturer only): Recurrence could result in death or serious injury
- Required timeframe for reporting
  - 5-30 days, depending on severity
  - Follow-ups when needed
- FDA assesses reports and decides if action is needed
- Anyone can report! We have a smart phone app!

Slide 26

SEB6 give some examples, and explain difficulty with relation to diabetes
Beck, Stayce E, 2/24/2014

Recalls

- Method of removing or correcting products that are in violation of laws
- Products present a risk of injury or gross deception or are otherwise defective
- Usually voluntary by manufacturer, but must be reported to FDA
- Recall information posted on the website:

  http://www.fda.gov/

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SEB7 give example of abbott test strip recall

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Diabetes Diagnostic Devices: Where are we now?

Glucose Meters

- Improvements in consumer features over the last few years
- Improvements in interference detection
- FDA published two draft blood glucose meter guidances in January 2014

These improvements have made patients safer,
and they will continue

Draft Glucose Meter Guidances

- Increased Accuracy
- Accuracy of meter on the outside of the box
- Studies to make sure meter works in different environments
- Provide comments- what you like and don't like by April 6, 2014!
- Draft documents can be found at:
  - Regulations.gov
  - Please comment
    - **If you don't like something, please send suggestions** that you would like to see along with your comment
    - If something isn't clear, let us know we should try to clarify it
    - **If you like something, please comment specifically on that** as well so we can have a balanced picture of feedback from all stakeholders

- Finalization process

Post Market Safety

- **>25,000 Medical Device Reports/year for blood glucose meters**
- **Variability in quality of reporting, decision-making at firms**
- **Challenges:**
  - High volume of data
  - Low quality data
  - Inconsistent compliance
- **Solutions**
  - New methods for data analysis
  - Developing guidance for manufacturers
    - Clarify reporting criteria/methodology
    - Increase consistency across manufacturers
  - Potential new surveillance program?

Continuous Glucose Meters

- CGMs are home use devices that continuously measure glucose in interstitial fluid
- Have demonstrated benefit for the patients that use them
- Recent Approvals
  - DexCom G4, down to 2 years of age!
  - Medtronic Enlite (part of 530G system)
- Challenges remain:
  - Sensor accuracy needs improvement
  - New materials/technologies to reduce sensor biofouling needed
  - Improved reliability needed (e.g., signal dropout)
  - Better standards would help advance technology

Artificial Pancreas

- Challenges:
  - Many still struggle to maintain good glycemic control
  - Hypoglycemic unaware individuals at risk
  - Risk of nighttime hypoglycemia
  - Better quality of life needed
- The development of an Artificial Pancreas will improve outcomes for people with diabetes
- Current challenges to get there:
  - Device limitations – pump imprecision, sensor inaccuracy/unreliability
  - Biology – complicated
  - Inter-individual variability – one size fits all possible? Smart algorithms?
- Brilliant people working on these problems….

Artificial Pancreas

- First step recently approved
- Medtronic 530G Threshold Suspend System
  - 530G pump
  - Enlite CGM
- In-clinic data submitted
- Post Approval study: FDA requested Pediatric access in the Post Approval study

Mobile Applications

- To facilitate new technologies, mobile platforms are key
  - Nearly everyone now carries a cell phone
  - Enable functions to allow for medical device interaction from that platform
- Challenges include:
  - Security, hacking – specialized communication protocols essential
  - Android vs. Apple OS
  - Mechanisms for verification of software/OS updates and upgrades
- FDA:
  - Is working closely with industry on requirements/process for market entry, upgrades, etc. – need to reach the right regulatory touch
  - Has already cleared/approved many apps in for use with diabetes devices
  - Published final guidance on Mobile medical Apps – provides more clarity and transparency (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf)
- Promises to be more convenient for patients

New Technologies

Needed Quality of Life Improvements:

- Consolidation of devices (meters, pumps, lancets, cell phones, etc.)
- Easy data interpretation, standard data format and metrics
- Consolidation of software/applications
- Remote upload/data access capabilities (cloud computing)
- Easier/faster download capabilities
- Improved patient interaction with healthcare professionals

Patient Interaction

- Efforts to better reach Patients
  - FDA is trying to find ways to increase input from patients so that we can do a better job of taking the patient perspective when making premarket and postmarket decision.
- We get a lot of perspective from working with patients:
  - Face to face discussions
  - Conferences
  - Working with investigators and their patients, etc.
- Grassroots efforts (e.g., #StripSafely campaign)

What Can You Do?

- Report adverse events (to the manufacturer *and* the FDA)
- Comment to the Docket for the draft blood glucose meter guidances
- Become informed on the facts (from all perspectives)

Questions?

Thank you!