FDA Regulation of POC Blood Glucose Meters

Leslie Landree, Ph.D.
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

June 2013
FDA Regulation of Medical Devices

• Federal Food, Drug, and Cosmetic Act (The Act)

• Medical Device Amendments of May 28, 1976
  – Risk based regulation by intended use
    o Class I - low risk, usually exempt from Premarket review
    o Class II - moderate risk, requires “substantial equivalence” to predicate device (510(k) clearance)
    o Class III – high risk and novel intended uses, require premarket approval (PMA)
Evaluation of Glucose Meters

- Class II devices (moderate risk)
- Require 510(k) clearance prior to marketing
- Substantial equivalence to predicate
- FDA evaluates intended use, performance, labeling
510(k) Premarket Review – SE Determination

- Blood Glucose meters are cleared through 510(k)

- The bar for clearance of blood glucose meters is the demonstration of Substantial Equivalence to a legally marketed predicate

- Not an independent evaluation of the device. The data submitted to support SE is generated by the sponsor
Cleared Intended Uses

- FDA clears glucose meters for the following indications:
  - Quantitative measurement of glucose in whole blood (e.g., capillary, venous, arterial)
  - Intended for self testing outside the body (in vitro diagnostic use) by people with diabetes
  - As an aid in monitoring the effectiveness of diabetes control program
  - NOT intended for the diagnosis of or screening for diabetes
Cleared Intended Uses

- FDA clears glucose meters for the following indications:
  - Testing sites - fingertip and alternative sites (e.g. forearm, palm, calf, thigh)
  - A few are cleared for use on neonates
User Populations

Glucose meters are used:

- By diabetics at home
- In healthcare settings
  - Hospitals
  - Nursing homes
  - Physician’s offices
  - Emergency Departments
  - Emergency Response Units
Cleared Intended Uses

- FDA clears glucose meters for the following intended uses:
  - For multiple-patient use in professional healthcare settings
  - Single-patient use at home
Intended User Population

- Majority of meters are designed and validated for OTC use
  - The majority of meters used in hospitals are OTC devices
  - CLIA waived by regulation – used anywhere in the professional healthcare setting
  - ISO 15197 accuracy criteria for OTC use
  - User is not the intended user
Intended User Population

• Currently no distinction between the performance requirements for OTC systems and those for professional use
  – Manufacturers choose to submit the meters as OTC

• Devices should be designed for a specific intended use/user population.
  – OTC meters used in hospitals:
    Meters are not designed for or evaluated with physiologic conditions, treatments or medications specific to the hospital population
FDA Evaluation of BGMS Performance

- Glucose meters and test strips are cleared as complete test systems, requiring performance testing of the whole system.

- System components:
  - Meter
  - Test strips
  - Quality control solutions
  - Sometimes lancing devices, lancets and alcohol wipes

- Strips are labeled specifically for use with a particular meter or meters.
Factors for Evaluation of BGMS Performance

- Intended Use
- Precision
- Accuracy
- Linearity
- Interferences
- Cleaning and Disinfection
- Environmental
- Software
- Labeling
BGMS Performance

**Precision**

- **Repeatability**
  - Evaluate concentrations spread across the measuring range (e.g. 30-50, 51-110, 111-150, 151-250, 251-400 mg/dL)
  - Multiple meters, one day

- **Intermediate**
  - Multiple meters, multiple days
  - Should use multiple strip lots
  - Usually control solutions are used
BGMS Performance

Accuracy – in the hands of intended users

• To evaluate whether users can operate and obtain correct results when using only instructions to be provided when device is marketed
• Lay users obtain and run own samples
• minimum of 100 capillary samples spanning measuring range
• Compare results to reference
• Questionnaire to assess understanding
BGMS System Accuracy

Current FDA minimum acceptable system accuracy and accuracy in the hands of users is based on ISO 15197 (2003) criteria:

• 95 % of individual glucose results shall fall within ± 15 mg/dL of the results of the reference measurement at glucose concentrations < 75 mg/dL

• 95% of individual results shall fall within ± 20 % at glucose concentrations ≥ 75 mg/dL
Other Sample Types

- Alternative site testing (AST) (e.g. forearm, palm, calf, thigh)
  - Lay users obtain and run their own samples
  - Each claimed site compared to a recognized reference
- Venous, arterial, neonatal
  - Results compared to a reference method
BGMS Performance

**Linearity**

- Multiple points across entire claimed measuring range
- Multiple replicates
- Multiple test strip lots
- CLSI EP6-A recommended
BGMS Performance

**Potential Interferences**

- Common endogenous and exogenous substances
  - Common OTC substances, frequently administered diabetes drugs, icterus, lipemia, hemolysis, sugars other than glucose
  - Endogenous – high levels
  - Exogenous – therapeutic and toxic
  - Commonly see acetaminophen, ascorbic acid, L-dopa, methyldopa, xylose
  - CLSI EP7-A recommended
BGMS Performance

**Potential Interferences continued**

- Hematocrit
  - Span claimed hematocrit range
  - Compare to a reference method
BGMS Performance

Environmental effects

- Operating conditions: temperature and humidity
- Altitude
Additional Factors Evaluated

- Conformance to IEC Medical Electrical Equipment standards
- Electromagnetic Compatibility
- Software:

  *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089543.htm
Labeling

- User manual
- Test strip insert
- Quality control solutions insert
- Quick Reference Guide, if applicable
- Box and container labels
- 21 CFR 809.10
  - OTC labeling at 8th grade reading level
Infection Control Background

• During the week of August 23, 2010, the FDA, CDC, and CMS issued clinical reminders and public health notifications highlighting the risk of transmission of disease from shared use of fingerstick (lancing) devices and point of care blood testing devices.

• These notifications were in response to recent outbreaks of viral hepatitis among patients where these devices were shared between users.
Infection Control Background

• Accordingly, the FDA modified its regulatory review requirements for all blood glucose monitoring systems (BGMS) to ensure that validated cleaning and disinfection instructions are provided to users so that they may adequately respond to these recommendations.

• Letters to BGMS manufacturers were issued (September 2010) by FDA. New review requirements were applied to submissions that were in house (under review or on hold) or submitted thereafter.
Infection Control Validation

- EPA registered disinfectant effective against HBV
- Disinfection Efficacy Testing
- Device Robustness Testing
EPA Registered Disinfectant

- EPA registered disinfectant effective against HBV
  - Readily available for purchase by user
  - Acceptable disinfectant time (< 3 min)
  - No personal protective equipment
  - Follow EPA registered label instructions (pre-clean step, contact time…) for all validation testing

http://oaspub.epa.gov/pestlabl/pplsls.home
Disinfection Efficacy Testing

- Demonstrate that the chosen EPA registered disinfectant is effective against Hepatitis B virus:
  - Using the materials used to make the device
  - EPA registered contact time
  - No cleaning step
Device Robustness Testing

• Demonstrate that the device can withstand the minimum number of expected cleaning and disinfection cycles within a typical use life (3-5 years).

• Should simulate actual use by the user (wiping). Wrapping, soaking, dunking are not acceptable methods.

• Criteria to assess potential deterioration of performance and deterioration of external materials.
Single- vs. Multiple-Patient Use Systems

- Distinguished systems designed to be used at home by a single person from those that were intended to be used on multiple-patients:
  - Intended use
  - Naming
  - Cleaning and disinfection validation testing
  - Labeling
Single- vs. Multiple-Patient Use: Intended Use

Distinct products should be created with separate intended uses:

- For home use; single-patient use:
  - intended to be used by a single person and should not be shared

- Clean and disinfect once per week for a single-patient use home device (minimum of 156 cycles to support a 3 year use life).
Single- vs. Multiple-Patient Use: Intended Use

Distinct products should be created with separate intended uses:

- For healthcare professional use; multiple-patient use:
  - intended for multiple-patient use in professional healthcare settings
  - system should only be used with single-use, auto-disabling lancing devices

- After use on each patient for a multiple-patient use device (minimum of 10 cycles per day; minimum 10,950 cycles to support a 3 year use life).
Infection Control Labeling Recommendations

• Emphasize the risk of disease transmission when using BGMS and reference any relevant public health notifications, standard practice guidelines, or other resources available to users.

• All parts of the kit are considered biohazardous and can potentially transmit infectious diseases, even after you have performed cleaning and disinfection.

• Validated cleaning and disinfection instructions
Labeling recommendations

• Emphasize Lancing device usage:
  
  – The meter and lancing device are for single patient use. Do not share them with anyone including other family members! Do not use on multiple patients!
  
  – Lancing devices should never be shared. Only single-use, auto-disabling lancing devices can be used with multiple-patient use BGMS.
In Conclusion

- Invaluable tools for diabetes management
- Many factors affect BGMS performance
- Each factor currently evaluated separately
- User experiences cumulative effect
What happens when things go wrong?
Resources: Post-market signals and adverse reports

• What is a Serious Adverse Event?: http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm
• MEDWATCH Page: http://www.fda.gov/Safety/MedWatch/default.htm
• MedSun http://www.fda.gov/medicaldevices/safety/medsunmedicalproductsafetynetwork/default.htm
• Recalls: http://www.fda.gov/Safety/Recalls/default.htm
Resources

Apps