FDA Regulation of Blood Glucose Monitoring Systems

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Objectives

- Identify what information FDA evaluates to grant marketing clearance for blood glucose monitoring systems
- Explain the current performance criteria that blood glucose monitoring systems must meet
- Discuss who the intended users of blood glucose monitoring systems are, and why they are not intended to be used by everyone

FDA Regulation of Medical Devices

- Risk based regulation by intended use
  - Class I - low risk, usually exempt from Premarket review
  - Class II - moderate risk, requires “substantial equivalence” to predicate device (510(k) clearance)
  - Class III – high risk and novel intended uses, require premarket approval (PMA)

510(k) Premarket Review of Blood Glucose Meters

- Class II devices (moderate risk)
- Require 510(k) clearance prior to marketing
- The bar for clearance is the demonstration of Substantial Equivalence (SE) to a legally marketed predicate
- Not an independent evaluation of the device - data submitted to support SE is generated by the sponsor

User Populations

- Diabetics at home
- Healthcare settings
  - Hospitals
  - Nursing homes
  - Physician’s offices
  - Emergency Departments
  - Emergency Response Units

Intended User Population

- Manufactures typically seek clearance for OTC use
- Designed and validated for OTC use
- Healthcare professional use not evaluated

Draft Guidance Documents

Published January 7, 2014

- Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM380327.pdf

- Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use

  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM380325.pdf

Comment period ends April 6, 2014

Draft Guidance Documents

- These guidances are:
  - A description of FDA's current thinking on the information manufacturers should submit to FDA for future glucose meter submissions
  - Draft

- These guidances are NOT:
  - Guidelines or rules for how hospitals, Health Care Professionals (HCPs), or patients should use glucose meters
  - Rules for how laboratories should validate glucose meters
  - Retroactive
  - Final

Evaluation of Blood Glucose Monitoring Systems

- Intended Use
- *Accuracy*
- Precision
- Linearity
- *Interferences*
- Cleaning and Disinfection
- Environmental
- Software
- *Flex Studies*
- *Test strip manufacturing lot release criteria*

Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use (BGMS)

- Meant to address only those systems intended for prescription POC use in professional healthcare settings
- Not meant to address those blood glucose monitoring systems intended for OTC use by lay persons at home

BGMS Performance - *Accuracy*

- User evaluation - accuracy in the hands of intended users
- Studies should represent actual use claimed with subjects that accurately reflect the intended use population
- 350 samples spanning measuring range for each claimed sample type/matrix (e.g. arterial, venous, capillary whole blood)
- Additional 50 high and 50 low samples (may be contrived)

BGMS Performance - *Accuracy*

- Neonatal (<28 days old)
- 100 to 150 fresh neonatal capillary blood samples compared to reference

BGMS - *Accuracy Criteria*

- 99% of results are within:
  - +/- 10% of the reference method for glucose concentrations > 70 mg/dL and
  - +/- 7 mg/dL at <70 mg/dL

- 100% of results are within:
  - +/- 20% of the reference method for samples >70 mg/dL and
  - +/- 15 mg/dL <70 mg/dL.

- Outliers should be specifically addressed by manufactures in the pre-market submission

Complexity and CLIA Waiver (BGMS)

- Prescription-use is not automatically waived
- Manufacturers will need to seek CLIA waiver
- Importance of waiver to point-of-care users
- Designed studies in the guidance to support both clearance and waiver

BGMS Performance
Potential Interferences

- Should evaluate the effect of potentially interfering endogenous and exogenous substances and conditions (e.g. lipemia, common medications, varying hematocrit levels, etc.)

- Ascorbic acid, dopamine, L-dopa, methyl-dopa, tryglycerides, uric acid, xylose

BGMS Performance
Potential Interferences

- Hematocrit
  - Span claimed hematocrit range, compare to reference
  - Minimum claimed range of 10-65%

BGMS Performance
Potential Interferences

- Oxygen
  - Span claimed blood oxygen range at various glucose concentrations
  - Minimum claimed range of 40-200 mmHg

Infection Control

- Not different from what manufactures are currently doing
- Validation studies differ mainly in the number of cleaning and disinfection cycles - should be representative of the amount of cleaning and disinfection that the meter will be exposed to in its use life (typically 3-5 year use life)
- Include validated cleaning and disinfection instructions in the labeling

BGMS Flex Studies

- Demonstrate that the BGMS device design is robust (e.g., insensitive to environmental and usage variation) and that all known sources of error are effectively controlled

- Design test systems to incorporate fail-safe mechanisms whenever technically practicable (e.g. lock-out functions)

Flex Study Examples

- Test strip stability testing
- Temperature and humidity effects
- Altitude effects
- Short sample detection
- Sample perturbation study
- Intermittent sampling
- Used test strips
- Mechanical Vibration Testing
- Shock testing
- Electromagnetic compatibility (EMC) Testing
- Electrostatic Discharge/Electromagnetic Interference Testing

Test Strip Lot Release Criteria

- Test strip lot release criteria should be sufficient to ensure consistent quality of the test strips
- Manufacturers provide a description of the lot release criteria and a summary of the sampling scheme in the pre-market submission

Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use (SMBG)

- Meant to address only those blood glucose monitoring systems intended for use by lay-users at home

- Not meant to address blood glucose monitoring systems intended for use in prescription point-of-care settings

SMBG Performance - *Accuracy*

- User evaluation - accuracy in the hands of intended users
- 350 samples spanning measuring range for each claimed sample type (e.g. fingerstick, palm, thigh)
- Additional 50 high and 50 low samples (may be contrived)

SMBG - *Accuracy Criteria*

- 95% within 15% and 99% within 20% of the reference
- Outliers should be specifically addressed by manufactures in the pre-market submission
- Claimed measuring range should minimally span
  50 – 400 mg/dL glucose

SMBG Performance
Potential Interferences

- Same study design – common endogenous and exogenous substances

- Hematocrit
  - Claimed hematocrit range of 20-60% (ideal)
  - Minimum claimed range 30-55% hematocrit

SMBG Performance

- Infection control validation – based on expected use and use life of the device
- Flex studies
- Test strip manufacturing lot release criteria

Labeling

- Prominent warning on the outer SMBG box labeling and package insert
  - Not for use in healthcare settings
  - Use of this device on multiple patients may lead to transmission of blood borne pathogens
- Performance description on outer box label
  - Currently no way for users distinguish meters
  - Labeling aimed at allowing better meters to have better labels – so people and their healthcare professionals can choose the best meter for their needs

Thank you

Questions?

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