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Draft Guidance Documents

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


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


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Draft Guidance Documents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 manufacturers 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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