FDA Perspective: Regulatory Challenges for Safe use of Blood Glucose Meters in Hospital Settings

Carol Benson, M.A., M.T.(ASCP), Associate Director, Division of Chemistry and Toxicology Devices

- Office of in Vitro Diagnostic Device Evaluation and Safety
- Center for Devices and Radiological Health
Overview

• Intended use manufacturers seek FDA clearance
• Implications under CLIA
• FDA’s acceptance criteria for accuracy
• Issues specific to hospital glucose meters/test strips
• Hospital meters/test strips and post market issues
Intended Use

Manufacturers of glucose meters/test strips seek FDA clearance for marketing for both:

• Lay users (OTC)
• Health care professionals
Why seek FDA clearance for both lay user and HP?

Glucose monitoring devices cleared by FDA for home use are:

- CLIA waived device according to regulation 493.15
Implications of CLIA Waiver

• Use at any setting with CLIA waiver certificate from CMS
• Follow manufacturer's instructions for testing and external QC
• Under CLIA no external QC requirements
• No PT is required
• Personnel no training requirements
CLIA Waiver Studies¹

More robust than typical lay user studies

- More samples are tested
  min. 360 samples
- More sites used
  min. at 3 sites
- Tested over time
  min. 2 weeks

CLIA Waiver Studies con’t.

- Accuracy criteria for glucose meters are tighter
  
  95% ± 15% for values ≥ 75 mg/dL, ± 12 mg/dL for < 75 mg/dL

- Look at other 5% of values

- Perform flex studies (stress device)
Regulatory challenges

Same meter/test strips for both lay user & HP

• many are designed for use by healthcare professionals only and not for lay users

Meters are:

large, docking stations, bar code capabilities, transmit data, QC lock outs, large memory capacity for storing data
Regulatory challenges

Same min. accuracy criteria for lay user and health care professional

- lay users results vs. reference (YSI) method – approx. 100 patients tested
- health care professionals vs. reference (YSI) 100 patients

Same people tested as lay user study – not sick hospitalized patients
FDA min. accuracy criteria from the ISO 15197 standard

Ninety-five percent (95 %) of glucose results are:

- within ± 15 mg/dL (0,83 mmol/L) of the results < 75 mg/dL (< 4,2 mmol/L)

- and within ± 20 % of the results ≥ 75 mg/dL (≥ 4,2 mmol/L)
Regulator challenges – large differences

- If 60 mg/dL on reference method then the meter can vary from 45 to 75 mg/dL
- If 200 mg/dL on reference method then the meter can vary from 160 to 240 mg/dL
- Only 95% need to meet - if 100 are tested only 95 results meet min. accuracy criteria
- ?? Other 5 results (5%)
ISO 15197 min. accuracy criteria

• Written for meters/test strips for lay users only
• Should be tightened ?? for lay users
• Broader than CAP requirements for laboratory based methods – 10% or 6 mg/dL (whichever is greater)
• Currently FDA applies to all meters/test strips
• Too broad ? for hospital use meters to be safe and effective
Regulatory challenges - other interferences are cumulative

- Hematocrit
- Drugs - dopamine, acetaminophen
- Other substances - lipids, Vitamin C
- Environmental effects - Temperature – Altitude-Humidity

If each affects glucose by 10% and evaluated separately – What is the cumulative effect for patient?
Cumulative amount??

- Hematocrit +10%
- Drugs +10%
- Lipids, Vitamin C +10%
- Temperature +10%
- Altitude +10%
- Humidity +10%

???
Hospital patients

- Sick – dehydrated, in shock, on oxygen
- Have different hematocrits – not known at time of testing
- Take multiple drugs – how affect system?
- May have glucose values changing rapidly
- Tested with multiple meters/multiple users introduce error – patient treated
- and …
Consequences of hospital patients tested with multiple meters by multiple users?

infection control issues (hepatitis)

¹Conclusion:
Hepatitis B virus infection outbreaks associated with blood glucose monitoring have occurred with increasing regularity in the United States and may represent a growing but under-recognized problem. Advances in technology, such as the development of blood glucose testing meters that can withstand frequent disinfection and noninvasive glucose monitoring methods, will likely prove useful in improving patient safety.

Nicola D. Thompson, Ph.D., M.S., 1 and Joseph F. Perz, Dr.P.H., M.A.2
Hospital patients

• Insulin dosing errors\(^1\)
  • meters with a 5% total error had <5% of the resulting insulin doses differing from the intended dose
  • at approximately 15% total error large errors in insulin doses, and
  • at 20% total error, >30% of insulin doses differ from intended doses and >16% of episodes of hypoglycemia are missed.

Regulatory challenges - hospital patients

- Intended use – may be different - tight glycemic control – Accuracy needed?
- Interferences - maltose (either from icodextrine derived or from IgG-containing medication), drugs, oxygen, dehydration, DKA
- Unawareness of user of potential interferant(s) or limitations
Regulatory challenges - hospital meters - labeling

- Currently same labeling for lay users with added information for health care professionals
- Same limitations – Not for use on critically ill patients, those in shock, dehydrated
- Accuracy presented in ISO 15197 tables
- Probably not present with device
- Not necessarily read by operators
- Limitations – understood by all users?
- QC materials – users know when to test?
For safe and effective use - Hospital meters

- Technology improvements
- Tighter accuracy criteria
- Less interference from drugs and hematocrit, oxygen, altitude, temperature
- Less lot to lot variability
- Lock outs – QC, expired reagents
- Cleaning procedures to prevent infections
Regulatory challenges - Post market signals

- Glucose meters have one of the highest number of device adverse events reported per year
- Thousands of Medical Device Reports (MDRs) sent each year (>12,000/yr)
- 12,672 serious injuries reported from 2004-2008
- 1992-2009: 100 deaths associated with glucose meters in the MDR database

Anyone can report problems

From Courtney Harper’s presentation
Summary

• Manufacturers seek FDA clearance for both lay user and Health care professional
• CLIA waived device
• FDA currently same min. accuracy criteria from ISO 15197 for both lay use and HP
• Hospital meters used on multiple patients
• Patients who are critically ill – dehydrated – have different hematocrits – take multiple drugs
• Infection control issues
• Post market signals high for glucose meters