Medical Devices: Who’s looking out for the patients?

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Hint: Not the FDA!

Objectives
- Increase awareness of:
  - sources of information about devices
  - regulatory process
  - systemic failure
  - human factors
- Using a “sentinel” device:
  - glucose monitor

Case History
- 57 YO WM with 5 year Hx of type 1.5 (insulin dependent) diabetes mellitus
- Well controlled on Humalog (lispro) Q1D and Lantus (glargine) qHS
- Recent addition of baclofen
- SMBG 3-4x/D

57 YO WM with 5 year Hx of type 1.5 (insulin dependent) diabetes mellitus
Well controlled on Humalog (lispro) Q1D and Lantus (glargine) qHS
Recent addition of baclofen
SMBG 3-4x/D
Recent increase in hyper- and hypoglycemia
? Baclofen (PDR – hyperglycemia)

6/4/02
0901 GM1 – 105 mg/dL
0916 GM2 – 200

6/8/02
HS GM2 – 142 (192?)

6/9/02
0108 GM1 – 26
0110 GM1 – 28
0117 GM1 – 79

6/10/02
0500 GM1 – 90 mg/dL
0706 GM2 – 176
0710 GM1 – 105
0711 GM2 – 180
0715 GM1 – 50 (GCS)
0716 GM2 – 93 (GCS)
0724 GM3 – 118* (GCS)
*test strip used with GM2

6/26/02
2211 GM2 – 509 mg/dL
2213 GM2 – 194
2214 GM2 – 198
2228 GM3 – 207
Case History

What's going on here?

A search for the truth!

- User’s manual – 114 pages
- Glucose testing:
  - IF... your blood glucose result is within the “normal” range,
  - AND... you exhibit symptoms of high or low blood sugar,
  - THEN... run a glucose control check with your glucose control solutions and a new test strip.

A search for the truth!

- IF... your blood glucose result seems unusually high or low, AND... does not reflect the way you feel, check the following:
  - Does the test strip code number match the code number on the meter?

A search for the truth!

- Was the blood sample applied to the test strip within 3 minutes of removing it from the vial?
- Was the size of the blood sample sufficient?
- Was the test strip vial cap tightly sealed?
A search for the truth!

- Was the test strip used before the expiration date?
- Were the test strips stored away from extreme temperature such as in the car in very cold or hot weather?
- Were the test strips stored away from areas of high humidity such as in the kitchen or bathroom?

A search for the truth!

- Test strip package insert:
  - Use.... Test Strips at temperatures between $57^\circ$ and $104^\circ$ F and less than 85% humidity (the amount of dampness in the air). Avoid rooms such as kitchens, bathrooms, and laundry areas.

A search for the truth!

- Manufacturer:
  - Patient hotline: no information
  - Physician hotline: no information
  - “provided data to FDA, but it is confidential”

- Medline:
  - No published data on effects of environment on accuracy of test strips
A search for the truth!

- ECRI - Health Devices
  - Portable Blood Glucose Monitors
    - Updates every 2-3 years
    - Acknowledges that individually wrapped test strip are less likely to yield inaccurate results.
    - No testing of environmental factors
  - Available from clinical engineering or Bob Kirby!

A search for the truth!

- FDA
  - Guidance documents
  - 510(k)/PMA
  - MedWatch (voluntary program)
  - MAUDE/MDR (manufacturer and user facility device experience/medical device reporting) - mandatory

FDA - Background

- Regulates products that account for 25 cents of every dollar spent by US consumers

U.S. Food and Drug Law History

- 1902 - Biologics Control Act - purity and safety of serums, vaccines, etc.
- 1906 - Food and Drugs Act - prohibits interstate commerce in misbranded or adulterated foods, drinks, drugs
- Meat Inspection Act - passes same day
- 1907 - Certified Color Regulations
FDA- Background

- Public Health Agency
- Enforces the:

Federal Food, Drug & Cosmetic Act of 1938

U.S. Food and Drug Law History

- 1938 - passage of the Federal Food, Drug and Cosmetic Act
  - Provisions:
    - Control of cosmetics and therapeutic devices
    - Drug must be shown to be safe
    - Set safe tolerances for poisonous substances
    - Standards for foods
    - Authorizes factory inspections
    - Adds court injunctions as a remedy

U.S. Food and Drug Law History

- 1965 - Drug Abuse Control amendments - drugs of abuse
- 1966 - FDA contracts with NAS/NRC to evaluate effectiveness of 4,000 drugs approved on basis on safety alone

U.S. Food and Drug Law History

- 1976 - Medical device amendments - safety and effectiveness of medical devices
- 1983 - Orphan drug act
- 1984 - Drug Price Competition and Patent Term Restoration Act
U.S. Food and Drug Law History

- 1990 – Safe Medical Devices Act – requires reporting of incidents that suggest the medical device caused injury or death
- Post-market surveillance on permanently implanted devices

The FDA Modernization Act of 1997

Focus on devices that present the greatest risk to patients

The FDA Modernization Act of 1997

- Exempts certain class I devices from premarket notification
- Focus postmarket surveillance on higher risk devices
- Expand “third party” pilot program – accredited experts

FDA Centers

- 6 centers
  - Pharmaceuticals – Center for Drug Evaluation and Research
  - Medical Devices – Center for Device and Radiological Health (CDRH)
Center for Device and Radiological Health (CDRH)

Develops and carries out a national program to assure the safety, effectiveness, and truthful labeling of medical devices for human use.

Center for Device and Radiological Health (CDRH)

Reviews and evaluates medical device premarket approval (PMA) applications, product development protocols (PDP), exemption requests for investigational devices (IDE), and premarket notification [510(k)]

CDRH

- Public advisory committees (private sector scientists)
  - 4 committees (i.e. Medical Device Advisory Committee)
  - 16 panels (i.e. Anesthesiology and Respiratory Therapy Devices Panel)

Medical Device Classes

<table>
<thead>
<tr>
<th>Class</th>
<th>Regulatory Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>General Controls</td>
</tr>
<tr>
<td>II</td>
<td>General and Special Controls</td>
</tr>
<tr>
<td>III</td>
<td>General Controls and PMA</td>
</tr>
</tbody>
</table>
**Medical Device Classes**

- **Class I** – minimal potential for harm
  - simple design (exam gloves, elastic bandage)
- **Class II** – general controls alone are insufficient to assure safety and effectiveness, but methods are available to provide assurance (wheelchair, infusion pump)

- **Class III** – insufficient information exists to assure safety and effectiveness from other controls

**Classification**

- 16 panels/specialty groups
- 1,700 classifications
- Class I - 45%
- Class II - 47%
- Class III - 8%

**Medical Device Approval**

- Exempt
- Premarket Notification 510(k)
- Premarket Approval (PMA)
- Investigational Device Exemption (IDE)
- Product Development Protocol (PDP)
# Medical Device Approval

<table>
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<td>I</td>
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<td>III</td>
<td>510(k), PMA, IDE, (PDP)</td>
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## 510(k)
- Purpose is to demonstrate that the medical device to be marketed is substantially equivalent (SE) to a legally marketed (predicate) device that was or is on the U.S. market.
- A comparison of one device to another.

## Predicate Device
- A device that was legally marketed in the U.S. prior to **May 28, 1976** (preamendment) **OR**
- A device which has been reclassified from Class III to Class II or I **OR**
- A device that was found to be SE through the 510(k) process.
Substantial Equivalence (SE)

A device is SE if, in comparison to a predicate device it:
- Has same intended use *and* has same technological characteristics
  **OR**
- Has same intended use *and* has different characteristics that do not raise new questions of safety and effectiveness

A search for the truth!

- FDA
  - Guidance documents
  - 510(k)/PMA
  - MedWatch (voluntary program)
  - MAUDE/MDR (manufacturer and user facility device experience/medical device reporting) - mandatory

FDA

Guidance documents -

"Review Criteria Assessment of Portable Blood Glucose Monitoring In Vitro Diagnostic Devices Using Glucose Oxidase, Dehydrogenase, or Hexokinase Methodology"

Draft released 2/28/97 for comments- no final document

FDA

Guidance document:

Labeling - “... It is suggested that the limitation section of the package insert/instruction manual contain the following cautionary statements as appropriate:
1. Extended exposure to air and light may alter results. It is recommended that the strips be stored in the original capped vial at temperatures below 30°C. Avoid exposure to excessive humidity; do not freeze."
A search for the truth!

- FDA
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FDA

- 510(k) - database search
- Class II device
- Product code - NBW
- 510(k) number - K021513

<table>
<thead>
<tr>
<th>Device Classification Name</th>
<th>SYSTEM, TEST, BLOOD GLUCOSE, OVER THE COUNTER</th>
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<tr>
<td>Regulation Number</td>
<td>892.1345</td>
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<td>510(k) Number</td>
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<tr>
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<td>ACCU-CHEK ADVANTAGE MODULE</td>
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<tr>
<td>Date Received</td>
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<tr>
<td>Decision Date</td>
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<tr>
<td>Decision</td>
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</tr>
<tr>
<td>Classification Advisory Committee</td>
<td>Clinical Chemistry</td>
</tr>
<tr>
<td>Review Advisory Committee</td>
<td>Clinical Chemistry</td>
</tr>
<tr>
<td>Statement/Summary/Purged Status</td>
<td>Summary only</td>
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SUMMARY

Type: Special
Reviewed by Third Party: No
Expedited Review: No

**SUMMARY**

- Device Classification Name: SYSTEM, TEST, BLOOD GLUCOSE, OVER THE COUNTER
- Regulation Number: 892.1345
- 510(k) Number: K021513
- Device Name: ACCU-CHEK ADVANTAGE MODULE
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- Decision: SUBSTANTIALLY EQUIVALENT (SE)
- Classification Advisory Committee: Clinical Chemistry
- Review Advisory Committee: Clinical Chemistry
- Statement/Summary/Purged Status: Summary only

**SUMMARY**
The enzyme glucose dehydrogenase converts the glucose in a blood sample to gluconolactone. This reaction liberates an electron that reacts with a coenzyme electron acceptor, the oxidized form of the mediator hexacyanoferrate (II), forming the reduced form of the mediator, hexacyanoferrate (I). The test strip employs the electrochemical principle of amperometry. The meter applies a voltage between two identical electrodes, which causes the reduced mediator formed during the incubation period to be reconverted to an oxidized mediator. This generates a small current that is read by the meter.

**FDA**

- 510(k) - Bottom line:

  No requirement by FDA for documentation to provide data on the effects of environmental factors on accuracy of readings

**A search for the truth!**

- FDA
  - Guidance documents
  - 510(k)/PMA
  - MedWatch (voluntary program)
  - MAUDE/MDR (manufacturer and user facility device experience/medical device reporting) - mandatory
MAUDE

Database is scheduled to be updated quarterly

Enter one or a combination of the MAUDE Search Values

OR

use Full-Text Search below and select Search:

MAUDE Search Values
Brand Name
510K Number
Manufacturer
PMA Number
Event Type
Report Code

Date Report Received by FDA (mm/dd/yyyy)

Full Text Search
Information About Full Text Searching

Enter a single word (e.g., catheter), an exact phrase (e.g., catheter line) or multiple words connected by and (e.g., catheter and tubing).

Select Number of Records per Report Page

Medical Device Reporting Search, for incidents before July 31, 1996

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**ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION**

REPORT DATE: 06/14/2002  MDR TEXT KEY: 1392577  Patient Sequence Number: 1

THE PT USED THE SUSPECT DEVICE TO CHECK THEIR BLOOD GLUCOSE. PT OBTAINED HIGH RESULTS AND PROGRAMMED THEIR INSULIN PUMP ACCORDINGLY. PT THEN BECAME HYPOGLYCEMIC AND PASSED OUT. PARAMEDICS CAME AND THEY CHECKED THEIR BLOOD GLUCOSE AND THEN TREATED PT WITH AN IV. GLUCOSE CONTROLS WERE NOT USED ON THE SYSTEM. THE SUSPECT DEVICE WAS REPLACED WITH NEW PRODUCT AND THEN AUTHORIZED FOR RETURN TO THE MANUFACTURER FOR EVALUATION.

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**ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION**

REPORT DATE: 06/14/2002  MDR TEXT KEY: 1392536  Patient Sequence Number: 1

THE PT USED THE SUSPECT DEVICE TO CHECK THEIR BLOOD GLUCOSE. THEY OBTAINED A RESULT OF 541 MG/DL AND THEN TOOK A DOUBLE DOSE OF INSULIN. THEY THEN EXPERIENCED A HYPOGLYCEMIC EVENT AND CALLED THE FIRE DEPARTMENT. UPON ARRIVAL THEIR GLUCOSE WAS CHECKED AND THE RESULT WAS 26 MG/DL. THEY WERE TRANSPORTED TO THE ER AND WAS TREATED UNTIL THEIR GLUCOSE ROSE TO 70 MG/DL. GLUCOSE CONTROLS WERE NOT USED ON THE SYSTEM THE SUSPECT DEVICE WAS REPLACED WITH NEW PRODUCT AND THEN AUTHORIZED FOR RETURN TO THE MANUFACTURER FOR EVALUATION.
**MAUDE**

**ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION**

**REPORT DATE:** 06/07/2002  **MDR TEXT KEY:** 1387359  **Patient Sequence Number:** 1

**THE PATIENT USED THE SUSPECT DEVICE TO CHECK THEIR BLOOD GLUCOSE AND OBTAINED A RESULT OF 298 MG/DL. PATIENT THEN PASSED OUT AND WAS TAKEN TO THE ER BY SPOUSE. A LAB TEST WAS PERFORMED AND THEIR GLUCOSE LEVEL WAS 21 MG/DL IN THE ER. PATIENT WAS TREATED WITH A D.50 IV. GLUCOSE CONTROLS WERE NOT USED ON THE SYSTEM. THE SUSPECT DEVICE WAS REPLACED WITH NEW PRODUCT AND THEN AUTHORIZED FOR RETURN TO THE MANUFACTURER FOR EVALUATION.**

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**MAUDE**

**ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION**

**REPORT DATE:** 06/04/2002  **MDR TEXT KEY:** 1386989  **Patient Sequence Number:** 1

**THE PT USED THE SUSPECT DEVICE TO CHECK THEIR BLOOD GLUCOSE AND OBTAINED A READING OF 283 MG/DL. PT WAS FEELING SYMPTOMS OF HYPOGLYCEMIA AND WAS TAKEN TO THE HOSPITAL. AT THE HOSPITAL, PT'S BLOOD GLUCOSE WAS 45 MG/DL ON A HOSP METER. PT WAS GIVEN ORANGE JUICE, CRACKERS AND AN IV. GLUCOSE CONTROLS WERE NOT USED ON THE SYSTEM. THE SUSPECT DEVICE WAS REPLACED WITH NEW PRODUCT AND THEN AUTHORIZED FOR RETURN TO THE MANUFACTURER FOR EVALUATION.**

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**MAUDE**

**ADVERSE EVENT OR PRODUCT PROBLEM DESCRIPTION**

**REPORT DATE:** 05/30/2002  **MDR TEXT KEY:** 1386965  **Patient Sequence Number:** 1


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**MAUDE**

**EVENT DESCRIPTION – 9/12/96**

**CLINIC RETURNED DEVICE ALLEGING THAT IT WAS PROVIDING HIGHER RESULTS THAN A SIMILAR DEVICE. DIABETIC USING DEVICE HAD BEEN ADJUSTING INSULIN DOSAGE BASED ON ELEVATED RESULTS, AND HAD EXPERIENCED "CONTINUAL INSULIN REACTIONS." EVALUATION OF DEVICE INDICATED THAT TEMPERATURE AND/OR HUMIDITY STORAGE REQUIREMENTS HAD NOT BEEN MAINTAINED. THIS MIS-HANDLING OF DEVICE RESULTED IN FALSELY ELEVATED RESULTS. EXPIRATION DATE IS 3/31/97. DEVICE MFG DATE IS 9/95. NO LAB INFO AVAILABLE. PT IS A DIABETIC TAKING INSULIN.**
Glucose Control Solutions

- Lifespan (J&J) fined $30.6M for not disclosing to FDA defects in a glucose monitor (12/00)
- An industry conspiracy
- Industry knows that test strips exposed to humidity give high glucose readings!
- Vague guidelines on when to use GCS
- Requires use of additional test strips ($0.75 each!)
- Pharmacies do not stock GCS and pharmacists don’t know where to order it!

- 26/110 patients used GCS
- 18/26 used expired solutions
- Most patients had no idea what a GCS was or how to use it!
- Only paper addressing this issue!

Human Factors

- Curse of Knowledge - ACEM
- Physicians routinely work around product defects
- Glucose monitors:
  - Eliminate GCS by having device detect inaccurate test strips
  - Automatic code entry
  - Intuitive design

- Glucose monitors - “As easy as 1,2,3.”
- Three general steps, but user required to learn 52 substeps!
- “OneTouch”
Oh, by the way......

- That glucose reading stored as 142, thought to be 192......
  - Roche Diagnostics has identified a situation that can occur no more than once every seven days, during a ten minute time period, which can cause an individual test result to be stored incorrectly in the memory......

Oh, by the way......

- Inaccurate results:
  - Altitude >10,150'
  - Oxygen 🍴 Glucose
  - Galactose
  - Maltose
  - Bilirubin >20 mg/dL
  - Lipemic specimens >5,000 mg/dL

Oh, by the way......

- Inaccurate results:
  - Acetaminophen
  - Uric acid
  - Hct
  - Glutathione
  - Vitamin C
  - Dialysis fluid