Advanced Technology for Point of Care Testing

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Director of Medical & Scientific Affairs, North America
Outline

• Nova Biomedical overview and history
• Nova Biomedical’s technologies and platforms
• Description of Nova’s test strip technology for POC glucose
• Other Nova’s technologies for critical care
  • BHB
  • Lactate
  • Creatinine
  • Gases, Electrolytes, and Metabolites
Nova Biomedical Corporate Profile

Ownership: Private  
Founded: 1976  
First Product Shipment: 1978  
Business Segments:  
• Hospital blood gas/electrolyte analyzers  
• Hospital Point-of-Care blood testing analyzers  
• Consumer diabetes blood glucose monitors  
• Biotechnology chemistry analyzers  
• Contract development/manufacturing  

New Biomedical Analyzers Introduced: 102  
FDA 510(k) Instrument Clearances: 90  
Nova Biomedical Corporate Profile

Employees: ~900
   Research and Development - 130
   Technical Support Staff - 150
   Manufacturing – 400
   Global Sales and Marketing - 170

Locations:
   Headquarters: Waltham, MA
   International Sales and Service Subsidiaries:
      - Austria    - Canada    - France
      - Germany    - Japan     - U.K.

Other International Markets Served: Dealers/Distributors covering 89 other countries

Manufacturing Sites:
   - Waltham, MA, USA (230,000 sq. ft.)
   - Billerica, MA, USA - Diabetes Division (>90,000 sq. ft.)
Nova is a Pioneer in Whole Blood Biosensors Technology

**Nova Biosensor Firsts**

- 1978 First biosensor for Ionized Calcium
- 1980 First biosensor to measure Chloride in blood
- 1984 First biosensor to measure Total Calcium
- 1985 First biosensor to measure Hematocrit by ISE/Conductivity
- 1987 First biosensor to directly measure whole blood Glucose
- 1988 First biosensor to measure Lithium
- 1990 First biosensor to measure BUN (urea)
- 1992 First biosensor to directly measure whole blood Lactate
- 1994 First biosensor to measure Ionized Magnesium
- 1996 First biosensor to measure Creatinine
- 1996 First biosensor to measure Total CO₂ in whole blood
- 1997 First multi-wavelength fiber optic SO₂% assay
- 1998 First fiber optic Hemoglobin assay
- 1998 First Ammonium biosensor
- 1999 First non-diluting direct Glutamine biosensor
- 1999 First non-diluting direct Glutamate biosensor
- 2001 First Acetate biosensor
POCT– a new adventure

• **2002** Design, manufactured and distributed SMBG devices under BD label

• **2005** Nova entered the POCT market with the development and FDA approval of a hospital glucose meter and strip

• **2007** first creatinine strip and meter

• **2009** first calibration free beta-hydroxybutyrate strip

• **2010** first hematocrit corrected lactate strip and meter
Glucose POCT Locations

- OR
- Inpatient Floors
- ED
- Labor & Delivery
- Outpatient Clinics
- NICU and Nurseries
- Intensive Care Units
- Specialty Clinics
- Ambulances
Interferences & factors reported to affect glucose POC meters

- User errors
- Substrate specificity
  - Non-glucose carbohydrate interferences (e.g. maltose)
- Hematocrit abnormalities
  - Inverse relationship observed between Hct and result (e.g. low Hct → falsely high readings)
- Drug interferences
  - Redox active substances
    - Ascorbic acid
    - Dopamine
    - Acetaminophen (paracetamol)
Nova’s glucose test strip is

- purposefully designed to address hospital glucose POC challenges reported in the literature
  - Interference from electrochemically active molecules
  - Effect of hematocrit
  - Substrate specificity
Miniaturization of proven technology

1980s

2005
Nova StatStrip® Multi-Well™ Technology Creates Significant Performance Improvements

**Top Layer**
- Prevents biohazard exposure
- Vent hole creates fast sample draw

**Capillary Layer**
- 1.2 µL sample fill
- Design eliminates overfill errors

**Measurement Wells Layer**
- Well 1: Interferences and glucose
- Well 2: Interferences
- Well 3: Hematocrit
- Well 4: Reference (and initiates analysis to eliminate short sampling errors)

**Gold Layer**
- Noble metal; superb electrochemical stability in all conditions
- Classic electrochemical measuring surface
- Excellent electrical properties

Patent: US#6,287,451;6,837,976;EP#1 212 609;CA 2,375,092
Reproducible validation of Nova’s StatStrip glucose technology

The scientific proof of a technology breakthrough is not established by a single study. The technology must be evaluated and the study results duplicated in numerous settings to be considered scientifically valid. In the last two years, 50 published studies by leading diabetes hospitals throughout the world validate that Nova’s StatStrip glucose sensor technology dramatically improves accuracy by reducing hemocrit and other interferences. These studies have been conducted at some of the most prestigious diabetes centers in the world including the Mayo Clinic, John Hopkins University School of Medicine, University of California Davis Center for Point of Care Technology, University of Toronto Sunnybrook Health Sciences Center, Addenbrooke’s Hospital, Cambridge University Hospitals, UK, WEQAS and University Hospital, Cardiff, Wales, Isala Klinieken, Netherlands.

Some conclusions:

"Here we further demonstrate for the first time that anemia is the primary cause of glucometer error in hemodynamically stable adult ICU patients and that eliminating hemocrit error decreases the frequency of hypoglycemia."
Falcão M et al. Crit Care Med 2010

"The new generation StatStrip glucose meter, which has been designed to compensate for hemocrit and chemical interferences, reduces the likelihood of erroneous results arising from interference factors that influence current conventional glucose meters."
Bewley B et al. Point of Care 2009

"The StatStrip system was not susceptible to hemocrit, ascorbate or maltose interferences, either alone or in combination with one another. The other strip meter systems tested were significantly influenced by these interferences."
Lyon MF. AACC, Annual Meeting 2008

"With the exception of the Nova StatStrip, all meters were affected by variable hemocrit."
Molin B. NZ J Med Lab Sci 2010
Questions?
Nova’s Technologies

**Stat Profile® pHOx Ultra**
Test Menu: pH, PCO₂, PO₂, SO₂ %, Hct, Hb, Na⁺, K⁺, Cl⁻, Ca²⁺, Mg²⁺, TCO₂, Glu, BUN, Creat, Lac, HHb, O₂Hb, Methb, COHb, O₂, O₂Cap, tBil
Samples: Whole blood, Serum, Plasma

**Stat Profile® pHOx**
Test Menu: pH, PCO₂, PO₂, SO₂ %, Hct, Hb, Na⁺, K⁺, Cl⁻, Ca²⁺, Glu, Lac
Samples: Whole blood, Serum, Plasma

**Nova Chemistry Analyzers**
Test Menu: Na⁺, K⁺, Cl⁻, TCO₂, Ca²⁺, Mg²⁺, Li⁺, TCa, Glu, BUN, Crea, Hct, pH
Samples: Whole blood, Serum, Plasma

**Nova BioProfile FLEX™**
Test Menu: Gluc, Lac, Gln, Glu, NH₄⁺, pH, PO₂, PCO₂, Na⁺, K⁺, Ca²⁺, CD, CV, Osm, IgG, PO₄
Samples: Cell Culture Media

**Nova StatStrip®**
Test Menu: Glucose
Samples: Whole blood

**Nova MAX®**
Test Menu: Glucose/Ketone
Samples: Whole blood

**Nova StatSensor®**
Test Menu: Creatinine
Samples: Whole blood

**Nova MAX® Plus**
Test Menu: Glucose/Ketone
Samples: Whole blood

**Nova MAX® Link®**
Test Menu: Glucose
Samples: Whole blood

**Nova Lactate Plus®**
Test Menu: Lactate
Samples: Whole blood

*Currently Available outside the U.S.*
sisbell@novabio.com
Critical Care

- Critically ill patients have complex pathophysiological derangements
- Frequent biochemical assessment of gases, electrolytes, and metabolites when managing these patients

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Hypoglycemia, Hyperglycemia</td>
</tr>
<tr>
<td>Glucose + BHB</td>
<td>DKA</td>
</tr>
<tr>
<td>Lactate</td>
<td>Hypoperfusion/Sepsis</td>
</tr>
<tr>
<td>Creatinine</td>
<td>CKD</td>
</tr>
<tr>
<td>Device</td>
<td>Handheld glucose meter + single use disposable test strip</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>QC material</td>
<td>Liquid</td>
</tr>
<tr>
<td>Measurement principle</td>
<td>Enzymatic/Amperometric</td>
</tr>
<tr>
<td>Specimen type</td>
<td>Whole blood</td>
</tr>
<tr>
<td>Frequency</td>
<td>Level 1 and 3 every 24hr</td>
</tr>
<tr>
<td>Operator</td>
<td>Nurse</td>
</tr>
<tr>
<td></td>
<td>Assess the quality of test strip and is then one test strip at a time</td>
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</tbody>
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Factors or interferences reported to affect glucose meters

<table>
<thead>
<tr>
<th>Factor or Interference</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operational errors</td>
<td>Calibration coding errors, improper</td>
</tr>
<tr>
<td></td>
<td>sampling, dosing errors</td>
</tr>
<tr>
<td>Environmental factors</td>
<td>Altitude, temperature, humidity</td>
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<tr>
<td>Exogenous interferences</td>
<td>Non-glucose carbohydrates, drugs</td>
</tr>
<tr>
<td>Endogenous/pathophysiological changes</td>
<td>Hematocrit, pO₂, triglycerides, uric acid</td>
</tr>
</tbody>
</table>

*Isbell and Lyon. Glucose meters. Where are we now? Where are we heading? MLO. 2012*