Advanced Technology for Point of Care Testing

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nova
biomedical

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

Quality Certifications: FDA registered, ISO 9001:2000, and ISO 13485:2003 compliant

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 CO_2 in whole blood

1997 First multi-wavelength fiber optic SO_2% 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

OR

Inpatient Floors

ED

Glucose POCT Locations

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 $\rightarrow$ 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
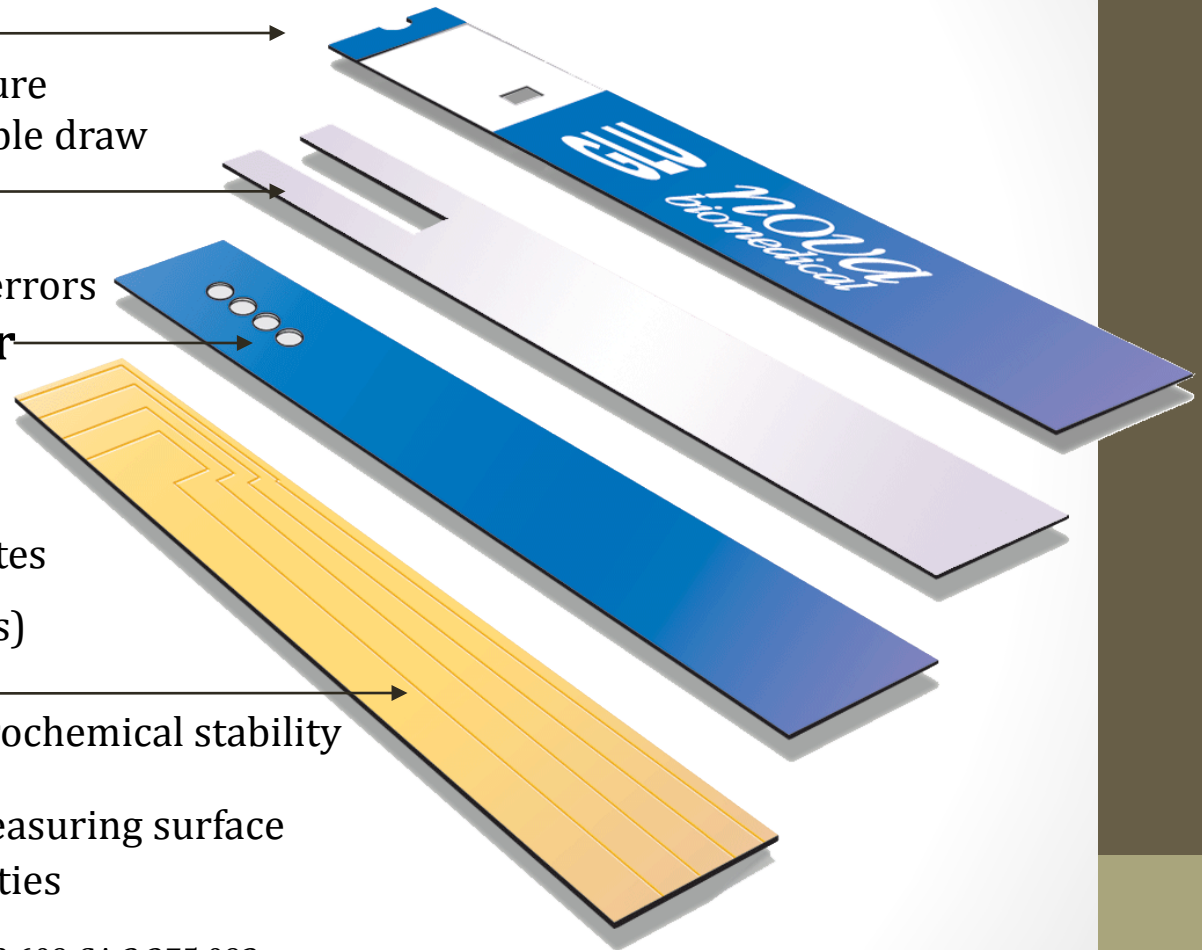
Patent: US#6,287,451;6,837,976;EP#1 212 609;CA 2,375,092

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Reproducible validation of Nova's StatStrip glucose technology

now 60!

Scientific Papers Validate Nova's Technology Breakthrough In Glucose Sensor Accuracy

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 hematocrit 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:

Copies of this booklet are available by contacting Nova Biomedical Tel: 781-894-0800 www.novabiomedical.com

"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 hematocrit error decreases the frequency of hypoglycemia."
Pidcoke M et al. Crit Care Med 2010

"The new generation StatStrip glucose meter, which has been designed to compensate for hematocrit 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 hematocrit, 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 ME. AACC, Annual Meeting 2008

"With the exception of the Nova StatStrip, all meters were affected by variable hematocrit."
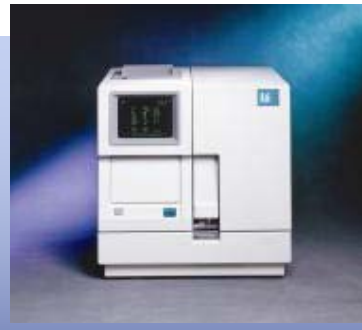Mohn B. NZJ Med Lab Sci 2010

Questions?

Nova's Technologies

Stat Profile® pHOx Ultra
Test Menu: pH, PCO_2, PO_2, SO_2%, Hct, Hb, Na^+, K^+, Cl^-, Ca^{++}, Mg^{++}, TCO_2, Glu, BUN, Creat, Lac, HHb, O_2Hb, Methb, COHb, O_2Ct, O_2Cap, tBil
Samples: Whole blood, Serum, Plasma

Stat Profile® pHOx
Test Menu: pH, PCO_2, PO_2, SO_2%, Hct, Hb, Na^+, K^+, Cl^-, Ca^{++}, Glu, Lac

Samples: Whole blood, Serum, Plasma

Nova Chemistry Analyzers
Test Menu: Na^+, K^+, Cl^-, TCO_2, Ca^{++}, Mg^{++}, Li^+, TCa, Glu, BUN, Crea, Hct, pH

Samples: Whole blood, Serum, Plasma
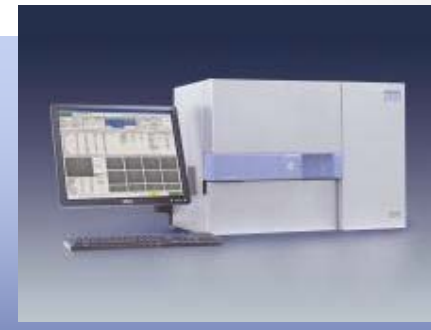
Nova BioProfile FLEX™
Test Menu: Gluc, Lac, Gln, Glu, NH4+, pH, PO_2, PCO_2, Na^+, K^+, Ca^{++}, CD, CV, Osm, IgG, PO_4
Samples: Cell Culture Media

Nova StatStrip®
Test Menu: Glucose
Samples: Whole blood

Nova StatStrip®
Test Menu: Glucose/Ketone
Samples: Whole blood

Nova StatStrip®
Test Menu: Lactate
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

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Critical Care

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

Analyte	Pathology
Glucose	Hypoglycemia, Hyperglycemia
Glucose + BHB	DKA
Lactate	Hypoperfusion/Sepsis
Creatinine	CKD

Device	Handheld glucose meter + single use disposable test strip	Chemistry analyzer
QC material	Liquid	Liquid
Measurement principle	Enzymatic/Amperometric	Hexokinase
Specimen type	Whole blood	Plasma or serum
Frequency	Level 1 and 3 every 24hr	Bracketed QC (every 300 samples)
Operator	Nurse	Clinical laboratorian
	Assess the quality of test strip and is then one test strip at a time	Assess the quality of entire measurement system (aliquot, dilutions, reagents, optics, etc)

Factors or interferences reported to affect glucose meters

Factor or Interference	Examples
Operational errors	Calibration coding errors, improper sampling, dosing errors
Environmental factors	Altitude, temperature, humidity
Exogenous interferences	Non-glucose carbohydrates, drugs
Endogenous/pathophysiological changes	Hematocrit, pO_2, triglycerides, uric acid

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