



**What it takes to make a new “state
of the art” diagnostics platform for
Point of Care use.**

Stig Morten Borch

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Axis-Shield plc

- 450 employees
- Turnover £ 58 million
- Profit before tax £ 1,9 million
- R&D spend £7,4 million (19 % of sales excluding third party business)



Axis Shield:

- Head quarters (UK)
- **Corporate R&D (Oslo & Bodø)**
- Laboratory Division (Dundee)
- **Point of Care Division (Oslo)**
- **Direct distribution: Medinor (Oslo)**

NycoCard™ (First version launched 1989)



- Point of care platform
- Quantitative measurements of CRP, HbA1c, U-Albumin, D-Dimer within 3 minutes
- Finger prick blood
- >16.000 instruments installed
- > 80 countries

Cons.:

- Accuracy depending upon operators performance.

Axis-Shield PoC vision

Become the #1 supplier of IVD products to the PoL (doctors office) segment.

2001

Develop a fully automated, multi-analyte IVD platform giving reliable results within 5 minutes.

Afinion™

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The sensor technology is just one of many critical elements within modern diagnostic platforms.

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Making the right product.

Key requirements of futures PoC IVD platform.

- **Multi-analyte menu.**
 - Relevance and uniqueness
- **Rapid, simple and safe in use (Convenience)**
 - Sample handling / Finger-prick blood sample
 - Closed disposable system / minimized contamination risk
 - Instrument auto-calibration and control
 - Max three steps procedure: Add sample - Push button - Read result
 - < 5 minutes
- **Quality: Reliability / robustness**
- **Performance matching reference lab. methods**
- **Compact and modern design**
 - Size: Kits & instrument
- **Data storage and transmission.**
- **Economy for end user**
 - Instrument & test costs vs. reimbursement
- **Meeting regulatory requirements (FDA)**
 - Design control

Concept idea from internal R&D by Nov. 2000:

- Multi-functional disposable assaying cartridge
Applicable to a variety of very rapid quantitative chemistry principles
=> Multi-analyte.
- Digital camera technology based measurement system.
- Concept for whole blood handling
- Fully automated instrument processing.
- Acceptable cost figures
- Proprietary (Patent protection)



- Compact (Instrument & Cartridge)
- Wide menu of quantitative assays:
 - HbA1c (Diabetes)
 - CRP (Inflammation)
 - ACR (Diabetes)
 - PT INR (Coagulations)
 - Ferritin+Hb (Iron status)
 - hs-CRP (Risk CVD)
 - Hcy (Risk CVD)
- Unique patented technology
- Winner of DnB-NOR's innovation award 2003
- Winner of a US design award 2006

- One compact cartridge for each test
- All reagents within the cartridge
(before, during & after use)
 - Liquid and dried reagents.
- Barcodes
 - Automatically read by the instrument.
Test ID, processing, batch data, expiry,....



afinion

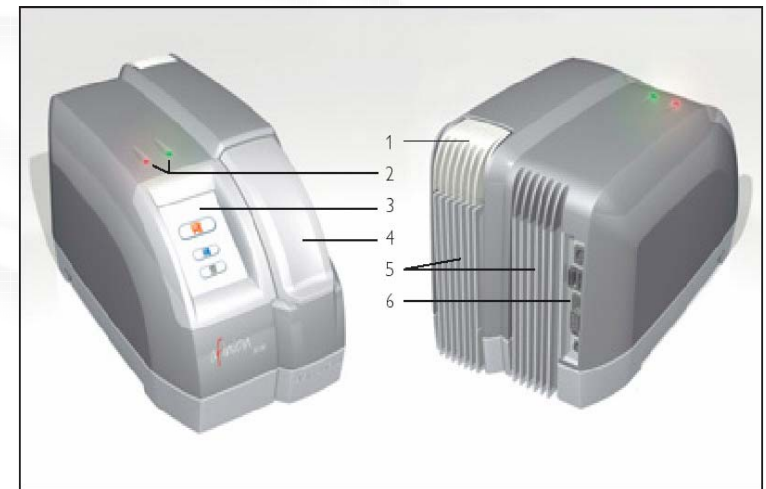
POINT OF CARE CENTER

- Integrated sampling device holding “end to end” capillary
- Fingerprick Whole Blood samples (+ S/P & Urine)
- Sample volume: 1.5 -15 μ L

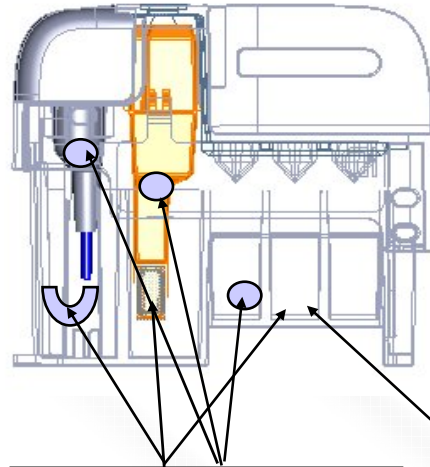


The instrument:

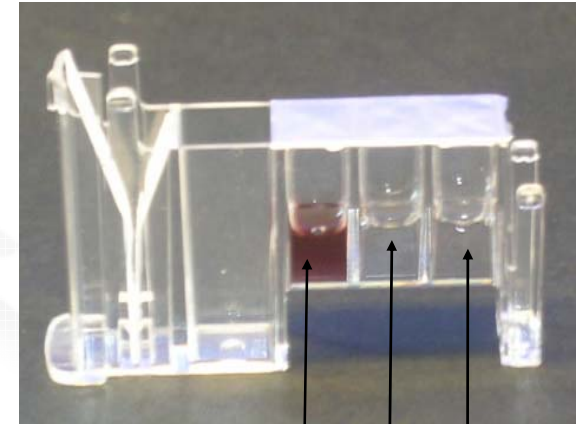
- Easy and safe handling
- Automated identification
(Assay & sample / Digital camera)
- Fully automated cartridges processing
(according to bar code)
- Digital camera for fail safes and measurement
- 1 to 5 minutes total assay time
- Data storage and relevant connectivity capabilities



The cartridge is the heart of the Afinion concept

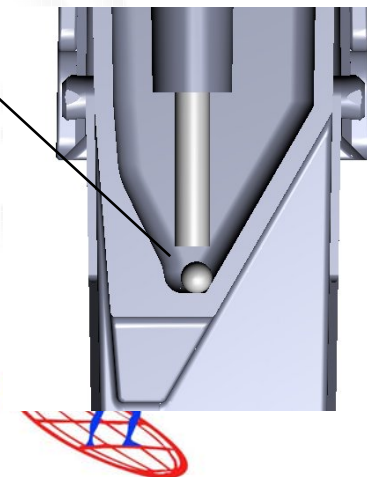


Dried reagents



Liquid reagents

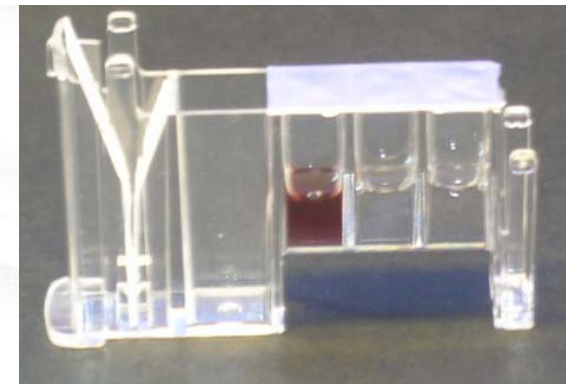
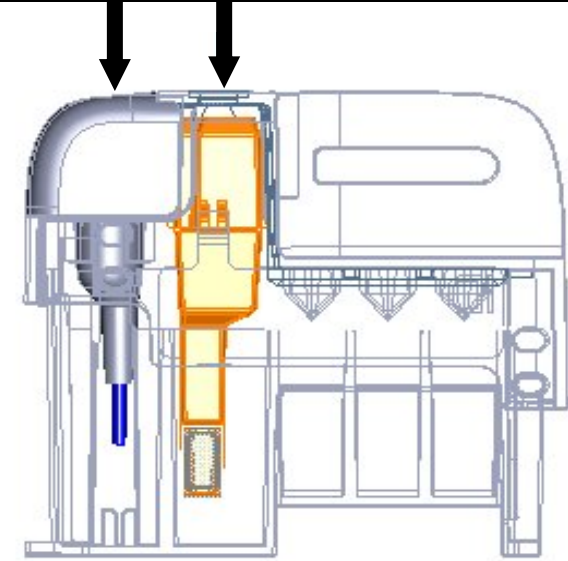
- Multicavity cuvette, Unique shape
- Several cavities for reagent storage
- Steel ball (magnetic) => PT (Coagulation)



Fully robotised cartridge processing within the instrument

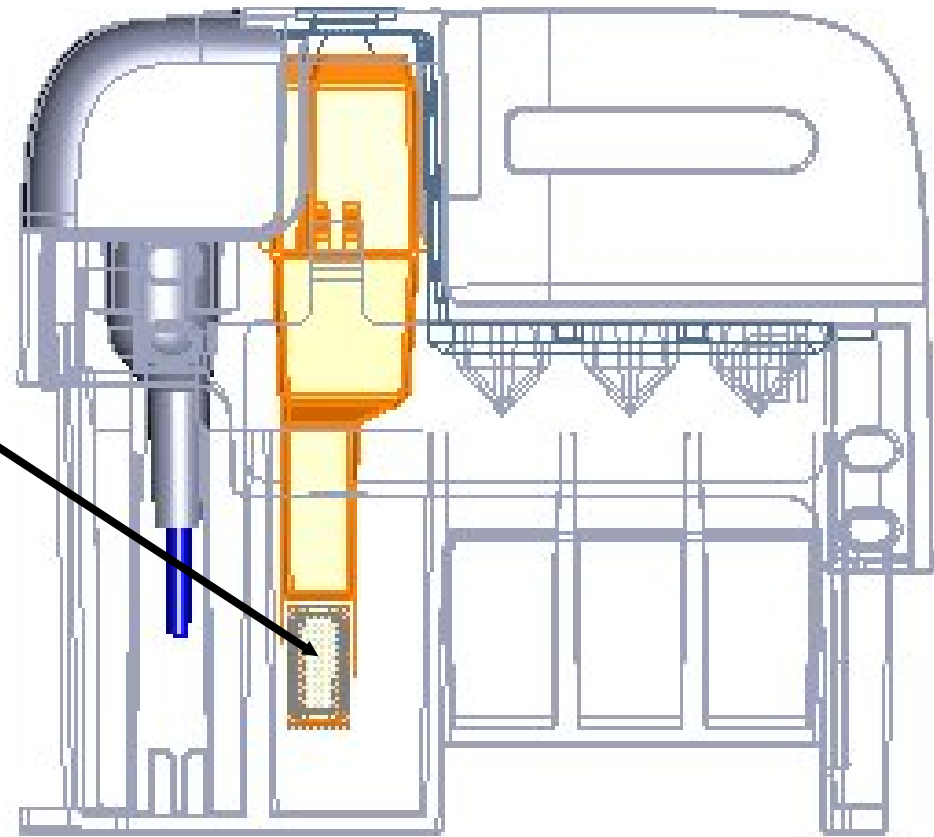
- Cartridge ID + OK, sample (Digital camera)
- Pump docking
- Cartridge splitting
- Reagents processing according to cartridge bar code.
- Digital camera reading responses
- Proper sealing after use

Two separate pump connections



”Sensor” technology:
Visibility of analyte response as measured by digital camera
Patented concept

Active porous membrane on a tube.

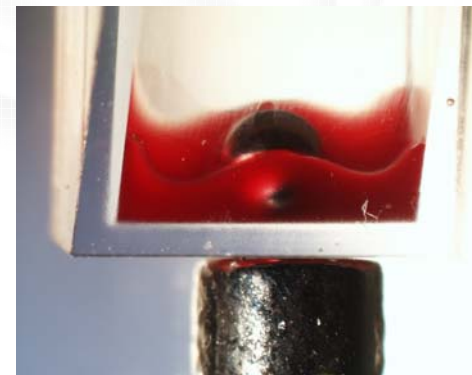
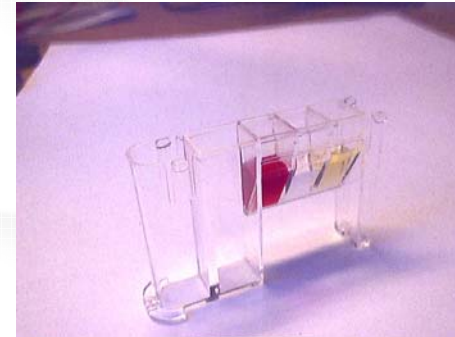


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The Digital Camera concept allows multiple measurement principles:

- Coloured surfaces (membranes)
(Reflectance)
- Optical density of liquids,
Transmittance:
 - Colourimetric measurements
 - Haematocrit corrections
 - Enzymatic reactions
 - Turbidimetric measurements
- Monitoring moving objects;
PT assay:
Steel ball in a magnetic field

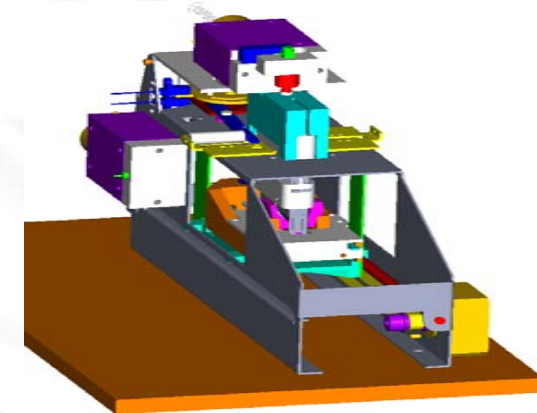
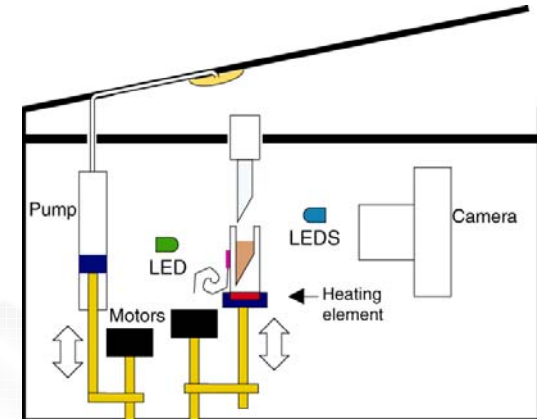


Multifunctional detection system

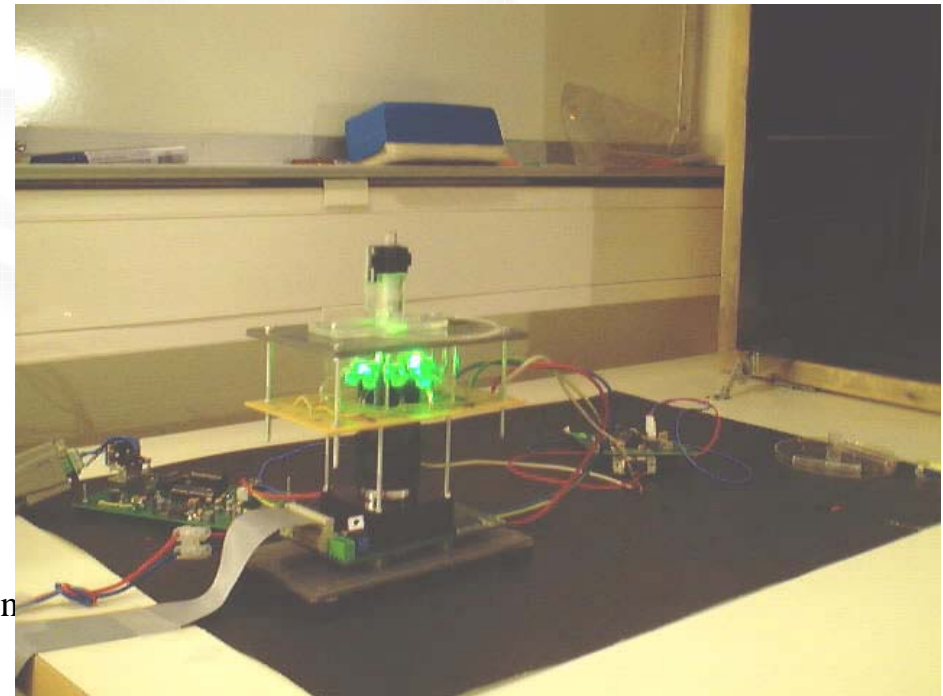
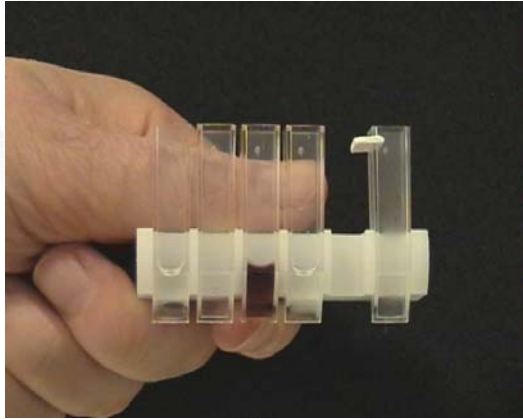
- Digital camera:
 - Identification (barcode, sample)
 - Failsafes and process monitoring
 - Advanced colourimetric measurements
 - Multipixel analysis, intensity, patterns, motions.
 - Process monitoring
- => Advanced multi-pixel analysis

Project Phases (Research).

1. Which technologies should be used.
2. Principles designs.
3. Detailed designs.
4. Prototypes building
Work Like => Look Like => Made Like



2 first years of testing experiences based on “in house” made model systems



orten

Modern diagnostics development:

Several fields of competence have to work very closely together:

- Chemistry
- SW-programming (Picture analysis)
 - Electronics
 - Mechanics
 - Mechatronics
- Materials engineering / Plastics design
 - Process engineering

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Challenges handling top level scientist:

- Scientist goals = Company's goals
=> **Motivation, incentives, information**
- Working according to "Design control regulations"
=> **Education**
- Communication between different fields of competence.
 - Chemists and SW-programmers
=> **Physical nearness, team building**
- Closing doors:
 - Choosing / excluding technologies
 - Stop development (improvement) when good enough.
=> **Clear milestones and acceptance criteria**
- Time limits acceptance.
=> **Planning seminars, incentives**

Large project => Many external partners

- **Chemistry / assays:**

- Axis Shield

- **Cartridge / Assembly line:**

- Axis-Shield
- Teleca (S)
- Epsilon PD (S)
- Carclo/Plasro (UK)
- Sortimat (D)
- Beck E. (No)

- **Instrument:**

- Axis-Shield
- Teleca (S)
- Epsilon PD (S)
- Sanmina (S)
- Beck E (No)

A-S had to build internal competence in electronics, mechatronics and SW programming.

R&D staff (2003):

- >50 coworkers full time internally
- >50 externally

Industrialization:

Cartridge + Chemistry assembly:

Produce >20 million test cartridges per year.

- Cost effective production.
Fully automated assembly machine
- Robust processes and materials
>95% yield, efficiency
- Automated in process control



Assembly line video

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Instrument:

- Robust and cost efficient production
 - Inexpensive design & materials
 - Robust parts (Mechanics)
- Uniform sensor responses
 - Automated calibration

Clinical use of *in vitro* diagnostic products in point of care settings.

Clinical use	
Risk screening	
Detection	
Diagnosis	
Disease / treatment monitoring	
Relapse	

Clinical relevance of reliable point of care *in vitro* diagnostic products.

Clinical use	Afinion™ products
Risk screening	Hs-CRP, Hcy
Detection	CRP
Diagnosis	CRP, HbA1c, ACR, Ferritin/Hb
Disease / treatment monitoring	INR PT, HbA1c, ACR, CRP, Ferritin/Hb
Relapse	CRP, HbA1c, ACR

The Afinion™ concepts impact on futures health care.

Early detection and precise diagnosis:

- Correct treatment / medication in time / on time:
 - Patients health and function (life saving).
 - Faster recovery
 - Reduced sick leave
 - Reduced hospitalization
 - Reduced medication (Antibiotics)
 - Reduced costs
 - Patients
 - Employers
 - Community

Diagnostic services today: <1% of total health care spendings

Key success factors for PoC IVD products

- Ease of use (CLIA waiver)
- Quality
 - Robustness
 - Performance
- Menu (Multi-analyte, relevance & uniqueness)
- Factory efficiency and expense management
- Proprietary technology. Patents
- Market coverage
- Launch