Market Perspectives on the (In Vitro) Diagnostics Industry

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For MTIC
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Topics

• Overall market size and segmentation
• Major trends and drivers
  – Consolidation of Suppliers
  – Growth Driver; POC
  – Growth Driver; Molecular Diagnostics
  – Growth Driver; Companion Diagnostics
• Investment environment
Not Topics

- Technology and Tech. Platforms
- Regulatory
- IP
- User Consolidation
- IT/i-Phone/Cellphones
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Big is beautiful

Clear dominance of the leading 15 companies, which account for almost 90% of the global IVD market – 8 companies = 80%
Consolidation drives for scale, segment presence and profitability

• Abbott
  – Medisense, Murex, Sequoia Turner

• Siemens
  – DPC, Dade Behring, Bayer
    • Dade Behring; Baxter, Behring, Syva
    • Bayer; Ames, Technicon, Corning

• Ortho
  – Kodak, Micro Typing Systems, DuPont
Consolidation Is Not Over

• 2009/10 Beckman-Coulter
  – Olympus Life Science IVD Business
  – $800 million acquisition
  – $500 million additionnel sales
  – $50-60 bottom line +
  – Another $50 million « synergies »
  – New customer IA base
  – Broader CC customer base
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POC Industry Snapshot

- Estimate Point of Care (POC) to be roughly $3B, excluding non-IVD applications and Whole Blood Glucose testing
- What is it? Patient self test (PST), physician office lab (POL), and hospital based POC
- Overall IVD market growth is at 6%-7% annually
- POC category growth better, at 10%-12%

[POC Industry Snapshot Pie Chart]

- Hospital Labs: 48%
- Commercial Labs: 29%
- Self Testing: 16%
- POC: 7%
Clinical use of *in vitro* diagnostic products in point of care settings*

- Risk screening
  - Hs-CRP, Hcy

- Diagnosis
  - CRP, HbA1c, ACR, Ferritin/Hb, TSH, pro-BNP, TnT/I, Mb, CK-MB, D-dimer, HAI’s**, Flu

- Disease / treatment monitoring
  - INR PT, HbA1c, ACR, CRP, Ferritin/Hb, TSH/TT4, HAI’s, urine albumin

- Relapse
  - INR PT, HbA1c, ACR, CRP, Ferritin/Hb, pro-BNP, TnT/I, Mb, CK-MB, D-dimer, HAI’s

*Excludes OTC and home testing

** Hospital/Healthcare Acquired/Associated Infections
Whole gamut of instruments and technologies

No dominant over-reaching standard = many niches = many opportunities
POC; what has Wall Street’s attention?

- Infectious disease Rapid testing (HIV coming?)
- PST: New and more accurate meters (WBG and Coagulation)
- Rapid hospital acquired infection (HAI) testing seen as potentially explosive – in hospital POC and POL
- POCCompanion Diagnostics? Warfarin metabolism testing could be the poster child. FDA is clearly supportive.

- Market Perspectives on the POC Diagnostics Industry
  MassMEDIC; September 12, 2007
PST Coagulation

- Coagulation monitoring is a sizeable market. 3MM patients on some form of anti-coagulation therapy in the US alone - 34MM tests annually.
- WW sales of coagulation testing equipment and reagents exceed $1B annually. PST component of this market is 8-10% today, and could grow to 20% by 2010.
- Additional indications (especially A Fib) could be the driver, with data available in 2009.

<table>
<thead>
<tr>
<th>Addressable patients</th>
<th>2005</th>
<th>2008</th>
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<tbody>
<tr>
<td>Mechanical heart valve</td>
<td>969,000</td>
<td>1,028,311</td>
</tr>
<tr>
<td>Atrial fibrilation</td>
<td>4,781,700</td>
<td>5,301,556</td>
</tr>
<tr>
<td>DVT</td>
<td>1,786,400</td>
<td>1,868,000</td>
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<tr>
<td>Other CV</td>
<td>501,600</td>
<td>572,409</td>
</tr>
<tr>
<td>Prophylaxis and post surgery</td>
<td>1,537,500</td>
<td>1,779,848</td>
</tr>
<tr>
<td><strong>Total tested patients</strong></td>
<td>7,290,840</td>
<td>8,609,080</td>
</tr>
<tr>
<td><strong>Total patient opportunity</strong></td>
<td>9,576,200</td>
<td>10,550,124</td>
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MRSA infections are ubiquitous, dangerous, and costly. The incidence of MRSA (Methicillin Resistant Staph Aureus) infections is rising in both hospitals and long term care facilities. In the ICU, infection rates approach 60% with 90K patients dying annually as a result of hospital-acquired infections, including those caused by MRSA.

Both POL and hospital STAT applications

MRSA screening is the single most important new market for molecular diagnostics. Currently valued at $1.2 billion in the US, potential $2.2 billion if screening technologies can be applied in smaller hospitals, out-patients facilities and long-term care facilities.
FOR IMMEDIATE RELEASE
January 2, 2008

FDA Clears First Quick Test For Drug-Resistant Staph Infections

Test Identifies MRSA Bacterium in Two Hours

Remarkable annual cost savings have been demonstrated in hospitals implementing active MRSA surveillance programs.

BD GeneOhm™ MRSA Assay
POC Challenges

- POC formats still tend to cost more than central lab tests
- Reimbursement, reimbursement, reimbursement – a mixed bag. POC coagulation a poster child for challenges
- POL – getting beyond the 30,000 or so larger POLs – will smaller practices ever really want to get into the blood handling/billing business?
- Getting CLIA waived tests can take time, money
- Hospital POC: turf issues between central lab and POC advocates
- Technical – especially in the more esoteric segments – making rapid POC more accessible. Will there ever be a user friendly molecular format?
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Molecular Diagnostics Unchained

- PCR patent expiry offers NA technology growth

- Patent expiry is expected to unlock considerable market opportunities

- *End of an Era*: PCR Patent; WHAT the dominance of Microsoft Windows is to personal computers, the dominance of the polymerase chain reaction is to biotechnology. The core PCR technique is now in the public domain
The molecular diagnostics industry is segmented into two major markets:
- service and in vitro diagnostics.
- different growth curves, target different niches,
- the service market is about 1.7 billion dollars in the U.S. globally, about 2.5 billion,
- the IVD market is ca $1.3 billion in the U.S. globally, about $1.9 billion.

The service segment of molecular diagnostics is growing by an average of 25% pa. Infectious diseases comprise 80% growing at a rate of only 10%-15%. Eg Third party sequencing services are provided by -600 Contract Research Organizations.

Today, genetics testing is responsible for driving growth of the overall molecular diagnostics market, currently constituting 7%-8% of the clinical testing service market.

In the service segment, genetics testing is growing by 60%-75% per year. Recently, the Abbott -Celera alliance hit the market with products for Cystic Fibrosis & HIV drug resistance,

There are no approved products on the market for genetics; they are mostly home-brews.

Oncology accounts for the remainder of the overall molecular diagnostics market. While oncology is only at 5% or less of the total market, this segment is growing at a rate of over 100%.
Totally new markets-technology Driven

- Jan 2010: Illumina launches the HiSeq 2000
  - decode a person’s DNA in one week using $10,000 worth of materials – five times cheaper than any other competing gadget on the market
  - BGI (formerly the Beijing Genomics Institute) has agreed to purchase a whopping 128 of the new sequencing systems
  - BGI’s order will ultimately allow it to sequence 11,000 human genomes per year
Totally new markets-technology Driven

- NHGRI Plans to Award $9.5M for '1,000 Genome' Sequencing Tech Development in FY 2010
- “Sequence-by-Service” - Nov 2009: Complete Genomics; sequenced three whole-genomes for an average materials cost of $4,400 and reports that it is selling whole-genome sequences at $20,000 apiece in minimum orders of five, with the price dropping as the order size increases

The Great Beyond
The Nature blog that rounds up science news from around the world

- Complete Genomics publishes a genome - November 05, 2009 « Meanwhile, dozens of new sequencing companies are working away in garages and office parks on ever-better technologies that will further cut costs and timelines. Personal genomics has been a long time coming, but if these companies can deliver, we shouldn't have to wait too much longer.”

IVD Market R. Sutherland JAN 2010
Many opportunities in ID outside HIV and HCV

- QIAGEN to Supply Singapore Ministry of Health With Avian Flu Surveillance Solutions (Jan. 8, 2008)
  - Awarded an exclusive contract by the Singapore Ministry of Health to supply sample preparation solutions and molecular tests for the specific detection of Influenza H5N1 viruses.
  - The contract with the Singapore Ministry of Health is the latest supply agreement of QIAGEN with public and private institutions engaged in H5N1 surveillance.
  - More than 80 institutes worldwide involved in the surveillance of avian flu infection use procedures and reagents developed and offered by QIAGEN
Qiagen first mover in Molecular IVD Consolidation

• May 2005; acquired the PCR diagnostics company Artus
  – paid approximately $39.2 million
  – diagnostic systems for use in the detection of infectious diseases such as SARS, Herpes simplex virus -1/-2, EBV, West Nile Virus, Malaria, Salmonella.

• June, 2007, acquired Digene for $1.6 billion
  – only FDA approved manufacturer of a molecular diagnostic test for human papilloma virus (HPV),

• November 2009, QIAGEN to acquire SABiosciences
  – a privately-held developer and manufacturer of disease- and pathway-focused PCR assay panels
  – > 100 real-time PCR assay panels analysis of DNA, RNA, epigenetic and microRNA targets associated with cancer and apoptosis

IVD Market R. Sutherland JAN 2010
Qiagen first mover in Molecular IVD Consolidation

- Sep 2009, acquisition of UK company DxS up to $130M
  - DxS has established over a dozen partnerships with leading pharmaceutical companies to develop *companion diagnostic* tests for a variety of disease states.
  - working with Bristol-Myers Squibb and Eli Lilly subsidiary ImClone Systems to develop a companion diagnostic for Erbitux. In July, the company announced an agreement with AstraZeneca to develop a *companion diagnostic* for Iressa.
  - real-time PCR tests, including a test for the mutation status of the oncogene KRAS, which is indicative for successful treatment of patients with metastatic colorectal cancer using EGFR inhibitors. TheraScreen: K-RAS Mutation Kit, is CE-marked.
  - Expects to contribute approximately $6 million sales 2009 and approximately $30 million in sales in 2010
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Will Companion Diagnostics finally be « Personalised medicine »

- February, 2009 **Novartis** Launches Molecular Dx Unit to Get Jump on **Companion Diagnostics**
- in-house molecular diagnostics unit in order to improve the co-development of companion diagnostics and drugs
- oncology is "obviously a very opportune place" for the drugmaker to begin developing companion diagnostics
- estimates Novartis’s early molecular diagnostics portfolio will be about 50% oncology related.
Will Companion Diagnostics finally be « Personalised medicine »

- Diagnostics kits will be developed on the same timeline as medicines, so that the drugs and their companion diagnostics can reach the market simultaneously – in-house strategy
- The areas that can benefit most from a drug-diagnostics combination are oncology and infectious-disease management
- Companion diagnostics may threaten the blockbuster-drug model because they limit the number of candidates for a drug
- But “It’s inevitable” potential benefits for the patients could be “fantastic”
Companion Diagnostics already exist?

- Warfarin metabolism testing could be first salvo – FDA has signaled their support
- Current turnaround time is generally described as not quick enough
- Rapid, easy to use testing formats are coming to market
Companion Diagnostics; its started already– January 24, 2008

- AutoGenomics Gets FDA OK for Warfarin MDx Assay
- US Food and Drug Administration clearance to market its Infiniti 2C9-VKORC1 Multiplex Assay for warfarin sensitivity
- In August 2007, FDA updated labelling for warfarin with information explaining that people with variations of the genes CYP2C9 and VKORC1 may respond differently to the drug
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• Investor attitudes
Wall Street’s Take

- IVDs historically not seen as glamorous as other medical device categories - less IP, less R&D
- IVD growth rates were lower than other Med Tech categories
- Consolidation in the central lab meant less pricing leverage for IVD vendors
- IVD companies were often viewed as cash cows without the capital needs that typically attract Wall Street attention
A New Point of View?

- Sector now being viewed much differently
- IVD companies are uber defensive plays - in turbulent markets providing even greater cash flow and earnings visibility than their more volatile Device/Biotech counterparts
- The Razor/Razor Blade business model provides the same demographic attractiveness as other health care groups, but with far lower volatility
- Perception: IVD companies have far less exposure to reimbursement risk.
- Recent “game changers” have made the IVD sector more visible:
  - High growth single markers i.e. BNP and MRSA
  - Molecular diagnostics – heading to POC and no PCR royalties
  - Companion Diagnostics now seem to be real
- Lastly – M&A. There is nothing more attention-getting than a lot of acquisition activity in a sector.
Some General Conclusions

- Small companies will lead on innovation & establish market presence through differentiated technology.
- POC is here to stay
- PCR is unchained
- Small is still good
- Totally new markets and significant growth from Asia-PAC

$40 billion in 2010?