

CLINICA

DIAGNOSTICS

HIGHLIGHTS

Genzyme Diagnostics and Genzyme Genetics profiled

Editorial – Gene sequencing costs decreasing

Interview – Five minutes with Mark Chandler of Biophysical

First for pharmacometabonomics

Market intelligence for in vitro diagnostics

MARKET INSIGHT

Improving healthcare through diagnostics: the future of IVDs

Clinicians, hospitals, patients and governments are all striving for improved healthcare. In the US, this has recently taken the form of an ongoing debate about health reform. In addition to expanding access to healthcare services and improving the quality of care, the reform effort aims to slow the growth of healthcare expenditure by "bending the cost curve". Recent estimates suggest that medical errors cost the US approximately \$37.6bn each year, approximately \$17bn-worth of which are preventable. These errors lead to roughly 70,000-100,000 deaths in US hospitals per year.

The in vitro diagnostics (IVD) market has the potential to play a major role in improving the delivery of care. Lab testing influences 70-80% of healthcare decisions and accounts for only approximately 4% of US healthcare spending. Healthcare costs have been rising unsustainably, partly because of the focus on treatment rather than prevention in the current care paradigm. Government regulators and healthcare stakeholders are beginning to turn their focus to providing higher-quality care and eliminating spending on unproven or lower-quality therapies.

IVDs can facilitate this approach by providing data about the pros and cons of treatment. The potential of IVDs to positively impact healthcare is exponential. The data can be used in pay-for-performance programmes which reward the delivery of better care. IVDs could also improve care standards by allowing therapy to be given in a more relaxed care setting by clinicians who require less training. As healthcare reform focuses on cutting costs and improving quality simultaneously, the decentralisation of IVDs will increase efficiency, initiating immediate and relevant treatment regimens. As these pressures for healthcare reform mount and evidentiary standards continue to climb, the IVD market will also trend toward more efficient, economical options. This could take the form of point-of-care (POC) testing, carried out by clinicians in office settings or by nurses in private clinics; or remote patient monitoring (RPM), performed in the home setting.

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Mesothelioma biomarker promise welcomed

The British Lung Foundation (BLF) welcomed the publication of research into a new mesothelioma biomarker – mesothelin – as "an important step forward" in diagnosing and treating the disease sooner, with the promise of lengthening survival time.

Researchers based at the UK universities of Oxford, London (UCL) and Bristol, sought to "assess the diagnostic role of pleural fluid mesothelin and the potential impact of common clinical factors on accuracy". They concluded that: "pleural fluid mesothelin provides additional diagnostic value relative to cytological examination". They also found that "mesothelin measurements are reproducible and not affected by inflammatory pleural processes".

The paper "Clinical impact and reliability of pleural fluid mesothelin in undiagnosed pleural effusions" appeared in the *American Journal of Respiratory and Critical Care Medicine* (September

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However, diagnostics could also contribute to the negative financial trends which are already putting a strain on the system. In particular, overutilisation of medical services has led to increased costs, and numerous studies have shown that the US healthcare system is overloaded with wasteful and unnecessary treatment. In fact, the director of the US government's Office of Management and Budget, Peter Orszag, has suggested that healthcare spending could be reduced by as much as 30% without any deduction in quality of care. There are a number of reasons for this: first, financial incentives, particularly a fee-for-service system, encourage physicians and labs to perform more tests to earn more money. In order to counter this, payers are beginning to carefully scrutinise what they are paying for and encourage only the highest-value tests using the most efficient modes of delivery. Another factor is the fear of malpractice legal action if a condition is not diagnosed properly or the standard of care is not met. This drives physicians to order tests without promising improved patient outcomes or treatment. One study has suggested that the cost of "defensive medicine" was \$100-178m per year. In future, diagnostics must successfully prove their value for purposes other than financial incentives and legal defence to be successful.

Positively developing IVDs can help avoid the backlash associated with the potential negatives of test "overuse". This involves three types of diagnostic developments: rapid POC testing; decentralised clinics; and RPM.

Promise of rapid POC testing

POC testing can potentially enable immediate and relevant treatment regimens. POC tests are defined as those that can be administered and interpreted at a patient's bedside in hospital, or a physician's office by non-laboratorians. They can measure continuous glycaemic load, prothrombin time, blood gas, haemoglobin, haematocrit, and other blood cell counts. A number of studies have demonstrated that using POC tests for continuous glycaemic monitoring reduces glucose values in the hypoglycaemic range and leads to significant improvements in overall glycaemic control. Furthermore, some of the most successful POC tests are used in the emergency room. Urgent disease states and conditions often present themselves in this setting, where a delayed diagnosis can have grave consequences. Often, turnaround time in the hospital lab is not quick enough to effectively diagnose and subsequently treat these urgent situations. Specifically, rapid tests measuring troponin and brain natriuretic peptide (BNP) have proven invaluable in helping clinicians determine if a heart attack has occurred, allowing them to treat the patient appropriately.

When a test can provide immediate results, it can be extremely beneficial. However, this immediacy may not be as valuable if it comes with a substantially greater cost. Many contagious diseases, such as methicillin-resistant *Staphylococcus aureus* (MRSA), are urgent because it is important to diagnose the patient immediately and quarantine them if necessary, to avoid the spread of an unwelcome pathogen. However, for many diseases there

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may not be the same need for immediate information. In these cases, the physician initially treats the patient based on their primary symptoms and later adjusts the treatment if the test results yield a different diagnosis. For example, when a patient presents with symptoms suggesting chlamydia, the clinician can treat them empirically with a standard course of antibiotics. In this case, testing can be confirmatory because the timing of the result is less important. While immediate test results would be an added benefit, they are not necessary for providing quality healthcare. As such, the healthcare system should not absorb a higher cost for POC tests for these types of conditions.

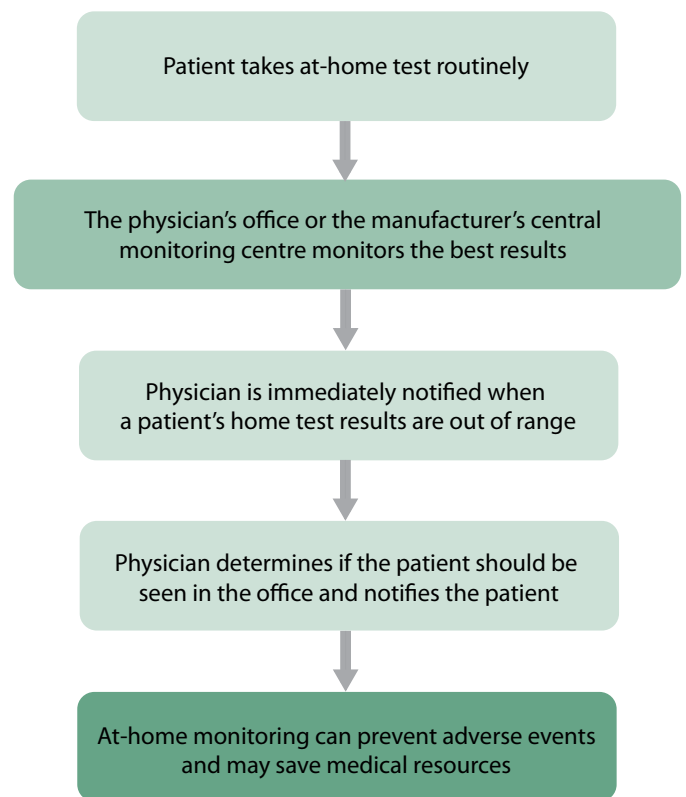
From the payer perspective, one issue with POC testing is that it may create a financial incentive for physicians to over-utilise the tests. When testing is done by a lab, the physician orders the test but the lab retains the profit from testing. This balance is lost when the physician can potentially profit from the test – the physician may test patients unnecessarily. To avoid this issue, payers often impose coverage restrictions to monitor and ultimately lessen the use of potentially lucrative tests. Therefore, POC test manufacturers must carefully position their tests to encourage appropriate use and avoid payer barriers. This can be accomplished through education and practitioner training on the appropriate test’s use and potential reimbursement barriers.

Promise of a decentralised model: retail clinics

Shifting the delivery of healthcare to less expensive settings is another option for containing costs. As detailed in “Innovator’s Prescription: A Disruptive Solution for Health Care” by Clayton Christensen, one of the main reasons hospital care is so expensive is because hospitals must be prepared to diagnose all manners of diseases and conditions. Hospitals must keep all diagnostic devices, tests and other tools on hand to identify the causes of different physical complications and conditions. As a result, their overheads are very high. Diagnostics that clarify a patient’s condition and the corresponding treatment have the potential to remove a lot of the cost and complexity associated with this care.

The arrival of alternative care delivery sites may provide an important opportunity for diagnostics. POC testing for common conditions in decentralised locations will expand general access to healthcare and play a key role in shifting care to less expensive settings. In some states, healthcare evaluations are now available through clinics established in retail pharmacies. For routine disease presentations, non-physicians can perform a comprehensive evaluation using advanced diagnostics, issue a diagnosis and begin treatment immediately. This system is an efficient way of delivering high-quality medicine, by sending only the patients with the most complicated cases to hospital. It also provides uninsured or underinsured patients with

Figure 1: Dynamics of RPM



Source: Boston Healthcare

access to more affordable healthcare. This concept would not be possible without POC tests.

A simple example of the benefits of this model would be a patient who comes down with strep throat over the weekend, leading to a severe sore throat and fever. In most cases, the only option for the patient would be to go the emergency room. As discussed, this is a costly trip. The patient may receive unnecessary healthcare services and may divert physician attention from more critical patients. A potential alternative to the emergency room could be a “minute clinic” located in a local pharmacy. At the clinic, the patient can be seen immediately without an appointment by a nurse practitioner and given a POC test. If the results of the POC rapid strep test are positive, antibiotics can be issued immediately. The total cost of these types of evaluations in a minute clinic are usually less than \$100, compared with several hundred dollars for an emergency room visit.

This healthcare model is not effective in all cases or for all conditions. However, for those conditions in which the diagnostic and treatment algorithms are well proven, rapid diagnostics can play important role in the success

and efficiency of treatment for these types of routine ailments. These tests must be reliable and simple to perform so patients and caregivers can feel assured that those with serious conditions are not misdiagnosed.

Promise of remote patient monitoring

Another way of diffusing the cost of healthcare is by moving care to the home setting. RPM devices perform rapid blood tests and other diagnostics in the patient's home and can transmit the results to the physician's office or allow the patient to monitor their own health status. The market for at-home remote diagnostic devices is currently limited, but growing rapidly. Forecasts project that the RPM market will more than double over the period 2007-2014.

Presently, most RPM devices are used by home health agencies that need to track and monitor patients' health status in order to determine the frequency and urgency of care. This care paradigm works well for these agencies because it means they can deliver more efficient and effective care. They can monitor all patients while focusing in-person visits on those with the greatest need. This model can also be applied to other segments of the healthcare system, to improve quality and eliminate unnecessary home visits and adverse events resulting in visits to the emergency room.

An example of the potential benefit of RPM is in monitoring the use of warfarin therapy. If not enough of the drug is administered, there is a loss of efficacy, but if too much is administered, "bleed-outs" can lead to hospital visits or even death. One way to avoid this is to frequently test a patient's prothrombin time or international normalised ratio (INR). However, since this is done in a warfarin clinic or lab it is often inconvenient to the patient. Last year, Medicare expanded coverage to at-home blood testing of patients who take anticoagulants daily. This provides proactive monitoring which can help the patient avoid adverse events and unnecessary office visits.

A key component of this care model is the development of tests which give healthcare providers the option to direct expensive care to the patients that need it the most, while also monitoring other patients. The ability to monitor patients remotely and receive results from essential IVD tests should make the system more efficient by eliminating unnecessary office visits and other resources required for typical IVD tests.

One of the reasons that RPM has been slow to expand is that although payers endorse the concept of at-home testing, regulatory restrictions and evidentiary standards currently block coverage. Like all novel technologies, payers want to see clinical utility. Structured coverage, coding and payments for RPM testing have not yet been established because so much of the reimbursement system is based on payment for care on a per-service basis when delivered in the clinical setting. For the RPM testing market to be successful, mechanisms for coverage, coding and payment that work for a home care delivery model will need to be developed.

However, like POC tests and the decentralised clinics, RPMs are not cost-effective in all situations. While payers recognise the potential value RPM devices may bring to the healthcare market place, they are also concerned about adding costs to the system that are not correlated with improved outcomes or efficiencies. RPM devices should be designed only for conditions that can be appropriately monitored in this way and easily adopted into the current care paradigm. Appropriate conditions would include those that lead to catastrophic consequences and expensive care if not monitored. RPMs can save costs if used and priced appropriately, and can also expand access to care by freeing up physician time and allowing priority treatment to the most critical patients.

The future of IVDs

Diagnostics will allow the delivery of more efficient and effective care, and enable healthcare access to a greater number of people. Innovators must, however, balance the desire to rapidly grow a market for these tests with the potential negative reaction if tests are "overutilised" due to financial or liability concerns. But diagnostics have the potential to play an essential role in achieving some of the key goals of healthcare reform: cost containment, and improving access and quality. The development of diagnostic technologies that are simple to use provides clear insights into care pathways. And treatment that can be used in less expensive care settings will be important to the success of POC, retail clinic and RPM models.

- This article was written by Charles Mathews, Terry Geldart and Michelle McInnis of Boston Healthcare Associates, a Boston, Massachusetts-based consultancy company for biopharmaceutical, medical device and diagnostic companies. For more information, contact info@bostonhealthcare.com

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Henri Termeer	President, CEO and chairman of the board
Dr Alan Smith	Senior vice-president of research and chief scientific officer
Michael Wyzga	Executive vice-president of finance and chief financial officer
Donald Pogorzelski	Vice-president and president of diagnostics division

Company Overview

The first division of Genzyme Corporation to be established was its diagnostics business, in 1981. Genzyme Diagnostics offers three types of products: intermediates or critical raw materials; finished reagent kits for use on clinical chemistry analysers; and point-of-care (POC) rapid tests. The company manufactures the intermediates at its facility in Kent, UK, while the POC tests are manufactured in San Diego, California.

Genzyme also has a genetics division which provides reproductive and oncology diagnostic testing, as well as genetic counselling services. Genzyme Genetics employs over 1,500 people and has eight laboratories located across the US and operations in Europe and Japan.

Genzyme's other divisions are biosurgery, oncology and pharmaceuticals. Overall, the company employs more than 11,000 people, and had revenues of \$4.6bn in 2008.

Key Competitors

Abbott Laboratories

Beckman Coulter

Becton Dickinson

Inverness Medical Innovations

Product Overview

Genzyme Diagnostics' intermediates, which include enzymes, substrates and antibodies, are used to manufacture further reagents, which are supplied to clinical labs worldwide.

The division's reagent kits include the firm's high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol tests, and the firm claims to be the market leader in this field. Genzyme Diagnostics also markets assays for amylase and lipase to help diagnose pancreatitis, and an assay for glycated serum protein to monitor medium-term glycaemic control in diabetics.

The division's POC rapid tests are designed to combine accuracy, speed and ease of use, allowing better patient management decisions and reductions in healthcare costs. They include the OSOM brand of tests for pregnancy, group A *streptococcus*, mononucleosis, *Trichomonas vaginalis* infection and bacterial vaginosis.

Genzyme Genetics claims to be an industry leader in maternal serum screening tests – its products include CFplus, a cystic fibrosis carrier screening test. It also offers therapeutic and prognostic tests for breast cancer, and testing services for leukaemia and lymphoma.

This division uses various testing methods including: screening biochemical markers in serum; cytogenetics, which detects abnormalities in the number and structure of chromosomes; flow cytometry, which quantifies and classifies different types of blood cells; fluorescence in situ hybridisation, which uses fluorescently tagged DNA probes to detect chromosome abnormalities and

rearrangements; immunohistochemistry, to identify antigens; and molecular genetics, to detect known genetic mutations.

Key Milestones

January 2009	Genzyme Diagnostics launches a new test to aid the diagnosis and monitoring of kidney disease, the cystatin C assay
November 2007	Genzyme acquires Diagnostic Chemicals Limited's IVD business, thereby expanding its diagnostics division
December 2006	The company launches a <i>KRAS</i> gene mutation test in the US to identify non-small cell lung (NSCLC) cancer patients with resistance to tyrosine kinase inhibitors, available through Genzyme Genetics' testing service
July 2005	Genzyme Genetics launches a noninvasive test for minimal residual disease in patients with B-cell chronic lymphocyte leukaemia. The test detects small numbers of leukaemic cells that remain in the patient during treatment, or when the patient is in remission – it is the major cause of relapse in cancer and leukaemia
May 2005	Genzyme licenses worldwide diagnostic rights to mutations in the epidermal growth factor receptor (<i>EGFR</i>) gene, which are found in some NSCLC patients, from the Massachusetts General Hospital and Dana-Farber Cancer Institute
May 2004	The firm purchases Impath's cancer diagnostic services business, which becomes part of the Genzyme Genetics division
May 2001	Genzyme acquires Wyntek Diagnostics, expanding its position in infectious diseases and pregnancy testing

1997	The firm establishes its molecular oncology division
1993	Genzyme Diagnostics launches its direct LDL cholesterol kit
1989	Genzyme merges with Integrated Genetics, helping to make it a leader in the genetic testing industry. It also establishes a prenatal testing lab in Framingham
June 1986	Genzyme becomes a public company, and opens the first genetic testing lab for cystic fibrosis and other inherited disorders
June 1981	The company is founded

Agreements

- Genzyme has a licence agreement with UK personalised medicine firm DxS to develop and commercialise products that detect mutations in the *EFGR* gene. In January 2009, the companies expanded the deal to include the US and Canadian markets
- Genzyme purchased the rights to intellectual property from genomic-based diagnostics specialist Exact Sciences in the field of prenatal testing and reproductive health in January 2009
- The company has an agreement with the UK's National Health Service to help the diagnosis of lysosomal storage disorders

Technologies/Product Pipeline

Genzyme Diagnostics aims to introduce further POC rapid tests, particularly for infectious diseases. It hopes to test for respiratory syncytial virus and *Clostridium difficile* toxins A and B in 2009, and is also developing diagnostic markers for renal disease and NSCLC.

GENZYME CORPORATION FINANCIALS (\$ THOUSANDS)

Year	2008	2007	2006	2005	2004
Total revenue	4,605,039	3,813,519	3,187,013	2,734,842	2,201,145
Operating income (loss)	581,479	653,865	(190,509)	600,862	252,913
Net income (loss)	421,081	480,193	(16,797)	441,489	86,527

SEQUENCING COSTS COME DOWN, WHILE PATIENTS' WAIT CONTINUES



Stephan Fritsch

On August 10, the publication of a letter in *Nature Biotechnology* described the first "single-molecule sequencing of an individual human genome", using a third-generation sequencing instrument by Helicos. While the sequencing of a whole human genome per se is no longer extraordinary, it is agreed that to make patient's DNA data available for a personalised medicine approach, the effort, time and money invested in sequencing a single person's genome needs to come down considerably.

The big aim is the \$1,000-genome, but this is some way off, and there is divided opinion as to what the current figure is. With last week's announcement, Helicos is admittedly far off the \$1,000 mark, with costs of approximately \$48,000 for reagents alone, not factoring in capital investment costs for the sequencing instrument itself, which costs close to \$1m. It has potential, however, that sets it apart from currently available technologies, according to Helicos president, Stephen Lombardi.

Mr Lombardi points out that the latest whole human genome sequence was achieved using a single instrument, with the means of a single genome laboratory, namely a laboratory at the Stanford

Cancer Centre, rather than using the infrastructure of a whole sequencing centre, and taking no more than two weeks. "We are working now on achieving a 50 times cost reduction, so that we can present a product in 2 to 2½ years that can produce a complete sequence of a human genome for \$800," Lombardi said.

To put the Helicos result into context, we need to consider the progress sequencing has made over the last 25 years.

The first drafts of the human genome, revealed in a video-linked media event in 2000, involving US president Bill Clinton and UK prime minister Tony Blair, took the best part of 15 years and used capillary electrophoresis. While there are no reliable estimates for the total costs, the figure is likely to be way above the original \$3bn allocated. Having started as a public effort dispersed over various academic centres around the globe, the work ploughed slowly on, until it was spurred into a faster pace by a private consortium, lead by Dr Craig Venter and using Celera's shot-gun sequencing method.

The three second-generation sequencing technologies in the market today, from Roche/454, Illumina/Solexa and Life Technologies/ABI, have left capillary electrophoresis behind and but use an amplification step of DNA strands via polymerase chain reaction (PCR). The current price points for a whole human genome sequence using these methods are roughly en par with Helicos.

However, if given a choice between two sequencing instruments with the same performance and same price, Mr

Lombardi is adamant that "any scientist will choose the method not using PCR amplification". While the three companies vie for sequencing scientists' favour, third-generation concepts avoid amplification – and the related potential source for errors in the resulting data – and use a single molecule of DNA. Contenders for this market include Pacific Biosciences, Oxford Nanopore and Complete Genomics, and some are known to offer a whole human genome sequencing service for closer to \$20,000.

But money is not all. Quality of data is key, as stressed by every provider of instrumentation; however there seems to be no generally agreed standards with which to measure this quality. And once we ask, how this raw data can be translated into clinical practice, we hear the same comments that have accompanied every milestone in DNA sequencing technology.

"We supply the technologies with which to generate the raw data. But this data is currently only useful for research. Academic groups around the world will have to ask the questions that allows the sequence of single bases of a human genome to give clinically useful answers in field such as pharmacogenomics or toxicogenomics," stressed Mr Lombardi. He expects the research sector to work on these solutions over the next 5-10 years.

This is what makes every announcement of advances in sequencing technology so frustrating: The presenting company or scientist is showing us the light at the end of the tunnel and evokes the brightness that will await us there. But we'll inevitably have to wait a few more years for the clinical benefits to be realised.

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BECKMAN COULTER ADDS MORE DIMENSIONS TO ITS CELL ANALYSIS



Ashley Yeo

Beckman Coulter marketing director of Life Science & Cellular Analysis, Arno Schoenberger, describes the company's cell analysis activities to Ashley Yeo, in the last of a series of interviews with European-based executives of the biomedical systems firm

In the area of cellular analysis, Beckman Coulter's strategy is to cover both haematology and flow cytometry. This enables the wider study of different cell populations.

The company is alone in aiming to focus on both these technological platforms: its main competitors, Sysmex and Becton Dickinson, specialise in only one or the other.

"The market has shown a trend to use both techniques, which is why we are investing in both platforms," Arno Schoenberger, director of Beckman Coulter's cell analysis activities, told *Clinica Diagnostics*.

The company used international market research to support its decision to redefine its new UniCel DxH 800 and Navios platforms (see below), he said.

Beckman Coulter is currently No 2 in Europe in haematology, behind Sysmex and has a goal to become the leader in the European market. In flow cytometry, Beckman Coulter is, again, No 2 in Europe, behind Becton Dickinson, which has over 60% of the market.

"In some countries, we are already No 1, for instance, in France and Spain in haematology," said Dr Schoenberger.

He explained that the company's DxH haematology platform technology is targeted at mid-high volume labs.

It offers a new, high-resolution and more automated way of analysing cells, improving the quality and consistency of results.

"Beckman Coulter made its name with VCS (volume, conductivity and scatter) legacy technology, which could analyse in three dimensions. Now, we can analyse cells in seven dimensions. But that is not the endpoint, said Dr Schoenberger, adding that the system "offers the potential to move to 400 parameters, depending on what we use. He said: "It is a very open system."

DxH is a completely new flexible technology that is designed to meet future throughput needs. "The beauty of the system is its modularity, and it is designed to be scalable for customers as workflow expands." The system allows for other modules to be connected, which is an innovative concept in haematology. The company plans to enable DxH connectivity in Q1 2010, making it possible for up to four instruments to work together. Q1 2010 will also see the release of a slide maker/slide stainer.

The system was launched in the US in late 2008, and is now being unveiled, during Q2 2009, in Europe via phased launches. Already, Europe's first DxH 800 has been installed in a hospital in Hamburg, Germany, and there are more orders in the pipeline, including from the Netherlands, and the UK, where an installation planned for September. The company describes these moves a "major breakthrough".

"We applied the disciplines of lean six-sigma before developing the instrument; the DxH therefore delivers modularity with a very small footprint," he said. Its waste can be handled easily, as it contains no carcinogens, cyanide or formaldehyde.

He added: "We believe that the scalable workcell platform in cellular analysis is unique in the market place. We demonstrated this at this year's EuroMedLab (EML) when the company was able to show how the DxH can offer labs a customised, scalable solution."

DxH – the most recent member of the UniCel family – has the 'same look and feel' for its software, and is based on the same concept as other UniCel-branded systems.

"The instrument is based on a completely new design for hardware and software architecture: it includes a modern fluidic management and only one aspiration point, so it is very convenient and easy to use. It is also a highly reliable system."

The major advantages of the DxH are that it reduces cost and includes automation. There is less hands-on time and a faster TAT, as the number of manual steps is reduced. DxH is a flexible concept that allows the lab to grow with demand, says the company. Also new is the reagent management programme; there are only five reagents for all programmes, and they are environment friendly. The reagents offer an excellent signal-to-noise ratio, and so can

provide a good differentiation of cell populations.

"Workshops, seminars and local customer events have shown that customers like the concept and the future opportunities available under the DxH workcell concept," said Dr Schoenberger.

The system also provides cell population data as additional parameters to describe morphological cell properties. This is important in investigating cells in respect of certain diseases, for example sepsis, lymphoma, anaemia, and myelodysplastic syndromes.

Beckman Coulter has its own in-house flow cytometry expertise, so it has been relatively easy for the company to combine haematology measurement with flow cytometry measurement.

"We aim to replace most manual smears, and in the future will have a specific testing module in the DxH module," said Dr Schoenberger. The company's trademarked "Hematoflow" concept – which

involves a way of using monoclonal antibodies to do a differential with up to five-colour, six-antibody combinations – will also play a part in this. Hematoflow automates the process and, as such, reduces errors.

"This is the future of cellular analysis and is unique to Beckman Coulter," said Dr Schoenberger.

"Conceptually, we are going in a new direction with DxH, and, based on the quality of results, will change modern haematology and disease management," he added. "DxH is a way of assessing diseases earlier and better – that's our positioning."

Haematology is a conservative market, he said, but added: "Beckman Coulter technology led the way for years – now we are back with a highly competitive platform."

Navios

The Navios is described by Beckman Coulter as a new frontier in flow cytometry. This high-speed and high-resolution benchtop analyser was on view at EML this year. "We have been successful with the FC500, but it has

its limitations, and we recognise there is a demand for more colour," said Dr Schoenberger.

Navios can measure up to 10 colours, using three lasers, or eight or six colours, both using two lasers.

It is a redesigned platform (which uses Gallios as its research platform) that offers superb scatter detection and fluorescence resolution for high-end cellular applications such as T cells, stem cells, and lymphoma and leukemia. To support this, Beckman Coulter will also launch a five-colour lymphoma and leukaemia reagents panel (Solastra, first IVD L&L kits) in Q3 that can run on the FC500.

Aiming for the top

Reagents are an important element in helping to differentiate cell populations. This is already a recognised strength at Beckman Coulter, particularly in flow cytometry. The company will build on their excellent performance in both flow and haematology to help the company move to first place in the cellular analysis market, said Dr Schoenberger.

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FIVE MINUTES WITH... MARK CHANDLER OF BIOPHYSICAL



Mark Chandler

Mark Chandler is the chairman and CEO of biomarker-based technology firm Biophysical. In 1994, Forbes Magazine described him as the "Indiana Jones" of medical research after his work in the rainforests in south-east Asia and South America discovering deadly toxins that became cutting-edge treatments for cancer



Joseph Harvey

Clinica Diagnostics: In your opinion, what will be the next big game-changer in the field of biomarker technology?

Mark Chandler: The game is radically changing in biotechnology, with the importance of the proteome ascending as rapidly as the genome is descending. Nowhere is this clearer than in the evaluation of neuropsychiatric conditions. Many large studies analysing the genetic component of schizophrenia have observed only the most tenuous thread between the disease and specific genes or single-nucleotide polymorphisms (SNPs).

Cambridge University and Psynova in the UK, however, have presented similarly large studies that revealed highly specific and sensitive serum biomarker patterns that are diagnostic for schizophrenia (>90%). Though not on the near horizon, any new technology that will allow precise quantification of

the thousands of components of the serum proteome (including specific antibodies) will be the game-changer we all expected from the genome.

Clinica Diagnostics: What is the best part of your job?

MC: The best part of my job is being right about an industry trend.

Clinica Diagnostics: What is the worst part of your job?

MC: The worst part is being wrong. My first company manufactured the earliest batches of Botox, but declined future involvement because I was certain nobody would risk injection with botulinum toxin just to smooth a wrinkle.

Clinica Diagnostics: How do you think the global economic downturn has affected the diagnostics market?

MC: The downturn is probably helping those companies whose

products provide critical information at lower cost. It may not be the best time to introduce expensive boutique products, however.

Clinica Diagnostics: What methods of marketing have you used to sell your products?

MC: Biophysical's marketing efforts have been centred on public relations. After five appearances on the Oprah Winfrey Show (US television talk show) and favourable mention in upscale publications like The Financial Times, Forbes, and Business Week, our clients and physicians are getting a clear idea of who can benefit from comprehensive biomarker testing. Physician adoption is now the fastest growing sector of our business, which is of most benefit to the patient as their physicians are working to detect disease early and provide a roadmap for health with their patients.

** Mark Chandler was talking to Joseph Harvey*

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Pharmacometabonomics shown to predict how patients respond to drugs

Researchers have found that measuring levels of compounds excreted in urine before the administration of paracetamol (acetaminophen) predicts how patients will metabolise the drug.

Those with high levels of para-cresol sulphate, a toxic molecule produced by microbes in the gut, metabolised the drug less effectively than individuals with lower levels, the study found. Para-cresol sulphate is metabolised by the same enzymes as paracetamol, as well as other drugs.

The principle that led to this discovery is called pharmacometabonomics, which the lead researcher, Jeremy Nicholson of Imperial College London, UK, told *Clinica Diagnostics* was "the metabolic equivalent of pharmacogenomics". While pharmacogenomics uses the genetic profile of an individual to predict how drugs will work, pharmacometabonomics analyses how an individual's pre-dose metabolic profile (which is both genetically and environmentally determined) can help predict how drugs are metabolised, Prof Nicholson explained. "This work shows that it is mainly gut microbial metabolic activity rather than human genetics that determines how this major drug is metabolised."

This is the first time that pharmacometabonomics has been used to show how a drug is metabolised in humans. "This is something nobody has been able to predict before, even for a simple drug like paracetamol at therapeutic doses, although we have previously proved the principle in rats," Prof Nicholson said.

The findings have many implications, he explained: "Para-cresol also potentially interferes with the metabolism of any compound

that has a hydroxyl group – that's hundreds of different drugs. But gut microbes can produce hundreds or thousands of other compounds, all of which can have these sorts of effects.

"And microbes do other things as well – not just competing for metabolism with drugs. They can metabolise drugs directly, for example the heart drug digoxin is metabolised by gut bacteria, so their activity can affect its availability. Microbes can also make drugs into more toxic compounds before they get into your bloodstream."

He was emphatic about the study's findings: "They mean you cannot consider the issue of personalised healthcare without considering gut microbes."

"Integral" to personalised medicine

The study analysed the urine of 99 healthy male volunteers before and after taking a standard therapeutic dose of paracetamol (two 500mg tablets). It found that those with high pre-dose levels of para-cresol sulphate had low post-dose ratios of acetaminophen sulphate to acetaminophen glucuronide – both metabolites of paracetamol. The results appeared online in the *Proceedings of the National Academy of Sciences* on August 13.

The authors proposed that "assessing the effects of microbe activity should be an integral part of pharmaceutical development and personalised healthcare".

"We have shown that by carrying out a urine test – which takes minutes and isn't very costly – we can say what metabolites are present and therefore potentially how a whole range of drugs will be metabolised, once we understand what that metabolic signature actually means," Prof Nicholson said.

"The other thing is if the microbes change drug metabolism, why don't we change the microbes?" This could

improve drug efficacy and reduce the rate of side-effects, he said. "A simple example of this would be a drug that stops microbes from making para-cresol – we filed a patent on this very recently."

The group is currently taking part in the Consortium for Metabonomic Toxicology (COMET) 2 project, which is funded by several major pharmaceutical companies, looking at mechanisms of drug toxicity.

The researchers are also working with Nestlé to understand the role of gut microbes in areas like obesity. "Abnormal gut microbial activity has also been related to colon cancer, Crohn's disease, ulcerative colitis, and even asthma," Prof Nicholson said. "So they really are important in a huge number of situations."

Strong Q2 prompts Qiagen guidance hike

Dutch diagnostics firm Qiagen has raised its revenue and EPS guidance for fiscal 2009 after posting healthy second-quarter results. The company upped revenue expectations for the full year from \$920-970m to \$930-970m and EPS forecasts from \$0.88-0.94 to \$0.90-\$0.94 per share. Venlo-based Qiagen said that robust market demand and solid economic trends within the diagnostic sector helped to boost sales. Revenue for the period was \$240.2m, up 10% from Q2 2008. Increased sales of the firm's HPV screening products, KRAS diagnostics and H1N1 tests helped grow the top line. Qiagen's net income also benefited from the stronger sales and reached \$48.3m compared to \$40.4m in the same period last year.

Eight-year European cancer biomarker project receives €10m funding

The French innovation agency OSEO has injected €10m (\$14.3m) into an eight-year research programme,

IMAKinib, to develop specific biomarkers and radiotracers that would enable personalised and effective treatment for cancer patients. Heading the project, which is expected to cost €24.7m in total, is Oncodesign, a French oncology-focused biotech company. The firm will work together with fellow French companies Guerbet, which develops radiotracers for medical imaging procedures, and Ariana Pharmaceuticals, which specialises in data management software used to enhance the drug discovery and development process. Oncodesign will be responsible for developing the biomarkers specific to the drug treatments, while Guerbet will develop radiotracers. These radiotracers will be used in clinical trials for scanning tumours and to allow the evaluation of the drug's clinical efficacy. Ariana will provide the software for analysis of chemical and biological data.

Genetic variant predicts hepatitis C treatment response

A genetic variant could explain why African-Americans are less likely to respond to treatment for hepatitis C than Americans of European ancestry.

A 1,671-patient genome-wide association study has found that a polymorphism near the *IL28B* gene is linked with an approximate twofold change in response to the standard treatment – a 48-week course of peginterferon- α -2b or peginterferon- α -2a plus ribavirin. The gene encodes interferon- λ -3, a cytokine that is important for immunity against viral infections.

Furthermore, the genotype that led to a better response is more common in European compared with African populations, and drug treatment is less successful in blacks than whites.

"This genetic polymorphism explains approximately half of the

difference in response rates between African-Americans and patients of European ancestry," the authors wrote. The study did not address what accounts for the other half, one of the researchers, Dongliang Ge of Duke University, Durham, North Carolina explained, but added: "It's a reasonable guess that the other 50% might be due to environmental factors."

The "good response" genotype is even more common in Asians – around 75% respond well to treatment, compared with 55% of European-Americans and 25% of African-Americans.

Side-effects

As hepatitis C treatment can be associated with severe side-effects, including fatigue, flu-like symptoms and depression, the findings could be used to develop a test to identify responders and non-responders. "I think this finding is of immediate clinical use, so a test could be used by physicians right now," Dr Ge told *Clinica Diagnostics*.

Patients with the "poor response" allele might opt to postpone treatment until better drugs become available, especially if they do not have liver damage. Several new classes of antivirals are in development, the most advanced being the protease inhibitors – Schering-Plough's boceprevir and Vertex's telaprevir are both in phase III trials.

"I want to clarify that patients with a poor genotype do have the option to proceed with treatment," Dr Ge said. "But they need to know that their chance to get cured from hepatitis C infection is much lower than patients with the good genotype.

"I think this is important, because the treatment is a very uncomfortable and miserable process. If I were infected with hepatitis C, I would like to know beforehand whether I could possibly benefit from the treatment."

One drawback of the study is that it only evaluated patients infected with a particular subtype of the hepatitis C virus, called genotype 1. This is the most common of the six main hepatitis C genotypes in the US. The virus genotype can affect patients' responses to treatment. Other researchers are planning to validate the latest findings in patients with different disease genotypes, Dr Ge said.

His group now aims to investigate the function of the genetic variant discovered in the trial, to find how it contributes to the difference in treatment response.

The study was funded by Schering-Plough, which also produces peginterferon- α -2b. Additionally, the firm owns the intellectual property rights on any diagnostic test resulting from the discovery, although it is unclear whether it will develop such a test.

The findings appeared online in *Nature* on August 16.

EGFR mutation analysis could guide therapy in lung cancer

A personalised medicine approach could soon be taken to non-small cell lung cancer (NSCLC), as researchers have discovered that patients' genomes determine their responses to certain treatments.

Two studies, one conducted by East Asian researchers, one by a Spanish group, found that those with mutations in the epidermal growth factor receptor gene, *EGFR*, responded well to drugs in the EGFR tyrosine kinase inhibitor class – Tarceva (erlotinib) or Iressa (gefitinib). Both trials were published in the August 20 issue of the *New England Journal of Medicine*.

Additionally, the study which analysed an East Asian population

found that patients without these mutations responded better to carboplatin-paclitaxel chemotherapy.

The prognosis for NSCLC patients is poor – first-line chemotherapy has a response rate of around 30%, with average progression-free and overall survival rates of five-months and 12-months, respectively.

In comparison, the Spanish study found a median progression-free and overall survival of 14 months and 27 months, respectively, in 217 Spanish NSCLC patients with *EGFR* mutations who received erlotinib. The overall rate of complete or partial response to erlotinib was 70.6%. Unlike the East Asian study, this trial selected patients with mutations to receive treatment, and did not compare erlotinib treatment with chemotherapy.

"Large-scale screening of patients with lung cancer for *EGFR* mutations is feasible and can have a role in decisions about treatment," the authors concluded.

The trial in East Asia randomly assigned 1,217 previously untreated patients to receive either gefitinib or chemotherapy. The overall rates of progression-free survival at 12 months were 24.9% with gefitinib and 6.7% with chemotherapy.

The researchers then subdivided patients depending on their *EGFR* mutation status – this could only be evaluated in 437 patients. In the 261 patients found to have mutations, progression-free survival was significantly longer in those who received gefitinib than those on chemotherapy. There was a 71.2% objective response rate to gefitinib in this group, which the authors described as "remarkably high".

Conversely, in 176 patients determined to be without *EGFR* mutations, progression-free survival was significantly longer in those

who received chemotherapy. In this group, the objective response rate to gefitinib was 1.1%.

Gefitinib was associated with fewer side-effects, including alopecia, nausea, vomiting and neurotoxic symptoms.

"Our findings suggest that, whenever possible, *EGFR* mutation status should be determined before the initial treatment of pulmonary adenocarcinoma," the authors of the study concluded.

These findings could enable a more personalised approach for NSCLC treatment. "We are currently at a change in the paradigm," the lead researcher, Tony Mok of the Chinese University of Hong Kong, told *Clinica Diagnostics*. "However, not all lung cancer cases currently have sufficient tumour sample at diagnosis to enable *EGFR* mutation analysis. We now need to obtain more tissue [at diagnosis] so we can do this, and then make a decision on which treatment a patient should receive.

"Once a patient is known to have an *EGFR* mutation, you can treat them with either gefitinib or erlotinib," he continued. "Patients without the mutations should receive chemotherapy as a first-line treatment."

Around 20-30% of the Asians carry *EGFR* mutations, compared with approximately 10% in western populations. The mutations are more common in women, patients who have never smoked, and those with pulmonary adenocarcinomas, a subtype of NSCLC.

KRAS mutations

Personalised medicine is already used in colorectal cancer, where only patients with non-mutated *KRAS* genes are recommended for treatment with EGFR inhibitors, including Amgen's Vectibix (panitumumab) and Merck KGaA's Erbitux (cetuximab).

The *KRAS* protein is downstream of the EGFR receptor, and in patients with a mutated *KRAS* gene, the *KRAS* protein is always "turned on" regardless of whether EGFR has been inhibited.

"The presence of a *KRAS* mutation [in colorectal cancer] will preclude the advantage of cetuximab," Dr Mok said. "But in lung cancer the situation is slightly different – it is the presence of the *EGFR* mutation that predicts a favourable outcome to gefitinib."

Super Religare expands Rosetta's MicroRNA assay coverage

Rosetta Genomics has broadened its global sales network by signing an exclusive distribution deal with Super Religare Laboratories (SRL), said to be the largest Indian diagnostics network. The new partnership will see SRL make Rosetta's range of miRview tests available in India, Saudi Arabia, Qatar and the UAE. The miRview portfolio includes a test for identifying the primary tumour site in metastatic cancer patients and patients with cancer of unknown primary, another for differentiating squamous from non-squamous non-small cell lung cancer and a test for distinguishing mesothelioma from other carcinomas in the lung. Financial details of the deal were not disclosed.

Response shares hit year peak before solid results

Shares in molecular diagnostics firm Response Genetics reached their highest price of the year to date in the run-up to the company's second-quarter results. Response's shares climbed as high as \$2.72 each on the Nasdaq on August 7, the stock's best pricing since December 2008.

On August 13, the Los Angeles, California-based firm posted a 4% increase in revenues to \$1.9m on

the back of greater sales of the ResponseDX genetic test. Response's net loss for the period widened compared to Q2 2008, falling from \$2.2m to \$2.4m after being impacted by increased R&D spending and greater general expenses linked to the launch of ResponseDX and its sales force expansion.

The launch of ResponseDX could prove critical in turning the company's fortunes around. Response endured a tough start to 2009, as it recorded a drop in revenues and a wider net loss in Q1, blaming a delay in the receipt of clinical samples from one of its major pharmaceutical partners.

Since launching on the Nasdaq in June 2007, Response shares have not been able to eclipse \$7.49, a price which its stock reached on its opening day.

AdvanDx adds \$8m to series C

AdvanDx, developer of molecular diagnostic tests for bacterial infections, has raised \$8m in the second tranche of its series C financing round. The funds, which were provided by existing shareholders SLS Venture and LD Pensions, will be used to expand AdvanDx's international sales and marketing activities and grow its product portfolio. In conjunction with the financing, the Woburn, Massachusetts firm also elected Tina Christensen to its board of directors. Ms Christensen is the vice-president and CFO of International Health Insurance Danmark, a Danish health and medical travel insurance provider.

US weight loss centre starts using Tethys' diabetes risk score

Structure House, a weight loss centre in Durham, North Carolina, has initiated a study using Tethys Bioscience's PreDx Diabetes Risk

Score (DRS) on 50 participants in its 28-day programme. PreDx DRS is a blood test that measures a person's risk of developing diabetes within five years. Emeryville, California-based Tethys hopes that it will help doctors target preventative strategies, such as weight loss programmes, to the most at-risk individuals. The study will use PreDx DRS to assess whether Structure House's intensive lifestyle change programme can alter patients' probability of developing diabetes. It will also evaluate whether more specific feedback on diabetes risk at the start of the regimen will increase the subjects' motivation to change their lifestyle.

New England to benefit from Caritas and Quest deal

US in vitro diagnostic products and services provider Quest Diagnostics has broadened its domestic presence by purchasing the physician office outreach business of Caritas Christi Health Care, a community-based hospital network based in New England. Quest (Madison, New Jersey) also agreed an information exchange partnership with Caritas and its network of hospitals. This collaboration will allow patients and physicians in New England expanded access to Quest's diagnostic testing, information and services. The Caritas network includes hospitals located in Massachusetts, such as St Elizabeth's Medical Center in Brighton, Carney Hospital in Dorchester, Good Samaritan Medical Center in Brockton, Holy Family Hospital in Methuen and Norwood Hospital serving around 600,000 patients annually. Financial terms of the acquisition and the information exchange were not disclosed.

Focus Diagnostics expands H1N1 test launch

Focus Diagnostics has made its H1N1 pandemic flu test available to other US labs with CLIA certification. The

Cypress, California company is also "assessing its options" for marketing the Influenza A H1N1 (2009) Real Time RT-PCR test outside the US. The US FDA granted emergency use authorisation (EUA) for the diagnostic in July, making it the first commercially available H1N1 test. On August 17, the agency informed Focus – a subsidiary of Quest Diagnostics – that it had amended the EUA for the test. It now states that the test may be performed in labs certified under the US CLIA act to perform high-complexity tests and operate certain equipment.

AMDL strengthens IVD focus with Dx subsidiary

Pharmaceutical company AMDL has created a new subsidiary, AMDL Diagnostics (ADI), which will focus exclusively on the development and commercialisation of its cancer test Onko-Sure.

Onko-Sure is designed to detect and monitor 14 different types of cancer – including lung, stomach, colorectal, liver and breast cancer – by measuring the accumulation of fibrin and fibrinogen degradation products in the blood. The test is CE-marked for use as a general cancer screen, approved by the US FDA for monitoring colorectal cancer, and by Health Canada for lung cancer screening and cancer monitoring.

AMDL, which is headquartered in Tustin, California, and has most of its manufacturing operations in China, said it has already signed distribution agreements with partners in the US, Canada and certain countries in the Asia-Pacific region for Onko-Sure. Over the next five years, ADI plans to build on these agreements, and significantly expand commercialisation of the product. It will also focus on the development of a next-generation version of Onko-Sure, which will be carried out in collaboration with the Mayo Clinic. The new test is expected to have

increased sensitivity and specificity; its launch is scheduled for late 2010.

Sales of Onko-Sure in 2009 are projected to be around \$1m, but not yet profit-generating. However, in 2010, the company expects to see sales increase to \$17m, with earnings of \$13m. By the end of 2014, if ADI fulfils its five-year business plan, it anticipates sales figures of over \$100m.

AMDL chairman and CEO Douglas MacLellan will run ADI.

FDA requests more information on Aspen-Bio's AppyScore

AspenBio Pharma's appendicitis blood test AppyScore has run into more problems, as the US FDA has requested further information related to the firm's 510(k) application. The Castle Rock, Colorado firm filed for approval of the diagnostic in June despite reporting disappointing results from a pivotal trial in January. AspenBio expects to submit the additional data in the first quarter of 2010. The company started "certain additional analyses and testing, including supplemental trial work" when it made the 510(k) application, as it anticipated that the agency might require more data.

Gene variation predicts poor response to antiplatelet drug

People with a particular genetic variation have a reduced response to the antiplatelet drug clopidogrel, a study has found. The research could expedite the use of pharmacogenetic testing to enable antiplatelet therapy to be tailored to each patient.

Patients with the variant who underwent percutaneous coronary intervention were also more likely to experience an adverse cardiovascular event within the following year.

Clopidogrel is recommended, in combination with aspirin, for a variety of cardiovascular disorders – often on a long-term basis. It is given to acute myocardial infarction (MI) patients, and to patients who have been implanted with a drug-eluting stent or other cardiovascular device, to prevent blood clots forming.

The variant discovered in the study led to a loss of function in the gene for one of the cytochrome P450 (CYP) enzymes, *CYP2C19*. This gene encodes an enzyme that converts clopidogrel, a prodrug, into its active metabolite.

This is not the first time that *CYP2C19* variants have been linked with adverse cardiovascular events in patients receiving clopidogrel. However, it was the first genome-wide association study to identify genes that affect patients' responses to the drug.

First, the researchers analysed the DNA of 429 healthy Amish people to find common genetic variations, and measured their platelet response after administering clopidogrel for seven days. They found that the loss of function variant, called *CYP2C19*2*, was linked with a diminished response to clopidogrel, measured by ADP-stimulated platelet aggregation performed on a blood sample.

The investigators then analysed the relationship between the variant, platelet function and cardiovascular outcomes in 227 patients undergoing percutaneous intervention. Those with the *CYP2C19*2* variant were more likely to have cardiovascular ischaemia or to die during the one-year follow-up period (20.9% vs 10% for those without the variant), although this was not statistically significant.

The findings appear in the August 26 issue of *JAMA*.

"About a third of the general population [in the US] carries at least one copy of this genotype," the lead

researcher, Alan Shuldiner of the University of Maryland School of Medicine in Baltimore, told *Clinica Diagnostics*. "And these people have about a 40% decrease in response to clopidogrel compared with those without the genotype, as measured by platelet reactivity. That translates into about a 2.4-fold increase in risk of having a cardiovascular event.

"Most people in our study had one copy of this variation – only about 3-4% of the population have two copies. So the association we found was mostly driven by people with one copy. Our data suggest that if you have two copies of the variation, you're more affected than if you have one. But that's debatable at the moment, and I think it's important to try to figure that out."

The variant was found to account for 12% of the inter-individual variation in platelet aggregation. Another 10% is explained by age, body mass index, and high-density lipoprotein and triglyceride levels. "We believe that there are probably other genes that also influence clopidogrel response," Dr Shuldiner said. "That's an area that we're actively pursuing now." Eventually, there could be a whole panel of genetic variants that could be tested to determine a patient's response to clopidogrel, he believes. "Or it may be that the combination of genetics and ex vivo platelet aggregation testing could predict who responds and who does not."

CYP2C19 genetic tests are already commercially available; they include Roche's AmpliChip. However, Dr Shuldiner cautioned that "until we have good prospective clinical trials, I'm not sure that we're quite ready to implement or translate these findings into everyday clinical practice".

His group is now planning a prospective, randomised trial of genotype-directed antiplatelet therapy. It will have two arms: one where all patients receive clopidogrel; and one where therapy is tailored depending on

patients' genotypes, so those without the *CYP2C19**2 variant would receive clopidogrel, while those with one or two copies would receive a different therapy. "That could be a higher dose of clopidogrel, which may overcome the effect of the genotype, or a different medication," Dr Shuldiner explained. This could include other antiplatelet drugs such as prasugrel, ticagrelor or cangrelor, which are not as dependent on *CYP2C19* for activation.

"Promising area"

In an accompanying editorial, Deepak Bhatt of the VA Boston Healthcare System and Brigham and Women's Hospital in Boston, wrote: "The study...moves closer to fulfilling the promise of pharmacogenetic testing

in tailoring antiplatelet therapy to the individual patient. Antiplatelet therapy seems well suited to such an approach, and future investigations should pursue this promising area."

"I think it's an interesting and well-done analysis," he told *Clinica Diagnostics*. "Of course, the bigger question about whether this sort of testing is something that's clinically useful now really depends on future studies. What we really need is a prospective study to prove that these polymorphisms affect clopidogrel activity in a way that we can modify. It may not make sense to measure something if you then can't use that information to decrease the patient's risk, especially for a test that's probably not going to be cheap."

Dr Bhatt pointed out that genotyping tests to predict patients' responses to another anticoagulant drug, warfarin, were commercially available, but had not caught on. "There are data that suggest that polymorphisms predict bleeding risk [with warfarin], but there's no definitive longitudinal data proving that you can use this information to decrease patients' bleeding," he said.

"I think clopidogrel genotyping is probably in a similar situation," Dr Bhatt concluded. "Until physicians have outcome data showing that use of genotyping can help modify the therapy that is prescribed, I think there should be some restraint in ordering these tests."



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1 issue). Further details and scientific analysis to follow.

"A simple and noninvasive test"

An early and more accessible diagnosis and management of mesothelioma holds the greatest promise for therapeutic techniques that are also being developed, including radiotherapy, chemotherapy and surgery.

"This study is an important step forward, as it could lead to earlier diagnosis and better treatment of mesothelioma," said BLF deputy chairman Professor Stephen Spiro.

"This simple and noninvasive test could help improve the survival time of those diagnosed with mesothelioma," he added, noting that "[this] is vital, as currently, most patients diagnosed with this disease live less than 12 months".

The BLF represents the interests of the approximately eight million people – around one in every seven of the population – who are affected by lung disease in the UK. Respiratory disease kills one in every five, making it the UK's second-biggest killer (117,500 deaths in 2004), behind all non-respiratory cancers combined (122,500 deaths). This is almost double the European average and the sixth-highest death rate in Europe, according to the BLF.

The present and emerging healthcare need

Mesothelioma is a cancer primarily of the lining of the lung, with a latency period of 15-50 years. Worldwide, more than 10,000 people a year are diagnosed with mesothelioma or other asbestos-related diseases (ARDs) and the incidence is rising, with over half a million ARD-related injury claims to date.

Until recently, ARDs have been associated almost exclusively with the intense exposure levels of certain heavy industries, but a link is starting to become more statistically significant with other professions, from domestic builders and, notably, schoolteachers.

This is due to exposure to mismanaged asbestos that is present in various forms in many buildings. In the US alone, it is estimated that 110,000 schools contain asbestos; in the UK, many of the 25,000 or so schools built at the height of asbestos use are thought to present a significant risk of exposure to asbestos. Low-level environmental exposure is also a growing concern; any level of exposure to asbestos was recently deemed to pose a carcinogenic risk.

Researchers across the UK and Ireland are seeking to integrate all asbestos-related diseases R&D under a single virtual centre.

Laboratory test co-payment is a "bad policy"

The American Clinical Laboratory Association (ACLA) is lobbying US Senators to prevent seniors eligible for Medicare paying 20% of the cost of the laboratory services they use.

The Senate finance committee is considering the move because it would reduce by 20% the Clinical Laboratory Fee Schedule (CLFS), under which labs are reimbursed – saving \$23.8bn over 10 years, according to the Congressional Budget Office (CBO).

This same proposal was put forward, and rejected, in 2003 and the ACLA is urging Congress to again reject this "bad policy" for the same reasons as last time.

The association said that savings would not be made for the healthcare system. The money would simply be shifted, increasing out-of-pocket costs to all Medicare beneficiaries.

The measure would also add costs to the system, the ACLA argues, because laboratories will have to generate "in excess of 134 million new bills each year to seniors or their supplementary insurers" – and attempt to collect from them.

The ACLA said laboratory services represent only 1.7% of Medicare spending "yet influence 70% of medical decision-making".

"A co-pay would contribute to already unacceptable cuts in payment for laboratory services and reduce the opportunity for advancements in the promising area of laboratory medicine," the ACLA said. The ACLA is part of a coalition of groups and companies opposed to the measure. Among the members are Becton Dickinson, Roche Diagnostics, Quest Diagnostics, Siemens Healthcare Diagnostics and Aureon Laboratories.

CMV IgG assays have "similar performance"

Cytomegalovirus (CMV) immunoglobulin G (IgG) assays on the UK market have been found to perform with equally good specificity and sensitivity, according to evaluation reports published by the Centre for Evidence-based Publishing (CEP).

According to a summary of the conclusions of the CEP – part of the Purchasing and Supply Agency (PASA) – the five CMV IgG assays for automated analysers and nine CMV IgG microplate assays were found to have similar performance in terms of both seroconversion and in a mixed-titre performance panel. The CEP reports good specificity (repeat reactive rates) and sensitivity values.

The analysers used in the former evaluation were Abbott Diagnostics' AxSYM, DiaSorin's Liaison, Siemens Healthcare Diagnostics' Immulite 2000; this report also features Abbott Diagnostics' Architect, which had been evaluated previously, but was included for information.

Both reports, of around 40-50 pages, feature supplier contact details, detailed results of the performance and seroconversion panels, and the manufacturers' claimed specificity and sensitivity.

Egypt confirms H5N1 flu cases, after global lull in reports

The Egyptian government has confirmed two new human cases of H5N1 "avian" influenza, the first since the end of June. Both cases – an infant and a child – are in a stable condition, following prompt hospitalisation and treatment. The cases are being attributed to close contact with dead or sick poultry. Egypt has a far lower than average case-fatality rate: of the 83 cases to date, 27 have been fatal; of the 43 reported this year alone, 12 have been fatal.

The latest cases were confirmed by Egypt's Central Public Health Laboratories, according to an August 11 report published by the World Health Organization (WHO). It would appear that the health ministry no longer needs to have its testing reconfirmed at the US Naval Medical Research Unit (NAMRU-3), in Cairo; the last mention of the NAMRU-3 unit in its case updates was in mid-May.

Scottish *C Diff* deaths inquiry back on track

Scotland has appointed a new chairman of its public inquiry into last year's *Clostridium difficile* outbreak in the Vale of Leven hospital, to which 18 deaths out of 55 infected patients have been attributed. Lord MacLean, replacing Lord Coulsfield who stood down for health reasons, will now be consulted on the terms of reference of the inquiry, the government said today. While "rapid and very significant progress" has been made in improving procedures, the inquiry could well serve to underline the value of diagnostic screening and monitoring of healthcare-associated infections (HAIs), *Clinica Diagnostics* suggests. Scotland says it is investing £54m (\$90m) over three years in measures to tackle HAIs, including an MRSA screening programme.

UK appraises LBC techs, reports "greater downtime" of Hologic slide processor

The UK's Centre for Evidence-based Purchasing (CEP) has published a "2008-09 annual report" on liquid-based cytology systems, as part of the Purchasing and Supply Agency's (PASA) analyser monitoring programme. The 23-page report, published last month and now available online via the PASA website (www.pasa.nhs.uk), "provides information on the reliability and performance" of the Hologic ThinPrep 3000 Laboratory Slide Processor and BD PrepStain Slide Processor. The summary of the report, which features a chapter on comparative data, notes that the former "incurred greater downtime and also a higher number of engineer visits" than the latter.

UK "not ready" to divulge vCJD assay findings

The UK government has said it will not yet publish the results of its ongoing evaluation of prototype variant Creutzfeldt-Jakob disease (vCJD) assays. Gillian Merron MP, on behalf of the health secretary, told Parliament that the evaluation "is ongoing, and interim results will not be issued at this stage". Results will eventually be published under the auspices of the CJD Resource Centre Oversight Committee, she said on July 15. (Parliament is currently in recess; it resits on October 12.)

Meanwhile, under growing pressure to help assess the national prevalence of prion protein infection linked to vCJD, coroners are said to remain entrenched in their opposition to the routine sampling of brain and other tissues during post mortems. They argue that the process of securing permission from relatives, as required by law, to perform the procedure for research purposes, would hinder their primary, statutory role of determining the cause of death.

US set for all-electronic PMS reporting

The US Food and Drug Administration (FDA) is proposing that all mandatory postmarket safety reporting to three of its centres, including the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER), be done only electronically.

The proposals were unveiled this month in the form of two draft rules. One applies specifically to medical device adverse event reporting, the other to drugs and biologics. They would not change what types of incidents are required to be reported to the FDA, and voluntary medical device safety reporting is not affected.

"Both proposed rules will improve the agency's ability to obtain safety information more quickly, which will help lead to faster identification of potential safety problems," said Dr David Buckles, director of the CDRH's postmarket surveillance (PMS) division. This information "may be critical to future action that improves patient safety", he added.

The CDRH currently receives "most" mandatory medical device adverse event reports on paper, before entering it manually into its adverse event database (Manufacturer and User Facility Device Experience, MAUDE) for further analysis. "Not only is this step costly, but it hinders CDRH's ability to review safety data quickly to uncover potential public health problems," argues the FDA.

Medical device manufacturers, importers and user facilities would be required to submit reports to the FDA through the eMDR system, to be entered into the MAUDE database. eMDR is available in two electronic formats: eSub, which is aimed at smaller reporting volumes; larger manufacturers can submit reports using a batch submission protocol.

UK fast-tracks swine flu R&D, but how big a role for diagnostics?

An "evaluation of methods used to select patients with suspected swine flu for hospital admission" is the closest the UK government went last week in allocating part of a £2.25m (\$3.7m) fast-track R&D scheme to diagnostics. A total of 14 projects – including the said evaluation to be headed by Professor Steve Goodacre, of the University of Sheffield – are being fast-tracked to the National Institute for Health Research (NIHR), with the aim of "providing vital clinical and scientific evidence that will inform the government's response to the virus in the coming months". The other projects include: an observational study of immunity in vaccinated pregnant women; and an analysis of a triage method to help determine intensive care candidate patients. The results will be expected by the end of the year, said the Department of Health.

"H1N1 test shortfalls highlight Brazilian system's needs"

The additional healthcare needs posed by the H1N1 "swine flu" pandemic in Brazil have been brought into the debate on healthcare funding reforms, as an example of the broader needs of the national health system (SUS).

Speaking in the chamber of deputies, the executive-secretary of the national council of state secretaries of health (CNSE), Jurandi Frutuoso, warned that the states were "losing the capacity to respond to the current crisis" and that the SUS needs to be strengthened to handle any lengthening or intensification of the pandemic. He called for the passage of legislation – the so-called "Emenda 29" constitutional amendment – that will raise the minimum healthcare investment thresholds by around US\$9bn per year.

Meanwhile, the deputy for Roraima state, Mauro Nazif, went further, announcing the state's first H1N1-related death, before highlighting the need for 2,000 additional testing kits – "far less than the health ministry has estimated". Roraima – the least-populated state, but with more than half of its population concentrated in the state capital, Boa Vista – is an example of the extremes of Brazil's demographics and the challenges that they pose to healthcare provision.

Significant rise in insulin-managed diabetes 1 & 2 in Australia

The incidence of insulin-treated type-1 and type-2 diabetes is growing significantly in Australia, at all ages, according to a report analysing

eight years of data from the national diabetes register.

The Australian Institute of Health and Welfare (AIHW) says that some 7,000 children aged 14 and under were diagnosed with type-1 (insulin-dependent) diabetes during the period covered by its Insulin-treated diabetes in Australia, 2000-07 report, published on August 21. In 2007 alone, there were 990 new cases in this age group, up 30% on the number of new cases in 2000. There has also been a six-fold increase in new cases of insulin-treated gestational diabetes among women aged 15-49 during the eight-year period.

The report also highlights the growth in type-2 (non insulin-dependent) diabetics using insulin to manage their condition – up 63% across all age groups. Insulin is now used to treat one in every five type-2 cases, says the AIHW. While people aged 35 and over accounted for 95% of the new cases in this group, there were 6,000 new cases of insulin-managed cases of type-2 diabetes in the 15-34-year age group alone.

"All these numbers are saying the same thing, which is that the incidence of insulin-treated diabetes in Australia is increasing, no matter what the age group or the type of diabetes," said Katherine Faulks, of the AIHW's cardiovascular disease, diabetes and kidney unit.

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PEOPLE

David Jackson

UK molecular diagnostics firm DxS has appointed David Jackson vice-president of business development and licensing. Dr Jackson will be based in the US and will be responsible for the company's companion diagnostics and technology licensing divisions. Dr Jackson previously worked for Response Genetics as executive vice-president, and before this was president and chief operating officer of CryoFluor Therapeutics, a company developing a novel cryosurgical platform. He also has "extensive consulting experience in personalised medicine", Manchester-based DxS said.

James Monton

Consumer genomics specialist GeneLink has appointed James Monton to its board of directors, where he will serve on the audit and compensation committees. Mr Monton has "decades of product development and branding experience" in health and beauty care for Proctor & Gamble, and currently serves on the boards of Northern Kentucky University's Business School and the International Business Center. Longwood, Florida-based GeneLink's products include lipid metabolism, bone health and cardiovascular assessments, which analyse single nucleotide polymorphisms (SNPs) associated with these fields. It is also developing panels assessing dementia and Alzheimer's disease, and metabolic syndrome.

MEETINGS

BIOMED-Connect

The BIOMED-Connect conference is the meeting place for French and UK players in the medical diagnostics and equipments field, according to its organisers, Sud de France Export and the London Technology Network. The meeting will include a medical and diagnostics show, networking opportunities and pre-arranged face-to-face business appointments. The EuroMeDiag workgroup, which was launched by medical diagnostics companies in the Languedoc-Rousillon area in the south of France, will be highlighted. The group includes both public and private sector players, and is part of the Eurobiomed competitiveness cluster on human health. The meeting will be held in London, UK, on October 12. For further information and to register, contact Aurélie Guillen on tel: +44 207 079 3344; or email: aguillen@suddefrance-export.fr