Healthcare on the move
Navigating the obstacles in mobile health

INSIDE
E-health: overcoming regulatory and ethical issues
Interviews: Philips and Telcare
BSI is now a full scope designated Notified Body under the European In Vitro Diagnostic (IVD) Directive, Medical Devices and Active Implantable Directives—enabling you to work with one organisation for your certification needs.

Our new IVD CE Marking Service is built on the same successful foundation that has made BSI Healthcare a leading Notified Body—with a worldwide reputation for providing services that combine speed with experience, integrity, independence and predictability. Benefits include:

- Combined Industry and Regulatory In-house Expertise in Wide-Range IVD Products
- Responsive, Fast, Efficient and Professional Service
- Speed-to-Market Programs
- Full Scope in all 3 CE Marking Medical Device Directives
- Making the Transfer Process Timely and Seamless
- Use of Industry Leaders for Batch Testing

Whether your product is simple or complex, please contact us to learn how we can assist you in getting your product to global markets safely and in a timely manner.

BSI – Europe
+44 (0)8450 765608
eu.healthcare@bsigroup.com
www.bsigroup.com/healthcare

BSI Healthcare - USA
800 862 4977
healthcare@bsigroup.com
www.bsiamerica.com/healthcare

raising standards worldwide™
Telemedicine, telehealth, e-health, mobile health. Call it what you want but the unfolding of this phenomenon – be it the digitalisation of workflow processes in healthcare or the implementation of new technologies that allow people to be diagnosed, treated and monitored away from traditional healthcare settings, wherever and whenever – is expected to pick up pace over the next few years. This acceleration is not only driven by the increasing recognition of the benefits of telemedicine (one word – cost-efficiency), but also by the fact that wireless connectivity and its related technologies are heavily interwoven into our day-to-day living.

As with any other business, the road to success is never smooth. The widespread roll-out of telemedicine could meet resistance from healthcare providers, insurance companies and healthcare professionals and even patients – stakeholders who feel this change would leave them worse off.

In this issue, we focus on the challenges of e-health, with our cover feature (pp 21-24) highlighting strategies that could help companies navigate their way around these obstacles. In our interview with UK medical device consultant Trevor Lewis (pp 25-26), we explore the current situation in the EU regarding the regulation of new software products, while Brian Kelly of law firm Covington and Burley considers the ethical and data privacy challenges related to e-health (pp 27-28). This issue also features Philips’ new Guardian wireless monitoring system for inpatient care (pp 36-37), and John Dwyer of Telcare speaks about fast-growing areas within healthcare (p 39).

News-wise, it has been an incredibly busy month. March’s headlines include the decision to disband the Global Harmonization Task Force, a move that has not been well-received by industry; the UK healthcare procurement system coming under fire (see Top Story and the Europe section); how the devastating earthquake in Japan, the world’s second largest medical devices market, is affecting the medtech industry; and a stronger than normal flow of M&A activity. Just as a reminder to our readers, the news featured in this issue is just a fraction of Clinica’s content. To read the full version of the stories and other articles and analyses, go to www.clinica.co.uk.

Tina Tan
Editor
Contents

News

Top Story 5
UK procurement under fire: concern over NHSSC dual role

US 6-8
Key stories
FDAs device chief defends US review process at government hearing
EC official hits back at US criticism
US senate adopts patent reform bill

EU 9-11
Key stories
EU IVD Directive consultation: Huge majority wants greater NB involvement
Commission considers options for overseeing EU medical device committee
CMC demonstrates its force and makes decisions over device management issues

Europe 12-13
Key stories
“Divide-and-rule ethos” in NHS supplies system under the spotlight
High-value equipment joins timely UK NHS audits
Overturn diabetes test reimbursement decision, says German IVDs industry
German device clinical trials system off to faltering start

International 13-14
Key stories
Exit GHTF, enter new regulators-only forum
Japanese medtech firms join forces to overcome quake challenges

Business 15-17
Key stories
Medtronic cancels $2bn group purchasing organisation contracts
Terumo soars to No 1 in global blood transfusion with $2.6bn CaridianBCT buy
FDA warns Cordis over Cypher stents; may delay approval of catheter

Science & Technology 18-20
Key stories
Medtronic’s Amplify bone graft turned down by the FDA; warnings lifted
High fracture rates with J&J’s ASR XL hip implant, UK ortho surgeons warn

Features

Healthcare on the move: navigating the obstacles in mobile health 21
The global population is ageing, governments are slashing healthcare budgets in an effort to redress the weak economy and healthcare providers have to deal with new issues such as growing rates of obesity and chronic diseases. These factors are combining to create a perfect storm for telemedicine and mobile health technologies. A carefully planned strategy is vital for companies looking to capitalise on this opportunity

Testing times ahead for medtech software and manufacturers 25
Medical device companies tend to be behind the curve in terms of developing and using sophisticated software in their products. Many other industries are far more advanced in this respect, says device industry and regulatory consultant Trevor Lewis

E-health: ethical and data privacy challenges in the EU 27
Brian Kelly, an associate in the Life Science Practice of UK law firm Covington & Burling, considers the regulatory framework for e-health, with a focus on the ethical and data privacy challenges

Philips to unveil Guardian for wireless hospital monitoring 36
Philips is to launch its new Guardian software, designed to simplify wireless patient monitoring in hospitals, this year. The firm’s marketing director for general care, Andreas Bindszus, spoke to Madeline Armstrong about the advantages of the system, which automatically alerts clinicians when patients show signs of deterioration

Regulars

IVD Insight 29
Patent Watch 32
People 38
Five minutes with... 39
The Association of British Healthcare Industries (ABHI) has voiced serious concerns about the way NHS Supply Chain (NHSSC) seemingly holds two conflicting roles; one as a supplier that competes with other healthcare product manufacturers for business, and the other as the body that actually oversees the tenders for contracts with the country’s biggest healthcare products buyer, the National Health Service.

Mike Kreuzer, director general of ABHI, confirmed to Clinica that the association is talking with UK government representatives, including health ministers, about NHSSC and has raised some of its concerns in an official memorandum commenting on the Health & Social Care Bill Committee.

It views the NHSSC’s dual role as giving NHSSC “the benefit of privileged market information including its suppliers’ intellectual property”.

NHSSC is operated by DHL as an agent of the NHS Business Services Authority (NHSBSA), under the terms of a master services agreement. It also sources products direct from manufacturers and sells them under its own brand Choice for Health.

Since it oversees the tendering process on behalf of the NHS, some believe that the NHSSC could be in a position to approach manufacturers anywhere in the world with vital product information and to invite them to undercut price. In theory, this could benefit the NHS and the taxpayer.

But in practice, this could be for NHSSC’s own profit too, some in the industry have suggested, although NHSSC points out that its profits are capped.

Shocked at abuse
The ABHI is not the only one with concerns about NHSSC. Speaking on behalf of the British In Vitro Diagnostics Association, director general Doris-Ann Williams, said that she was “shocked” to hear how the NHSSC has “been abusing the NHS brand”.

Although members of BIVDA have not been directly impacted by evidence of the NHSSC sourcing IVDs in cheaper markets and undercutting their prices, Ms Williams is in no doubt that it could potentially affect her part of the medtech industry too.

“I have heard that NHSSC has asked UK Trade and Investment to introduce them to manufacturers of X-ray and other imaging equipment in India and China,” she told Clinica.

But while IVDs could be next in line, she considers that the complexity of how analysers and tests operate and the fact that the profit margins are generally low mean that NHSSC is not likely to have IVDs high on its list of priorities among areas where it could be making profits.

Ms Williams said that one of the problems with the NHSSC and its title is that the name suggests that it is a UK government body operating on behalf of the NHS. “A lot of people are unaware that this is DHL by another name”, she said, a point that many are now making.

Moreover, since NHSSC is under contract to procure for the NHS, it has confidential information about companies, including pricing information, which it can then use to its own benefit, to act as a direct supplier and manufacturer of medical devices. “This is anti-competitive”, she stressed.

One consequence of this will be job losses in the UK and even more seriously, the potential loss of domestic companies who may not survive if the key domestic supplier to the NHS cuts them out.

NHSSC view
NHSSC states that it has official government backing for its procedures and that all own-brand products that it sources are procured in accordance with the EU regulations which require the principles of equal treatment and transparency between potential suppliers to be adhered to.

NHSSC has obtained an opinion from Senior Counsel on its direct-from-manufacturer/own-brand programme, it says, and the advice was that “no conflict of interest exists in the operation of NHS Supply Chain’s own-brand programme” and “the operation of the own-brand programme by NHS Supply Chain is not anti-competitive, and indeed is more likely to be considered pro-competition”.

It also says that, to date, 107 of its own-brand products have been launched following EU procurement tender processes it has run, which have collectively enabled NHS trusts to make average savings of 14%.

Its commercial returns for this activity, it says, are part of the overall cap on DHL’s profits under its arrangements with the NHSBSA.

This is an abridged version of the article. Go to www.clinica.co.uk, to read the full story and related article UK’s NHS Supply Chain under investigation for breach of CE marking rules
FDA device chief defends US review process at government hearing

US Food and Drug Administration device chief Jeffrey Shuren has admitted that the agency “could do a better job” at managing its premarket review programmes, but has opposed suggestions that the US system be replaced with one similar to that in place in the EU.

Although the EU system may in some instances be faster, the US system is more robust in ensuring that patients receive safe and effective products, Dr Shuren suggested at a government hearing that considered whether the FDA review system was damaging the US medtech industry.

The hearing, organised by the House Energy and Commerce Committee’s Subcommittee on Health, was designed to assess the impact of US medtech regulations on local jobs and patients. According to Health Subcommittee chairman Joe Pitts (Republican – Pennsylvania), the FDA process has been described as unpredictable and characterised by disruptions and delays. In addition, it has been shown that companies are able to make their products available to patients faster and at a significantly lower cost in markets such as Europe.

Dr Shuren said that the EU system focuses only on the safety and performance of a device and, unlike the FDA, does not require demonstration of device effectiveness. Devices may come on the market in the EU before they do in the US, but those allowed in the US are both safe and effective, he said, adding that the US system had served patients well by preventing EU-approved devices that were later shown to be unsafe or ineffective from harming American consumers. The FDA may take longer than the EU to approve some higher-risk devices because it asks for more robust clinical data to meet the “stronger US regulatory standards”, he said.

Representative Pitts questioned whether the stricter US standards were resulting in safer devices. “None of us would be concerned about longer, more arduous approval processes for medical devices in the US versus Europe if we thought that those processes kept American patients safer than their European counterparts,” he said. “But, according to recent studies, medical devices... [cleared by the] EU processes are statistically as safe as FDA-cleared or approved devices and have comparable outcomes” he said.

Representative Pitts expressed concern that shorter, more predictable and more transparent approval processes in the EU have led many device companies to seek a market for their products in Europe before submitting them to the FDA.

Commenting on the hearing, US industry association AdvaMed warned that the “growing lack of predictability and consistency” in product reviews at the FDA is a serious threat to the country’s “global leadership” in medical technology. The association noted that a study (www.advedmed.org/RD/151012/04/11/4046E6C33-380B-4F6B-AB58-9AB10A7A3CF/0/ makowerreportfinal.pdf) has shown that FDA reviews for medical devices take on average two years longer than reviews for similar products in Europe, “with no discernible benefit in patient safety or outcome”.

No comparison

Dr Shuren told the hearing that it was not possible to compare the US and EU device regulatory systems “as there are some very basic differences between” them. The EU, for example, he said, has no centralised authority for tracking safety information related to medical devices and no EU-wide post-market surveillance system, which makes comparisons of safety data problematic.

To make his point, Dr Shuren also referred to an industry-funded study that compared device recalls in the EU and the US markets. Of the 24 EU states reviewed in that study, he noted that 85% of medical device safety reports in the EU came from only five member states, underscoring the potential for under-reporting of safety events in the EU.

Also, he said the EU system allows manufacturers to “forum-shop” their applications among third-party reviewers who were subject to minimal oversight. The European Commission, Dr Shuren noted, has already acknowledged limitations in the EU regulatory framework and is in the process of preparing for a recast of the directives governing medical devices. Proposals in this regard could be finalised by the beginning of 2012 (www.clinica.co.uk, 11 October 2010).

Poor submissions add delays

Contrary to criticisms from the US medtech companies that the FDA is not meeting many of the quantitative and qualitative performance goals under the current medical device user fee programme (www.clinica.co.uk, 27 September 2010), Dr Shuren countered that there were only a “limited number of areas in which we are not meeting the goals agreed to with the industry”.

Dr Shuren blamed delays on increasing FDA workload, growing device complexity and the filing of poor quality submissions by device sponsors. A significant number of submissions received by the FDA “are incomplete or fail to address basic elements such as the device’s proposed indications for use”, he explained. Specifically, more than half of the pre-market, or 510(k), submissions received by the FDA have quality problems, he added.

Dr Shuren said that although the FDA was meeting most of its performance goals for 510(k)s,” these submission quality problems delay the completion of the marketing clearance process and unnecessarily divert resources from more productive activities in the review process”. He listed several recent efforts by the agency to boost its device approval process, including a 25-point action plan to improve the 510(k) process (www.clinica.co.uk, 20 January 2011) and proposals for establishing a priority review programme for approving breakthrough devices (www.clinica.co.uk, 9 February 2011).

Dr Shuren’s comments prompted regulators across the Atlantic to rise to the defense of the EU regulatory system. This included a letter from the head of the Directorate General for Health and Consumers, Paola Testori Coggi, addressed to FDA commissioner, Margaret Hamburg, which stated her concerns that “a senior official of the FDA should publicly discredit the regulatory system in Europe in this way”.

*See next page for further analysis.
FDA cites examples of strict US regulations

The US FDA has provided examples in support of its belief that medical devices in the US are subject to stricter regulations before they are allowed on the market compared with those in the EU.

Claims by the FDA’s device chief Jeffrey Shuren that the US system is more stringent than that of the EU have resulted in a transatlantic row of sorts (see adjacent column) but the agency says it has several product-specific examples to support its argument.

Medtronic’s Chronicle IHM
One example relates to Medtronic’s Chronicle implantable haemodynamic monitor (IHM). The Chronicle system was being studied in a worldwide multicentre clinical trial and the company planned to file for US and European marketing approvals simultaneously.

In November 2005, Medtronic’s premarket approval application for Chronicle IHM was accepted by the FDA and granted “expedited review” status. The PMA also supported Chronicle ICD – a Chronicle device with implantable cardioverter defibrillator therapy.

In March 2007, citing the statistically insignificant results as “lack of clinical effectiveness”, an FDA panel rejected Medtronic’s application in a 9-2 vote. Additionally, panel members reportedly expressed concern about the size of the clinical trial, which included 274 patients in eight clinical settings.

An FDA spokesperson pointed out that this was “a good example of the EU system not requiring [evidence of] effectiveness claims – whereas the US system does (at least for PMA devices)”.

Trilucent breast implants
Another example concerns LipoMatrix, which CE marked its Trilucent (soya bean oil-filled) breast implants in 1995. The products were marketed in the UK but were withdrawn in March 1999, by which time over 9,000 implants had been sold to 5,000 women in the UK.

The company agreed to the recall after the Medical Devices Agency (the precursor to today’s Medicines and Healthcare products Regulatory Agency) raised concerns about the long-term safety of the product in relation to the breakdown of the filler. It was found that the breakdown of the filler was significantly different from that predicted during preclinical testing. The products had to be explanted in many patients and LipoMatrix continues to follow those patients with implants.

The FDA points out that this device was never cleared by the FDA and, therefore, never reached the market in the US.

RoboDoc
In 1996, the FDA continues, Integrated Surgical Systems CE marked RoboDoc, a computer-assisted robotic milling machine used for drilling out the femur to make a hole for a hip implant.

In 2003, a group of German patients initiated a class action lawsuit in Sacramento, California, against the company, claiming that the device severed their muscles and arteries. In June 2007, ISS declared bankruptcy and sold RoboDoc to Curexo Technology Corporations.

In August 2008, RoboDoc was cleared by the FDA via its 510(k), or the premarket notification system, after implementing multiple software updates to increased precision, according to the FDA spokesperson, who added that the data still do not show that RoboDoc is superior to traditional surgical methods, but it does not pose additional risk to patients.

CoStar drug-eluting stent
In 2006, the FDA also notes, Conor MedSystems (part of Johnson & Johnson) CE marked CoStar, a cobalt chromium paclitaxel-eluting coronary stent.

In May 2007, citing issues related to a potentially sub-optimal therapeutic dose of paclitaxel, J&J announced that the COSTARI trial (the pivotal study for CoStar) failed to meet its primary endpoint. The trial did not identify safety issues.

As a result of this outcome, Conor terminated ongoing clinical trials and chose not to conclude the submission of its premarket approval application to the FDA for the product. Conor discontinued the sale of the stent in Europe, Asia and Latin America, where it was already approved and on the market.

EC official hits back at US criticism

The European Commission has asked US regulators for evidence to back derogatory remarks about the EU regulatory system made by Jeffrey Shuren, director of the US FDA’s Center for Devices and Radiological Health. These comments were made when, apparently backed into a corner while trying to defend his own medtech policies, Dr Shuren accused the EU of treating its patients as rodents in medical experiments (www.clinica.co.uk, 25 January 2011).

Head of the Directorate General for Health and Consumers, Paola Testori Coggi, has written to FDA commissioner, Margaret Hamburg, stating that she was “deeply concerned that a senior official of the FDA should publicly discredit the regulatory system in Europe in this way”.

In a letter dated 18 February, Ms Testori Coggi said that the US and European regulatory systems, “though on different paths, seek to secure a high level of patient safety”.

She added that it the FDA has evidence of unsafe devices on sale in Europe, “I would appreciate if you could share this information with European regulators,” according to a Reuters article.

Frederic Vincent, a spokesman for the European Commission, reportedly said the letter was sent to “clarify the issue and pass on a clear message”.

Dr Shuren’s comments were a serious diplomatic faux pas, unless they were motivated by a real desire on his part to engage in a transatlantic dialogue on the relative merits of the EU and US medtech regulatory systems (www.clinica.co.uk, 25 February 2011).

The question is: are we about to see the most high-level and intense debate in the history of medtech regulations as we know them? In light of Ms Testori Coggi’s letter, will Dr Shuren now back down and apologise for statements that he has made?

The head of the CDRH had made the comments while defending the US regulatory medtech system against accusations that it was inconsistent, unpredictable and far slower in enabling much needed innovative products to reach the market than the EU system and others around the world.
After six years of toil and debate, Senator Patrick Leahy (Democrat – Vermont) has been victorious in getting his patent reform bill through the US Senate, with the chamber overwhelmingly backing the measure in a 95-5 vote on 8 March.

If enacted, the legislation would, for the first time in nearly six decades, make major changes to the US patent system, which Senator Leahy has called “antiquated.”

The most notable change would be moving the US from a first-to-invent system for patent applications to a first-inventor-to-file standard – already used by most developed nations – which proponents have insisted would bring more certainty to the process.

That change also would ensure a more transparent and cost-effective process, said US commerce secretary Gary Locke.

Opponents of the change, however, have insisted the move would severely harm US innovation and be especially burdensome on small businesses, inventors and start-ups.

A measure introduced in the Senate last week by Dianne Feinstein (Democrat – California) to remove the first-inventor-to-file provision from the bill was beaten back in an 87-13 vote.

And while her fellow lawmakers that supported ditching the first-inventor-to-file provision all voted against the final bill, Senator Feinstein, in the end, backed the legislation, as did Senate Majority Leader Harry Reid (Democrat – Nevada), who also opposed the move from the current first-to-invent system.

If enacted, the bill, known as the America Invents Act ($23), would also allow the US Patent & Trademark Office to set its own fees – which would help ensure that the agency has reliable funding.

With the funding, the US PTO would hire more examiners. Mr Locke told reporters last week during a briefing. But just as important, it would bring the agency’s information technology system into the 21st century, allowing the US PTO to process applications more quickly and produce better patents that are less likely to be subjected to a court challenge, he insisted.

At the same 1 March briefing, US PTO director David Kappos said giving the agency the ability to set its own fees would create a larger resource base, “by which inventors can be granted higher quality patents in a faster period of time, all while adding zero cost to the taxpayer”.

The new fee-setting system also would ensure the US PTO has the funds necessary to process the backlog of more than 770,000 pending patent applications, said Mr Leahy, who authored the patent reform bill with Senators Orrin Hatch (Republican – Utah) and Chuck Grassley (Republican – Iowa).

Mr Locke noted that it currently takes about 36 months on average for a patent application to be processed, which he called “unacceptable”. Successful inventors need to secure patent rights to access the funds, hire the employees and lift their companies off the ground, but for too long, the patent system has been hamstrung by a huge backlog of unexamined applications, many of which represent a potential new business and new jobs not being created,” Mr Locke said.

The patent reform legislation also would permit the US PTO to offer an expedited patent application process of 12 months for a higher fee, he noted.

The bill that passed the Senate is backed by the Biotechnology Industry Organization. “Patents are often the main assets of small biotech companies, and they rely on this intellectual property to attract investors to fund the lengthy and expensive research and development process necessary to bring breakthrough new therapies and other biotech products to patients and consumers,” said BIO chief executive Jim Greenwood. Mr Greenwood, a former member of the House of Representatives, urged that chamber to work “without delay” in getting a bill passed.

FDA modifies list of medical device standards

The US FDA has published a document containing the modifications it is making to the list of standards it recognises for use in pre-market reviews of medical devices.

The document is designed to help manufacturers who elect to declare conformity with consensus standards to meet certain requirements for medical devices, the agency says. The modifications comprise the addition of around 45 new standards as well as withdrawals, corrections and revisions of other standards. They came into effect on 14 March.

The FDA is allowed by law to recognise consensus standards developed by international and national organisations for use in satisfying portions of device pre-market review submissions or other requirements. The newly published document, entitled Modifications to the List of Recognized Standards, Recognition List Number: 026, describes which standards are being withdrawn and their replacements; the correction of errors made by the FDA in listing previously recognised standards; and the changes to the supplementary information sheets of recognised standards that describe revisions to the applicability of the standards. Examples of modifications include ASTM F1903-10 on Standard Practice for Testing for Biological Responses to Particles In Vitro, which is being withdrawn and replaced with a newer version.

New entries

The document also lists modifications the FDA is making that involve the initial addition of standards not previously recognised by agency. New entries to the list include:

- ISO 80369-1 First edition 2010-12-15 on Small bore connectors for liquids and gases in healthcare applications – Part 1: General requirements;
- ASTM F2312-10 on Standard Terminology Relating to Tissue Engineered Medical Products; and

The FDA maintains its list of recognised consensus standards in a searchable database that may be accessed online at www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm.
Huge majority wants greater NB involvement

Europe looks set to adopt a risk-based classification system for IVDs, following overwhelming support for the adoption of this approach which is based on the Global Harmonisation Task Force (GHTF) model.

In a public consultation on the proposed revision of the EU’s IVD Directive, launched by the European Commission in June (www.clinica.co.uk, 29 June 2010), 93% of respondents were in favour of taking a risk-based route, and the vast majority also believe such an approach would address the main concerns raised about the “insufficient level of scrutiny” for companion diagnostics since this would result in companion diagnostics falling into the third-highest risk class of the GHTF model, Class C, and requiring the involvement of a notified body. At present there is generally no notified body involvement for these products. (Under the GHTF model, Class A is the lowest risk and Class D the highest risk category).

A risk-based model would have “a positive impact in terms of flexibility, allowing better protection of public health while ensuring timely access to the market for new tests”

Overall, a risk-based model would have “a positive impact in terms of flexibility, allowing for a better protection of public health while being able to ensure timely access to the market for new tests”, they say. The regulatory framework would become “more robust to the technological progress,” and would have the benefit of facilitating exports for European manufacturers and benefiting competitiveness, they add.

Acceptable increased costs

Adopting a risk-based classification system will result in manufacturers having to involve a notified body to conduct conformity assessment procedures for a huge swathe of tests, including a host of cancer diagnostics, which are currently considered general IVDs in the existing IVD Directive and so can be self-certified.

The majority of the respondents to the consultation argued that this would increase costs for manufacturers “significantly” and that these additional costs might need to be passed onto the end users.

However, these costs should be balanced with the “improvement of safety for public health brought by the implementation of more stringent regulatory requirements for some categories of tests”, they say.

Moreover, a sufficient transitional period (five years) might help contain costs and would avoid a disproportionate impact on SMEs and on manufacturers (www.clinica.co.uk, 20 September 2010).

New conformity assessment procedures

Not surprisingly, given the support for the GHTF classification, the majority of respondents underlined the need to align the conformity assessment procedure with the GHTF model.

There were concerns, however, that self-tests would not be treated as a risk class in their own right with appropriately targeted requirements as at present.

Many answers, in particular from notified bodies, underlined the need to align the conformity assessment procedures for self-tests to those applied for the current high-risk Annex II List B tests (eg tests for the detection and quantification in human samples of rubella, toxoplasmosis).

Moreover, a total of 88% of respondents are convinced that a quality management system (QMS) should be put in place for Class B, C and D IVD medical devices, in accordance with the GHTF model, and that this QMS should be controlled by a third party. As laid down in the GHTF documents. Some respondents even suggested that the QMS requirements be extended to Class A IVD medical devices while others believe a QMS controlled by a third party would not be sufficient for some IVDs.

For a full report on the responses to the consultation on the IVD Directive, go to www.clinica.co.uk

EMA to regulate companion Dx?

The European Commission’s consultation on revising the In Vitro Diagnostics Directive (98/79/EC) has revealed that some stakeholders want the European Medicines Agency to become involved in regulating companion diagnostics, ie IVDs that are developed and used in direct combination with a specific medicinal product.

While respondents to the consultation, almost unanimously, said that IVDs used as companion diagnostics must be subject to the IVD Directive, some stakeholders pointed out the need for “closer cooperation” between the IVD sector and the EMA.

Specifically, those working in the field of genetic diseases feel that the competence of the EMA should be extended to pharmacogenomics, as a companion diagnostic can have an impact on the health outcome of a medicinal product. They want the commission, when it revises the directive, to ensure that the analytical and clinical validity of the companion diagnostic is evaluated as part of the benefit-risk assessment of the medicinal product.

Currently, most companion diagnostics are self-certified by the IVD manufacturer. Should the EU move to a risk-based classification of IVDs, as proposed by the commission, it would be necessary to place companion diagnostics in Class C (ie high individual risk and/or moderate public health risk) of the risk-based model of the Global Harmonization Task Force, which would ensure that a third party would be involved in the CE-marking of these IVDs, stakeholders said.

Some respondents feel, however, that the clinical utility of the combination (ie of the medicinal product and the IVD) should be demonstrated in the context of the CE marking and the marketing authorisation of the medicinal product.

Commission considers options for overseeing EU medical device committee

The European Commission is looking at four possible options – one involving the European Medicines Agency – for providing administrative, technical and scientific support to medtech regulation at EU level.

The details of these options are in a so-called “non-paper” from the European Commission, which Clinica has obtained.

Among the options being considered is the creation of a Medical Device Committee (MDC) within the EMA, and thus extend the EMAs responsibilities into the medtech arena. The other options include:

- establishing an entirely new EU body for medical devices, and creating an MDC within this body;
- giving the European Commission a mandate to support the MDC; or
- creating a Central Oversight Committee managed by member states (ie carrying forward the member state initiative for a Central Management Committee).

While all four options are still open, at present, the weighting of the commission’s argument seems to be with the EMA option, although financial imperatives could alter the balance, Clinica notes.

Indeed, the latter two possibilities – having the commission support the MDC and creating a Central Oversight Committee – offer the key advantage of no additional costs to the EU budget.

At face value, in the current economic climate, these two options may seem the obvious answer to the current regulatory needs. However, aside from the financial advantage, the commission appears to not be able to find any more advantages in support of these approaches.

In contrast, for the option of having a MDC within the EMA, the commission lists five advantages, and for having an MDC within a new EU body, it lists four.

The arguments for going with the EMA option include, among other things, similarity with allocation of competences at national level (in 20 EU member states, the competences for pharmaceuticals and medical devices are within one authority) and at international level (US FDA, Japanese PMDA, Australian TGA, Health Canada), and the likelihood of achieving a high level of consistency in implementation of the legal requirements.

The cons listed are: costs; the possibly unwieldy size and structure of the EMA; industry’s concerns over creeping “take-over” by pharma.

For the option of creating a new EU body for medical devices as home to an MDC, one of the advantages is that it would give a clear distinction between the EU body responsible for medical devices and that responsible for pharmaceuticals. Disadvantages of this option would be: costs; no synergies with EMA (in terms of costs and expertise, especially for combination products); and uncertainty whether the body would have the critical mass in terms of required human resources from a budgetary point of view.

* Go to www.clinica.co.uk for further details from this story

CMC demonstrates its force and makes decisions over device management issues

Europe’s Central Management Committee is taking a firm stand on tackling notified body issues and has just endorsed a decision to make authorities designating and monitoring notified bodies in medtech to comply with the Notified Bodies Operations Group Best Practice Guides.

In addition, the committee is setting in motion a series of work items that are intended to rapidly tackle other aspects of notified body management, as well as areas of medical device regulation where shortfalls or the need of harmonised decisions have been identified by its members.

The CMC comprises competent authority representatives from every EU member state. Set up last autumn, the committee is acting independently and with a sense of urgency – in as far as its remit can go without yet having a legal basis – to bring about much needed change in medical device legislation in the EU.

In total, the organisation, a real contender to play a pivotal role in the future management of EU medtech implementation issues on behalf of the commission, has agreed on seven new work item proposals with tight deadlines.

Three of these items directly relate to notified bodies – criteria for designation, content of notified body certificates and content of declarations of conformity.

The others items concern:

- content of the manufacturer declaration of conformity (CMC to ask the Compliance and Enforcement Group (COEN) to develop scheme and for CMC to ask competent authorities to enforce harmonized application of scheme);
- improving the readability of instructions for use;
- agreeing on consistent rules for “periods of grace” to be allowed to manufacturers to allow non-conformities to be addressed, or in cases of reclassification of devices; time periods for corrective measures (proposal to ask COEN to set up guide for presentation in early 2012); and
- co-ordination of external communications between authorities.

The CMC has also made decisions on borderline and classification issues and on the details that manufacturers should provide in terms of giving their address – so there is uniformity in future.

The CMC will have a close follow-up on its decision and will ascertain whether the Commission’s MDEG Working Group on Classification and Borderline will introduce the CMC’s classification decision into the classification manual.

* To read the full story and comments from CMC chair Dr Matthias Neumann, go to www.clinica.co.uk
EU to press on with single patent despite setback for court plans

The EU’s Council of Ministers has given the go-ahead to a special procedure aimed at creating a single patent valid in all participating EU member states. The European Commission will now draft concrete proposals on the patent and the associated language regime, which it expects to be ready by the end of March.

The single patent, which is strongly supported by the commission and industry, is intended to provide protection in all the EU member states, thereby reducing the complexity and cost of obtaining and litigating patents in Europe.

However, the member states are not at one on the matter. As things stand, the patent, when eventually created, will not be valid in Italy and Spain. The two countries do not like the proposed translation arrangements and are staunchly withholding their support for the project, claiming that the trilingual language regime discriminates against the other EU languages.

Despite repeated efforts by the commission and the presidency of the council, the language dispute has prevented ministers from reaching the necessary unanimous agreement on creating the patent. The other 25 EU member states have, therefore, agreed to continue under “enhanced co-operation”, a last-resort procedure that allows a group of at least nine countries to go ahead with a legislative proposal when unanimity cannot be achieved.

Italy and Spain are also strongly opposed to the use of enhanced co-operation on the grounds that it contravenes EU law, even though the legal services of the council and the commission have said it is lawful.

Dissent

At the 10 March council meeting where the decision was taken to proceed, the Italian and Spanish ministers said that while they supported the idea of a single patent, they remained resolutely opposed to continuing with discussions on the basis of enhanced co-operation, which they said discriminated against their countries. Italy repeated its threat to refer the matter to the Court of Justice of the EU.

The two ministers also cited the opinion delivered two days earlier by the CJEU, which declared that the proposed patent jurisdiction, based on a new European and EU Patents Court (EEUPC), was incompatible with EU law (www.clinica.co.uk, 9 March 2011).

The Spanish minister said this opinion threw the whole project into doubt, and urged the commission and the other countries to pause for thought and “stop this headlong rush into the void”. In a colourful speech, he claimed the commission ‘did not have a clue’ as to what might happen on the jurisdiction issue, which he insisted was intrinsically linked to the patent and language proposals.

But the commission, the other 25 countries and the council presidency disagreed, saying that the unitary patent and the patent jurisdiction were separate legal matters and that it was perfectly possible to press ahead with the patent, leaving the jurisdiction issue to be sorted out separately. This view was also supported by a representative of the council’s legal service.

In his closing speech, the internal market commissioner, Michel Barnier, said the commission was currently drafting two regulations – covering the patent and the language arrangements – on which the council and the European Parliament would seek to reach agreement. The drafts should be ready by 30 March. Mr Barnier said the commission would look in detail at the ‘very interesting’ CJEU opinion and would “bear it in mind” when drafting them.

EMA: guidance on CAT-NB interaction for combi ATMPS

The European Medicines Agency has finalised its much-awaited procedural advice on how its Committee for Advanced Therapies should interact with notified bodies when assessing advanced therapy medicinal products that incorporate medical devices (ie combination ATMPs).

The document describes possible scenarios and timelines for such interactions within the context of the European ATMP Regulation (No 1394/2007). The aim of the interaction procedure is to facilitate the required conformity assessment of the medical device component (with the essential requirements provided in the relevant medical device directives) during the centralised evaluation of a combined ATMP.

A draft version of the procedural advice was issued for public consultation in July last year and was welcomed by stakeholders for the transparent and clear approach it provides on how the CAT intends to interact with notified bodies and how the ATMP sponsor will be involved (www.clinica.co.uk, 30 July 2010).

European medtech industry association Eucomed, however, expressed concern that the document did not address two very important issues: it does not offer guidance on determination of whether a product is a “combined product” and it does not explain the basis on which the CAT might decide that consultation with a notified body is not necessary. Eucomed requested that these two points either be included in the current document or dealt with in separate guidance in order to help manufacturers determine the need for a pre-application consultation with a notified body.

The EMA said these two points were outside the scope of the advice. The agency may publish guidance on these topics after it gains further experience. Also, the EMA clarified that the final document does not concern post-approval procedures/interaction between the CAT and notified bodies, which will be dealt with in separate guidance.

Interaction between the CAT and notified bodies will be done in conjunction with the product applicant, which in practice implies that the applicant “will always be involved/copied/informed” of all contacts the CAT may have with the notified body.

ABHI tackles uncertain times with new market information service

The Association of British Healthcare Industries (ABHI) is preparing to launch a new information service to help its members monitor the activity of the UK market.

The plans have not been finalised, the association told Clinica, but the information is likely to feature certain market indicators – such as waiting times and activity volumes – for specific specialisms, procedures or technologies. The information will be compiled from existing data, collated from different sources, and published on a regular basis, probably quarterly.

The service could be launched within the next quarter.

“The medtech industry is being listened to”

The aim of the initiative is to help its members with decision-making through the current period of uncertainty – most notably the cost-cutting pressures on the NHS and, to some extent, the evolving reforms of the UK health system.

Despite these challenges, the ABHI expressed optimism at how the medtech industry is “being listened to” and demonstrably influencing the discussions at governmental level on the reforms of the NHS.

High-value eqpt joins timely UK NHS audits

As Clinica went to press, the UK’s National Audit Office (NAO) was close to completing an investigation into the management and utilisation of high value equipment in the NHS. “The report will examine how the utilisation, costs and outputs of high value technological equipment vary, and identify areas of potential efficiency gains to help the NHS improve the use of this equipment,” said the NAO. The report was due to be published “towards the end of March”.

“Divide-and-rule ethos” in NHS supplies system under the spotlight

The activities of logistics giant DHL in the UK’s NHS supply system have taken centre stage in an ongoing parliamentary inquiry into procurement inefficiencies.

DHL’s activities as part of NHS Supply Chain (NHSSC) were highlighted by the Public Accounts Committee (PAC) during a hearing held on 15 March to question key figures of national and local responsibility for NHS procurement, in response to issues raised by the National Audit Office (NAO) in its report The procurement of consumables by NHS acute and Foundation trusts (www.clinica.co.uk, 4 February).

The focus of the NAO’s concerns, given its remit as auditor of the use of public resources, is the wide variations in the prices paid for the same product. The NAO report argues that improving the NHS’ procurement system could result in savings of £500m ($804m) per annum of the £4.6bn annual consumables bill in England.

This is based on a “conservative estimate” of 10%, equivalent to the average difference between the highest and lowest prices for all products among all trusts, as calculated by the NAO.

Seeking to elucidate on the complex interactions of the many bodies that operate in the supply system, the PAC found that a “divide-and-rule” ethos had pervaded NHS procurement, and that laudable measures to introduce transparency and competition had instead served to cultivate a “market-gaming” culture with perverse anti-competitive effects.

Addressing the expected rise in collective activity in purchasing and its role in reducing costs, the PAC noted that the activities of NHS Supply Chain as a leading player in this area, had not had this impact. Referring to the NAO’s findings that the prices of its supplies were higher in 51% of the 4,300 products it surveyed, the PAC said that the system marginally increased costs to the NHS, instead of reducing them.

Referring to the price variations, the PAC went on consider the suggestion by panel members that suppliers were “gaming the system”.

The issues around the activities of DHL alone in the PAC’s assessment are complex and a proper assessment of its views must await their report. But the impact of the interacting activities of the wider system on the various bodies involved, including the NHSSC itself (led by DHL since NHS Logistics was privatised in 2006), is even more convoluted.

On the one hand, the PAC’s take on the part played by DHL in this “divide-and-rule” culture is that this serves its interests. On the other, the NAO report effectively refers to the NHSSC as an apparent victim of this situation, in terms of how competitors were undercutting it.

“It has been suggested that some suppliers may be deliberately attempting to cut out NHS Supply Chain out of the market for their products, by selling to NHS Supply Chain at high prices, which means that the prices NHS Supply Chain can offer to trusts will be higher than those available direct from the supplier,” the PAC read from the NAO report.

“The temptation to not use Supply Chain is obviously there, and one can understand that suppliers might like to play this game,” a PAC member said. “But the suggestion that there is actually ‘gaming the system’ going on [must lead us to conclude that] they don’t want Supply Chain to work – they much rather divide and rule, and the question is: how are we going to beat that?” he added.

These issues of system fragmentation and complexity, and the lack of centrally-held payment information to help manage the system locally, and are set to be the key targets of the PAC’s recommendations to the government.

When the plans for privatising NHS Logistics first emerged in mid-2006, the Association of British Healthcare Industries (ABHI) warned the government that the changes would be “catastrophic” for UK healthcare.

These and other warnings do not appear to have been heeded – see NHS procurement: Chronicle of a catastrophe foretold (23 March) and the full version of this article (17 March) online.
Overtake diabetes test reimbursement decision, says German IVDs industry

The German in vitro diagnostics industry is calling on the ministry of health to reverse a decision to end reimbursement of blood sugar test strips for non-insulin-dependent type II diabetics. The decision was taken on 17 March, at the monthly plenary meeting of the G-BA, the joint federal committee, in Berlin.

The national IVD industry association, the VDGH, had been fearing the decision for some weeks. GPs had also been second-guessing the decision, after IQWIG, the G-BA’s Institute for Quality and Efficiency in Healthcare, had criticised ongoing reimbursement of the product as too costly to the health system (see Expert View, 16 March).

Hundreds of thousands of sickness-insured diabetics will now have to fund these products out of their own pockets, says the VDGH. For those that will not or cannot pay, the most effective method of self managing the condition has summarily been withdrawn from them. The decision affects most but not all users.

VDGH chief executive Martin Walger, urging the health ministry to act, said the decision was based on poor advice. A test strip is not a therapy, but the means on which to base therapy. The G-BA has incorrectly viewed the product as a pharma product, he said. He feared that reimbursement of test strips for insulin-dependent diabetics will likely come under threat next.

As indicated in a recent Clinica interview with IQWIG director Professor Jürgen Windeler, the institute is focused strictly on cost benefit, and not the wider social care benefits of a healthcare product’s use (www.clinica.co.uk, 6 January). Critics of this approach say the long-term consequences and costs to the health system of any such decision need to be factored in.

German medical device clinical trials system off to faltering start

Some 250 applications to conduct device clinical trials were filed with the German federal institute for drugs and medical devices BfArM in 2010, the first year in which new rules were introduced under amended medical devices legislation.

Last year, the fourth revision of the Medizinproduktgesetz (MPG4) came into effect, bringing with it provisions that companies must now seek authorisation from BfArM before running device clinical trials in Germany. Previously, mere notification sufficed. The legal and ethical aspects still need to be checked by the ethics commission, as before.

Industry has been highly critical of the extra work and expense needed to comply, and its frustrations have been partly borne out by BfArM itself. At a devices industry-hosted conference in Bonn on 17 March, the institute’s head of simplified procedures and active devices Dr Ekkehard Stößlein detailed the faltering progress of the new arrangements.

Of the 250 applications filed, 100 were for waivers. Many of the forms were incomplete, lacking information on safety or risk analysis. Better attention to filling out the forms would have accelerated the process, said Dr Stößlein.

A better solution would be to put more weight and resources behind market surveillance, believes industry. This is an efficient system that leads to improved transparency and better patient and user protection. Problems with products in the system can be dealt with early and swiftly. Moreover, industry is used to the system.

Manufacturers used the 17 March meeting, hosted by BVMed, as a platform to renew calls for hospitals to install a dedicated competent person who can act as the contact point for market surveillance on vigilance reporting. This would strengthen post-market tracking activities further.

Australia’s TGA makes it easier to search for devices in online register

The search functionality of Australia’s online register of approved devices and drugs has been improved to enable industry, health professionals and consumers to find information on products more easily.

Changes to the Australian Register of Therapeutic Goods involve, among other things, standardising the views of products; the selections are now for “Medicines” or “Medical Devices”. Also, two new search and select functions have been added to allow the users to search for new products recently added to the ARTG and search products by a nominated active ingredient.

The Therapeutic Goods Administration has provided more information on its website on how these search and select functions can be operated. The agency alerts users to take note of the two dates in the public summary document – the ARTG “start date” and the “effective date”. While the former refers to the date on which a product was added to the ARTG, the latter is the date on which the last change to the entry came into effect.

The changes to the ARTG were made by the TGA as part of its efforts to improve the way it communicates with stakeholders.

Catherine King, the parliamentary secretary for health and ageing, pointed out that while the ARTG has always been online, it has been “difficult to navigate and understand”. The changes, Ms King said, would make it easier for users “to find a product name and the ingredients, details about the company, the date a product was approved for use in Australia and importantly any warnings about the use of the product.”

Related story at www.clinica.co.uk

— Australia outlines roles and duties of IVD sponsors and manufacturers
Exit GHTF, enter regulators-only forum

The founding members of the Global Harmonization Task Force (GHTF) have agreed to terminate the body and are proposing to replace it with a regulators-only forum in the future. The GHTF for the past 18 years or so has been working towards developing a regulatory model and supporting documents to underpin globally harmonised regulation of medical devices.

The decision to terminate the joint regulators/industry initiative was taken at a recent meeting of regulators from the five GHTF founding member regions (namely, the US, the EU, Japan, Canada and Australia), according to GHTF vice chair and head of Medical Technology Association of Australia Anne Trimmer. The next (and possibly final) meeting of the GHTF will be held in Brisbane in May.

At the meeting, which took place on 15-17 February, the GHTF regulators expressed support for replacing the current model with a new forum. For this, they have proposed a new “regulator-only forum with a global reach”. Only last year, the GHTF adopted a procedure that allowed the organisation to open up its steering committee membership to representatives from outside the founding member regions. The Asian Harmonization Working Party (representing the medtech industry in Asia and other regions) was among those to receive a formal invitation to join the steering committee as a full-time member (www.clinica.co.uk, 25 June 2010).

The new forum would not work in isolation; it is envisaged that it “will consult with other interested groups, including industry, healthcare professionals and consumers in the advancement of regulatory harmonisation”. While the exact role of industry associations in the proposed regulators-only forum is not clear, the industry may find it easier to align its efforts with the Global Medical Technology Alliance, which has been recognised as a formal organisation that aims to ensure the industry’s views are reflected at the global level.

A number of medical technology industry associations that are represented on the GHTF have expressed their disappointment. In a joint statement, Eucomed and EDMA (EU), AdvaMed (US), JFMDA (Japan), MEDEC (Canada) and the MTAA (Australia) say they recognise that it is “timely for the structure of GHTF to evolve”. Indeed, they had “flagged opportunities and suggestions for changes”. However, they “regret that the regulatory authorities diminish the value of the contributions to be made by the industry under the new arrangements and emphasise the need for ongoing commitment by the regulatory authorities to the GHTF model and maintenance of the integrity of the documents developed by GHTF which underpin that model”.

A second group of associations later echoed these concerns.

Japanese medtech firms join forces to overcome quake disaster challenges

Japan’s medtech producers and distributors responded to the recent earthquake disaster with plans to collaborate to overcome the main challenges.

Members of the Japanese Medical Devices Manufacturers Association (JMED) discussed among themselves and with the government possible ways of alleviating the supply and production capacity problems caused by the disruption to transport and to power supplies, Clinica has learnt.

“We are investigating the current situation: Most medtech companies have not been damaged [in terms of their infrastructure], but the problem is logistics,” said Shouji Hatano, an executive officer of Terumo Corporation in Tokyo, speaking on behalf of JMED.

While the area affected by the quake is not a significant medtech manufacturing zone, the supply of finished products to distributors and then to the client is affected, said Mr Hatano. In addition, there is also some problem with the supply of components to manufacturers. “This is a big problem that is going to take some time [to resolve],” he added.

With regard to the threatened disruption to electricity supplies, Mr Hatano said that discussions are underway to address this problem.

“Maybe we can share our production capacity among one another,” he said, adding that the most likely target of these collaborations would be the production of disposables, such as dialysers, syringes, needles and catheters.

“JMED is also working closely with the ministries of health, labour & welfare (MHLW) and of economy, trade & industry to resolve the many problems,” Mr Hatano emphasised.

The Japanese stockmarket took a hit in the first days of trading after the earthquake. But analysts expected the general impact of the situation on technology companies to be relatively modest and short-lived, despite the likelihood of delays in shipping goods and possibly higher prices in certain products and components.

Brazil embraces WEEE and RoHS requirements

Brazil is seeking to ensure that its medtech industry is ready to meet by 2014 the environmental standards that healthcare products must comply with in order to access the EU’s medtech market.

The EU’s two key pieces of legislation on this issue – the WEEE (waste electrical and electronic equipment) and RoHS (Restriction of Hazardous Substances) directives – were the subject of a recent meeting hosted by healthcare products regulatory agency Anvisa.

“We must align our aims of achieving the highest clinical standards...with our efforts to stimulate the innovation and competitiveness of Brazilian manufacturers,” according to Anvisa’s acting director-president, Dirceu Barbano.

For Brazilian manufacturers the message from Anvisa is clear: “All medical equipment, devices and diagnostic products developed in Brazil must comply with these environmental standards in order to enter the EU market,” said the agency.

Related news at www.clinica.co.uk

— Industry regrets “unilateral” decision to disband GHTF
— More medtech associations lament GHTF changes
— Exciting but uncertain times for medtech regulation
Medtronic cancels $2bn group purchasing organisation contracts

Medtronic has terminated five contracts with Novation, the largest US healthcare group purchasing organisation (GPO). The contracts cover cardiovascular and orthopaedic products and are worth around $2bn in annual purchases.

Medtronic has also pulled out of its contract with another GPO, Premier, which covered spinal products.

GPOs act as "middlemen", negotiating prices with hospitals so companies do not have to do so themselves. They aim to get discounts from manufacturers by using the collective buying power of their members. Many GPOs are funded by administrator fees paid by vendors such as Medtronic.

Cutting out Novation from the supply chain could save Medtronic money and allow it more flexibility when negotiating directly with hospitals on prices for its products. Analysts at Gerson Lehrman Group described the decision as a "bold move"; "The downside of selling through a GPO is the effect of offering lower prices to hospitals that do not purchase higher volumes of products," they noted. "Medtronic has a large enough contracting and sales force to be able to negotiate directly with hospital customers rather than use GPO arrangements. By [doing so] Medtronic should be able to negotiate more aggressively and reward customers with lower prices in exchange for higher volume."

"We believe device manufacturers pay admin fees ranging from 0.5-3.5% to GPOs," said Morgan Stanley analyst David Lewis. This could equate to savings of $40m for Medtronic, assuming it pays fees at the midpoint of this range on sales of $2bn.

Cost-cutting

Minneapolis, Minnesota-based Medtronic also contended that selling directly to hospitals would reduce costs to the healthcare system. Novation disagreed, saying that this could in fact raise costs for hospitals by eliminating price protection and introducing pricing confidentiality clauses – these stop hospitals from discussing pricing information with third parties, which will keep prices "artificially high", Novation believes.

Healthcare providers appear to agree with Novation – 16 US not-for-profit hospitals and academic medical centres sent an open letter to Medtronic detailing their "extreme disappointment" with the decision.

Nonetheless, Medtronic might be the first of many companies to dispense with GPOs, according to analysts. "I expect that St Jude Medical and Boston Scientific will likely follow Medtronic's example for their cardiac devices," the Gerson Lehrman Group research note said, adding that the orthopaedic and spine industry might also follow suit "as the major device companies struggle to maintain their average sales prices".

However, despite its actions, Medtronic's chief financial officer, Gary Ellis, recently told investors that the firm does not plan to stop working with GPOs altogether.

"GPOs play a valuable role in the delivery of healthcare," Mr Ellis said. "We intend to maintain our relationships with GPOs that are providing a benefit."

He made the announcement at the Barclays Capital 2011 Global Healthcare Conference, held in Miami, Florida on 15-17 March, in response to speculation about whether the firm was planning to change its strategy to save costs by cutting out the organisations.

Quest buys personalised medicine firm Celera for $671m

Quest Diagnostics is to acquire genetic testing specialist Celera in a bid to consolidate its presence in the growing personalised medicine market.

Quest has definitively agreed to pay $8 for each Celera share, representing a 28% premium over Celera's closing price on 17 March. Excluding the $327m of cash and short-term investments which Celera has and Quest will acquire, the transaction value will be $344m. The price of the deal will also be further reduced on realisation of Celera's available tax credit and net operating loss carry-forwards, which totalled $117m at the end of 2010.

The acquisition is not anticipated to have a material impact on Quest's earnings per share in 2012. Should the deal close at the end of April, as anticipated, the company expects Celera to add just over 1% to 2011 revenue growth.

Celera's 2010 net revenues, reported on 18 March, were down 18% to $128.2m. The company also reported a net loss of $24.6m, compared with a net loss of $25m in 2009. Celera attributed its drop in revenue to lower sales of products distributed by its partner Abbott, and also to a reduction in licensing revenue.

The deal will see Quest gain immediate access to Celera's proprietary genetic tests and pipeline of biomarkers, as well as Celera's Berkeley HeartLab subsidiary, which sells cardiovascular tests via a specialised sales force.

Celera's existing products include the ViroSeq HIV-1 genotyping system; a cystic fibrosis genotyping assay for carrier or newborn screening; and human leukocyte antigen gene tests for donated organs.

Its pipeline includes the KIF6 genotyping assay, designed to detect a risk marker for coronary heart disease, which the company submitted for US FDA premarket approval in January. It is also developing ViroSeq hepatitis B and C virus assays, and genetic markers for thrombophilia, liver fibrosis, and breast and lung cancers.

Madison, New Jersey-based Quest believes the acquisition will "strengthen its leadership position in molecular diagnostics discovery and development, and drive sustainable revenue growth".

Jefferies analyst Arthur Henderson described the acquisition as a "strategically sound move for the company". He added that "near-term financial implications appear modest", but the buy could lead to "significant growth opportunity longer term" for Quest.

The acquisition is the second of the year for Quest; last month, it bought Thermo Fisher Scientific's Athena Diagnostics lab-testing division for $740m in cash (www.clinica.co.uk. 25 February 2011). Athena specialises in genetic testing for neurological disorders.
Terumo soars to No 1 in global blood transfusion with $2.6bn CaridianBCT buy

Terumo is to buy Gambro’s blood banking unit CaridianBCT for $2.6bn, a move which will propel the Japanese firm from its existing number-five position in the global blood transfusion market to number one.

The acquisition will give Terumo a blood transfusion business with annual sales of around ¥70bn ($850m); it is believed to be the biggest M&A transaction to date by a Japanese medical device company.

The deal is a good fit for Tokyo-based Terumo; the company made its debut in the blood transfusion market in the 1960s and has established an expertise in whole blood collection, offering products such as blood bags and blood transfusion sets.

It hopes the acquisition of Lakewood, Colorado-based CaridianBCT will allow it to offer a wider range of blood processing technologies and expand its global presence, particularly in the North American market. CaridianBCT makes automated systems for collecting blood components and filtering pathogens, which are used by blood banks and hospitals.

According to Terumo, the significantly expanded blood transfusion business will enable the firm to capitalise on opportunities arising in an industry that is currently experiencing high growth, driven in part by the ageing population and the increased need for treatments requiring blood products, and in part by the rapid development of healthcare infrastructure in emerging economies.

The purchase price is around 15 times that of CaridianBCT’s 2010 earnings before interest, taxes, depreciation and amortisation (EBITDA), which were $182m; Terumo will finance the deal with available cash and bank loans. Analysts have valued CaridianBCT at around eight times EBITDA, so while the acquisition may seem expensive, it may reflect the anticipated high growth in this segment. CaridianBCT’s sales have been growing at an average of 12% per year since 2000, and Terumo says it expects further expansion. In 2010, it recorded pre-audited sales of $524m.

The bulked-up blood transfusion business will now account for 18% of Terumo’s total sales (excluding CaridianBCT, it used to account for 8%).

The acquisition is expected to be completed in late April to early May 2011. As well as blood banking products, Terumo also develops endovascular products including catheters, sheaths and guidewires, and medical products such as blood pressure monitors and syringes.

Across all of its businesses, Terumo aims to generate revenues of ¥1 trillion within 10 years, and believes the CaridianBCT acquisition will help it achieve this. Until now, the firm has expanded mainly through organic growth. However, it was rumoured last year to be interested in buying UK beath technology firm Biocompatibles International, which was eventually acquired by BTG (www.clinica.co.uk, 19 November 2010).

The move could also reflect a trend for Japanese firms to buy overseas targets, driven by the mature home market and a strong yen. Earlier this month, Japanese pharma firm Daiichi Sankyo bought private US company Plexxikon for $805m.

CaridianBCT is owned by Swedish firm Gambro; the latter is jointly controlled, which is, in turn, owned by industrial holding company Investor AB and private equity group EQT.

Philips strengthens anaesthesia offering with Dameca buy

Philips has bought Danish anaesthesia systems developer Dameca for an undisclosed amount in a bid to strengthen its portfolio of products aimed at the operating room.

In 2008 Philips acquired Brazilian medtech firm Dixtal Medical, which makes healthcare equipment including anaesthesia machines (www.clinica.co.uk, 23 May 2008). However, the Dixtal devices are primarily sold in Brazil, whereas the Dameca acquisition will allow Philips to tap into new markets – Dameca has direct sales channels in Denmark and Sweden, and serves over 65 more countries via distributors.

Another advantage of the Dameca deal is that Philips will gain an anaesthesia device platform that it can use to develop future products. “This is one of the most important things about this acquisition,” a spokesman told Clinica. “It will help us complete our anaesthesia care portfolio.” He added that Dameca has some “very advanced technologies”, including an MRI-compatible anaesthesia machine.

One country where Dameca does not have a presence is the US, but Philips hopes to change this. “We’re eventually planning to expand into the US using the Dameca platform,” the spokesman said.

Privately-held Dameca was founded in 1947, is based in Copenhagen, and has around 70 employees. Its product line includes anaesthesia machines, wall panels, pendant systems, flow meters, suction units and other accessories for the operating room.

These products also complement Philips’ existing expertise in patient monitoring and informatics. “The expansion into this arena is a very natural one, because during intervention, a patient monitor is always there,” the spokesman said. “We already have a presence in intensive care units, and we would like to expand this into the operating room. And with this acquisition we can offer a comprehensive solution: patient monitoring, anaesthesia and clinical informatics, which we believe will help us gain share in the anaesthesia market.

It’s our ambition to grow faster than the market.”

Other players in the anaesthesia segment include GE Healthcare, Covidien and Teleflex Medical. The global market for anaesthesia devices is expected to reach $7.3bn by 2015, expanding at a compound annual growth rate of 7%, according to a 2010 report by Research and Markets.

For other M&A news on Medtronic, Physio-Control, Accuray, TomoTherapy, Roche, Utah Medical, Fresenius and Halma, go to www.clinica.co.uk
FDA warns Cordis over Cypher stents; may delay approval of catheter

Johnson & Johnson’s cardiovascular unit Cordis could face further disruption to the supply of its Cypher stent following an FDA warning letter concerning violations found at the Puerto Rico facility that manufactures the devices.

In the letter, dated 16 February and released publicly on 8 March, the FDA stated that Cordis had sold Cypher sirolimus-eluting stents that did not meet design specifications and that tests conducted in 2009 found devices that ‘did not completely expand’. On one occasion, testing ‘obtained failure results’ from all of the 15 Cypher DESs tested. Complying with design-specification tests is critical to ensure patient safety, the agency stated.

The FDA asked the firm to justify its decision to release products that had failed the design tests. “In your response to this letter, please explain how you can demonstrate that the quality of your distributed products was not affected,” it wrote.

The letter, addressed to Cordis’s chairman, Seth Fisher, contained a stark warning: “The specific violations noted in this letter…may be symptomatic of serious problems in your firm’s manufacturing and quality assurance systems.”

Cordis’s Sandra Pound told Clinica: “Our San German facility continues to manufacture and ship Cypher products for the US, where it continues to be available to patients and physicians. We are currently working with the FDA to resolve the warning letter as quickly as possible.”

The company said: “Based on the medical input we have received, we do not believe this issue impacts product safety and efficacy and we are confident our product remains safe and effective for use.”

Impact on catheters?

More importantly, the FDA has said that until the issues are resolved by Cordis, the agency will not approve any products that are made at this site.

Cypher DESs are manufactured solely at Cordis’s San German, Puerto Rico facility and the FDA’s refusal to approve any related products could pose a real problem for the firm. The catheter currently used to deliver Cypher in the US is made by rival stent developer Abbott, and Abbott recently decided to stop supplying it to Cordis after the end of April (www.clinica.co.uk, 1 March 2011). Therefore, Cordis is trying to get its own catheter approved – a regulatory submission is under FDA review. But this new catheter is, of course, manufactured at the Puerto Rico facility. Cordis has said that it has a stockpile of the Abbott catheters, but it must now work to get the warning letter lifted before its supply runs out.

Ms Pound said: “According to the letter, the timing of DES-related approvals, the catheter, could be delayed until the warning letter is resolved.”

The FDA has issued a warning over Cordis’s Puerto Rico site before. In April 2004, it sent a letter following inspections of facilities in Florida, New Jersey, the Netherlands, Belgium and Italy, as well as the San German site.

In an unrelated matter, J&J’s Animas subsidiary is also recalling 384,000 insulin cartridges that may leak and cause pumps to deliver too little insulin.

Animas said it would replace the leaking cartridges free of charge. The faulty pumps make up around 5% of the eight million cartridges the division manufactures each year.

Related news at www.clinica.co.uk:

— Head of J&J’s ortho division resigns amid weak sales

Thermo Fisher and Medtronic expand Chinese operations

Thermo Fisher Scientific plans to open a new manufacturing facility in China next year as part of its strategy to aggressively expand its presence in Asia-Pacific. This facility, based in Suzhou city in eastern China, will develop and manufacture lab instruments, equipment and consumables for China’s growing life sciences market, says Waltham, Massachusetts-headquartered Thermo. The site is expected to be completed in early 2012. China is one of Thermo’s fastest growing markets; in 2010, revenue generated in the country grew by over 14%. The company currently has over 1,400 employees in China. Last year, it opened a second demonstration lab in Beijing and a China Technology Center in Shanghai.

Meanwhile, Medtronic has established new headquarters in Shanghai, China, which will serve as a centre for its growing operations in the region. The company plans to expand its activities in China by hiring and training 1,000 new employees there in the next five years, and will also invest in R&D, clinical studies and manufacturing. Medtronic opened its first office in Shanghai in 1996. In 2008, the firm formed a joint venture with Weigao Group, a local leading medical device company.

Medtronic has also opened a new facility in Singapore that will manufacture its cardiac devices. Medtronic plans to invest a total of $871m ($56m) and employ over 120 people in the centre by the end of the year. Annual sales of medical devices in Asia-Pacific will amount to $6.3bn by next year, a quarter of the global total, according to research firm Frost and Sullivan.

OPKO plans $100m public offering

OPKO Health, which is developing technology to help diagnose Alzheimer’s disease, plans to raise $100m in a public offering. It intends to use the money for R&D expenses, clinical trial, and acquiring new technologies or businesses. The Miami, Florida-based firm did not disclose how many shares it will be offering or how they will be priced, but its shares on the American Stock Exchange closed at $4.25 on 3 March. Earlier this year, a small study found that OPKO’s technology could successfully “fish” for antibodies in the blood, and that the method could distinguish between Alzheimer’s patients and healthy controls (www.clinica.co.uk, 7 January 2011). In January, the firm signed a collaboration deal with Bristol-Myers Squibb for the Alzheimer’s test.
Medtronic’s Amplify bone graft turned down by the FDA; warnings lifted

The US FDA has rejected Medtronic’s marketing application for its Amplify spinal graft, saying that it requires further data from the company before granting approval.

Amplify is made of recombinant human bone morphogenetic protein-2 (rhBMP-2), used to stimulate bone formation, and a porous matrix comprised of collagen and resorbable ceramic. It is intended to be used to fuse vertebrae in the lower spine.

Last July, an advisory panel to the FDA recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time, recommended approval of Amplify, but so narrowly that, at the time.

The company has maintained that it will continue to seek FDA approval for Amplify, but refused to say when it was expected.

In a filing with the US Securities and Exchange Commission, Medtronic wrote: “In the third quarter of fiscal year 2011, the FDA sent Medtronic a letter advising that they were not able to approve Amplify at that time without additional information from Medtronic.

“We are in active dialogue with the FDA to address the issues in its letter, have been given the opportunity by the FDA to provide further information relevant to these issues, and are hopeful that the FDA will ultimately approve Amplify.”

Medtronic declined to specify which “issues” the FDA raised, but the agency’s panel was concerned about trial data that link the graft with a higher incidence of cancer than other bone healing technologies. A 463-patient clinical trial comparing Amplify with autograft therapy found that the cancer rate with Amplify was 5% at five years, compared with 1.8% in the autograft group. Medtronic (Minneapolis, Minnesota) said that the differences were not statistically significant.

The company has maintained that it will continue to seek FDA approval for Amplify, but refused to say when it expected US approval of the graft, saying that this timing was dependent on the agency’s actions.

**Infuse implications**

It is possible that delayed US approval of Amplify may have only a small impact on Medtronic, as its Infuse bone graft, which also contains rhBMP-2, is already used off-label for lower spine fusions. In fact, over 70% of Infuse grafts are used for this indication.

However, it is also conceivable that the concerns surrounding Amplify may lead to a re-evaluation of Infuse’s safety. Amplify was designed to address concerns about off-label use of Infuse, so its failure to win approval may mean off-label Infuse use and perhaps even its reimbursement will come under greater scrutiny in future.

Quite apart from this, Infuse is already the subject of safety concerns. In September 2008 the FDA posted a public health notification on its website warning doctors of potentially life-threatening complications associated with the unapproved use of rhBMP-2 in cervical spine surgeries, and the company had been the subject of a DoJ investigation and litigation concerning the promotion of off-label use of Infuse (www.clinica.co.uk, 16 September 2008, 4 December 2008, and 16 January 2009).

In fiscal 2010, Medtronic’s worldwide revenues from its biologics products in its spinal business, which include Infuse, were $868m.

**Warning letters resolved**

Separately, the US FDA has lifted two warning letters that had prevented Medtronic gaining US approval for devices manufactured at two of its facilities.

One of the letters dates from June 2009, and pertains to the company’s site in Juncos, Puerto Rico. The other, from November 2009, concerns Medtronic’s Mounds View, Minnesota facility.

The agency sent Medtronic the first letter after inspecting the Puerto Rico facility, where the firm manufactures neuromodulation, diabetes and cardiac rhythm disease management (CDRM) devices, in November 2008. The letter stated that Medtronic had taken too long to react to a recall of its Synchromed II programmable drug pump and its MiniMed insulin pump after it was discovered that some versions of the device lacked a propellant. It also said that Medtronic did not follow proper reporting procedures concerning complaints about the MiniMed pump (www.clinica.co.uk, 29 June 2009).

The other warning letter came after an inspection of the company’s facility in Minnesota, the headquarters of Medtronic’s CDRM operations, in August 2009, which raised issues related to Medtronic’s procedures for identifying, preventing and correcting problems with CDRM devices, reporting problems to the FDA, documentation and quality control (www.clinica.co.uk, 20 November 2009).

The agency says these issues have now been resolved.

Interestingly, Medtronic managed to get one of the devices built at the Mounds View site approved in the US before the warning letter was resolved. Warning letters give the agency the right to halt marketing applications for devices made at these sites, but in the case of Revo MRI SureScan, Medtronic’s MRI-compatible pacemaker, the agency did not exercise this right. The pacemaker was approved last month (www.clinica.co.uk, 9 February 2011).

US approval and launch of the Protecta family of implanted defibrillators, also manufactured at Mounds View, could now be on the cards. Designed to minimise inappropriate shocks, Medtronic CE marked these devices in March 2010 and launched them in Europe in June.

---

**Other Science & Technology news at www.clinica.co.uk:**

- Intercytx starts trial of cell therapy in epidermolysis bullosa
- FDA approves use of Covidien’s uranium-derived Mo-99
- AccessClosure’s vascular closure device beats St Jude’s established rival product
ECR: breast elastography useful – but expensive

ShearWave Elastography, an imaging technology developed by venture-backed French firm SuperSonic Imagine, improves diagnosis of breast cancer when added to ultrasound.

Trial data presented at the annual European Congress of Radiology, held in Vienna, Austria, on 3-7 March, confirmed that the technique is useful for lesion classification.

Cancerous tissue tends to be stiffer than healthy tissue, so when elastography is applied to the breast, the tumour deforms less than the surrounding tissue. This makes tumours easier to identify, particularly in younger women.

SuperSonic developed a statistical model based on 939 lesions, which showed that ShearWave Elastography increases the performance of breast ultrasound. The use of ShearWave Elastography to determine maximum elasticity (stiffness) or heterogeneity of a lesion, in addition to B-mode ultrasound, improves the accuracy of BI-RADS classification of lesions, the investigators concluded.

BI-RADS is a classification system designed to standardise reporting of breast imaging results by providing the following categories: 0 – incomplete; 1 – negative; 2 – benign; 3 – probably benign; 4 – suspicious abnormality; 5 – highly suggestive of malignancy; and 6 – biopsy-confirmed malignancy.

In the study, 1,223 lesions were examined, including 425 cancers (34.8%). Elastography was found to maintain the sensitivity of the ultrasound exam at 97.9%. It increased specificity by more than 8%, raising the figure from 59.9% to 68.2%. Ultrasound’s negative predictive value was maintained at above 98%, and its positive predictive value was increased by more than 5%, from 73.1% to 78.5%.

These results confirm the increase in specificity expected with the addition of ShearWave Elastography to BI-RADS criteria, SuperSonic said, thus reducing the rate of negative biopsies as clinicians can more confidently rule out cancer. The Aix-en-Provence-based firm said: “ShearWave Elastography can assist in diagnosing cancers that would have otherwise fallen into a follow-up category, thus earlier intervention and treatment could occur with significant implications for patient management.”

The Aixplorer ultrasound system developed by SuperSonic uses technology based on combining two types of waves: an ultrasound wave that provides imaging, and a shear wave which measures and displays the stiffness of tissue in kilopascals.

The system was CE marked in 2008 and is sold in countries including France, Germany and the UK. It is also available in the US, where it is distributed by Hologic (www.clinica.co.uk, 25 November 2010). The product is also sold in Asia via a network of distributors, including Canon in Japan.

Too expensive?

Elastography was also discussed in a seminar at the ECR meeting.

In a technical review of elastography, Dr Giorgio Rizzatto of the University of Udine, Italy, highlighted the ShearWave technology. He said that while the technique is reproducible and less operator-dependent than other techniques, a recent trial has shown that different operators can evaluate lesions differently.

The study, which appears in the March issue of the American Journal of Roentgenology, evaluated 65 breast lesions in 53 patients who underwent ultrasound-guided core biopsy. Ultrasound and elastography images of the lesions were analysed by three prior to biopsy. Each radiologist recorded final ultrasound BI-RADS assessments using ultrasound alone and combined ultrasound and elastography.

Of the 65 lesions, 43 (66.2%) were benign, and 22 (33.8%) were malignant. Specificity, positive predictive value and accuracy were all significantly improved when elastography was added to ultrasound. However, agreement between the three observers was not improved with combined ultrasound and elastography in comparison to ultrasound only.

Later at the meeting, Ingrid Schreer of the University Hospital Schleswig-Holstein in Kiel, Germany, said that the ShearWave technology increases confidence in grading lesions, as well as downgrading alarming BI-RADS scores, thereby eliminating unnecessary biopsies.

However, the system is so expensive that it will not be widely available for some time, Dr Schreer said.

Siemens’ PET-MRI combo system “feasible” in head and neck cancer

A small feasibility study has suggested that hybrid PET-MRI systems may be used for detecting head and neck tumours.

The pilot study assessed the use of the Biograph mMR system, developed by Siemens Healthcare, to image eight patients with malignant head and neck tumours.

The patients initially underwent routine PET/CT imaging using [18F] fluorodeoxyglucose (FDG) as a radiotracer. Immediately afterwards, additional measurements were performed with the PET/MRI system for simultaneous PET and MR imaging.

The MR datasets showed “excellent image quality”, the researchers wrote, without recognisable artefacts caused by the PET system. PET images obtained with the PET/MRI system exhibited more detailed resolution and greater image contrast compared with those from the PET/CT system. This could enable better visualisation of smaller structures than is possible with other imaging techniques.

The researchers concluded that simultaneous PET/MRI of the head and upper neck area “is feasible with the new hybrid PET/MRI prototype”.

The findings were published online in European Radiology on 10 February.

Hybrid imaging systems combine the imaging of anatomical structures using MRI with PET’s ability to evaluate metabolism and molecular processes.

The Biograph mMR features an MRI-compatible lutetium oxyorthosilicate-based PET insert, which fits into a slightly modified 3 Tesla whole-body MRI scanner.

At present, only one hybrid PET-MRI system is commercially available anywhere in the world; Phillips CE marked its Ingenuity TF PET/MR for sale in Europe in January (www.clinica.co.uk, 25 January 2011).

Siemens has previously told Clinica that it anticipates launching Biograph mMR globally in summer 2011 (www.clinica.co.uk, 30 November 2010). Both companies’ hybrid systems are awaiting FDA approval.
High fracture rates with J&J’s ASR XL hip implant, UK ortho surgeons warn

Nearly half of Johnson & Johnson’s ASR XL artificial hips fail within six years of implantation, two UK doctors’ organisations have warned.

The British Hip Society (BHS) and the British Orthopaedic Association (BOA) issued a joint statement on Wednesday cautioning that the ASR XL device has a “higher than anticipated early failure rate”.

DePuy recalled the ASR XL acetabular system as well as the ASR hip resurfacing system in August owing to the number of patients implanted with the devices needing revision surgery (www.clinica.co.uk, 31 August 2010). The company had claimed then that the five-year revision rate for the ASR XL is approximately 13%.

Worldwide, around 93,000 ASR XL acetabular systems and ASR hip resurfacing systems are thought to have been implanted. Production of the two devices had been discontinued in 2009 after a decline in demand and J&J had said at the time of the August recall that “very few devices remain on the worldwide market”.

Data from clinical trials presented at last month’s BHS annual meeting, held in Torquay, showed that 21% of patients implanted with the artificial hips required revision surgery within four years of implantation. This could rise to 35% if all implants currently known to be painful progress to revision. At six years post-implant, the revision rate was 49% at 6 years for the ASR XL device.

Other, similar devices have a revision or impending revision rate of 12-15% at five years, the organisations said.

The organisations advise that patients with metal-on-metal bearing replacement hips such as the ASL XL should be followed up regularly for five years and probably for the life of the prosthesis. Furthermore, future use of these devices “should be carefully considered and possibly avoided”.

Cost: $280m and counting

The researchers posited several possible reasons for the devices’ failure. Several hips removed during revision were damaged at the site where the large-diameter metal head of the hip attaches to the stem, “but it was not clear whether this was from wear or corrosion or both,” the statement said.

Other potential sources of problems include wear to the bearing surface and corrosion of the stem if the hip is un cemented.

Failed hip implants took the form of loosening of the acetabular component, loosening of the femoral component or metal reaction with necrosis and soft tissue damage. “Failures seem to be more frequent in females,” the BHS and BOA noted.

ASR XL comes in a number of sizes. When it recalled the devices, DePuy said that revision rates would probably be highest for ASR head sizes less than 50mm in diameter, which are usually implanted in female patients.

DePuy’s worldwide sales were $5.59bn in 2010, and made up 9.1% of J&J’s total revenue. Recalling the ASR XL cost the firm $280m. DePuy’s president, David Floyd, resigned in early March (www.clinica.co.uk, 7 March 2011).

S&N takeover?

Analysts said that the ASR XLs dismal trial data could increase sales of hip resurfacing technologies from orthopaedic rival Smith & Nephew, but more interestingly, they could also prompt J&J to renew its overtures to S&N. In January, reports circulated that J&J had made a 750p-a-share offer for the UK multinational at the end of last year, which was rejected as too low (www.clinica.co.uk, 10 January 2011). Speculation was so intense that S&N was forced to issue a statement denying that it was engaged in any discussion about a merger (www.clinica.co.uk, 14 January 2011).

Nonetheless, a second round of rumours, this time placing J&J’s bid at 800p per share, appeared just three days later (www.clinica.co.uk, 17 January 2011).

The latest events prompted Navid Malik, an analyst at Matrix, to say that S&N was “as a highly attractive takeover target”, adding that the news will put even more pressure on J&J to look for acquisitions. Of the data itself, Mr Malik said: “This is an astonishing level of failure for what is one of the market-leading products.”

ExonHit CE marks Alzheimer’s disease diagnostic

ExonHit Therapeutics has CE marked AclarusDx, its Alzheimer’s disease blood test, and will now launch it in France.

The Paris, France-based company intends to make the test available to specialist French clinics dealing with memory and dementia, starting in April.

ExonHit’s Corinne Hoff told Clinica: “AclarusDx is not a stand-alone test, and must be used in combination with other usual assessments to make Alzheimer’s disease diagnosis”. These other assessments could include neuropsychological tests, brain imaging and clinical examinations.

The test will be performed at “Memory Centres”, clinics with appropriate facilities dedicated to research and diagnosis of memory disorders, including Alzheimer’s. Ms Hoff said that in France, general practitioners cannot diagnose Alzheimer’s disease; such a diagnosis can only be made by a specialist – a neurologist or a geriatrician.

The firm also plans to test the diagnostic in "real life" patients undergoing diagnosis.

AclarusDx analyses whether messenger RNA from a patient’s blood sample matches a molecular profile that is specific to Alzheimer’s disease. ExonHit originally launched it for research use at the end of 2009, for pharmaceutical companies and academic centres conducting clinical trials in the disorder (www.clinica.co.uk, 3 December 2009).

As for US market entry, ExonHit says it is assessing different options, from laboratory-developed test to FDA clearance.

The firm believes AclarusDx to be the second blood-based test for Alzheimer’s to gain CE marking. DiaGenic (Oslo, Norway) CE marked its ADtect assay for early diagnosis of Alzheimer’s in 2009 (www.clinica.co.uk, 25 June 2009).

The company also posted its full-year 2010 financial results. Total revenues were €8.4m ($11.7m) in 2010, compared with €4.9m last year. Net loss was flat at €7.7m.

The firm’s sales and marketing expenses increased slightly to €7.5m, which it said was mostly incurred by the preparation for launch of AclarusDx in France.
The telemedicine market is expected to experience a growth rate of over 55% by 2014–2015. It therefore represents a significant business opportunity for industry stakeholders provided they are fully aware of and address issues still remaining. Healthcare and telecoms companies, as well as consumer electronics companies and software developers, can all gain from the growth in telemedicine and m-health, although this will also result in tough competition across sectors.

A new care model is emerging that includes electronic health records and remote diagnostics, remote disease management, and patient monitoring. Industry players need to rethink their strategies and business models to exploit the new opportunities.

We know the benefits…
The benefits of telemedicine and m-healthcare are well known. With deaths from chronic diseases expected to increase by 17% between 2005 and 2015, caring for these patients will put a considerable logistical and financial strain on healthcare systems. The ability to let these patients stay at home, while providing care and monitoring remotely, will help to ease the burden on limited resources.

In addition to reduced costs, mobile health can also bring about increased efficiency for healthcare facilities and professionals. According to PwC’s Health Research Institute (HRI), a third of US
As with any business, there are obstacles to consider when planning to expand into telemedicine and m-health.

**Cost issues**

**Costs of equipment and services**

Although it may eventually result in cost savings and greater efficiencies, telemedicine involves costs beyond the actual equipment expenditure, such as:

- Operational costs;
- Telecommunications costs;
- Healthcare professional training;
- Healthcare services provision.

Some of these costs are not currently accounted for properly or reimbursed consistently.

In the US, for example, laws are in place in 35 of the 50 states to reimburse healthcare providers “for certain types of telemedicine consultations that are billed to the state Medicaid program”. However, not all insurance providers reimburse telemedicine services, although legislation passed in January 2001 to increase reimbursement for telemedicine services should help the uptake of telemedicine.

The lack of widespread consensual reimbursement of telemedicine and mobile health can hinder its development as healthcare institutions and patients alike may be reluctant to incur costs that they may not be able to recoup.

**New telemedicine and m-health charges**

Doctors may introduce charges for e-consultations and other telemedicine services such as remote patient monitoring and disease management. Some have already started to do so in the US. This will be an additional barrier to the growth of this market. The introduction of specific charges for telemedicine and m-health in poorer countries in particular could derail the deployment of telemedicine programs in those regions.

The willingness of patients to pay for telemedicine services or to contribute to their costs will be a determining factor in the adoption of these services worldwide.

**Technological issues**

**Content challenges**

For maximum effectiveness and user experience, the e-health content delivered to mobile devices should combine both text and graphics, and possibly video and audio. Some m-health apps already include voice or audio capabilities. As the market grows, multimedia e-health content will become more common.

This presents challenges for both content publishers and network operators in a context of increasing bandwidth demand and bandwidth bottlenecks. For this content to be delivered satisfactorily, more bandwidth must be available. But content publishers must also design new content specifically for use by portable, mobile devices. The new content designed must be easily accessed on the move and across platforms, bearing in mind download rates, target users (consumer or professional) and user friendliness.

The use of e-health for education purposes also raises the issue of copyrighted content for which providers may need to pay fees or operate under a license.

**Mobile infrastructure and network challenges**

Network congestion can stall the growth of the m-health and telemedicine markets unless solutions are found to address the bandwidth problem.

Mobile networks are under growing pressure with the increased popularity of data-intensive applications such as (audio)video and gaming linked to the increased popularity of smartphones, an ever more mobile way of life and the greater availability of internet-enabled mobile devices, especially in developed countries.

Network operators worldwide are in the process of deploying 4G to alleviate network congestion and improve user experience. Vodafone, Orange, AT&T and Verizon Wireless in developed countries and Zain, Vodacom and China Mobile in emerging countries are all operators engaged in 4G deployment and serve as potential partners for healthcare products manufacturers who want to incorporate this capability in their devices.

The digital dividend resulting from the digital switchover in various regions of the world should enable mobile operators to put in place the right infrastructures to support m-health and telemedicine growth. As spectrum is being auctioned off, governments may want to consider allocating some frequencies specifically for m-health and telemedicine.

Alternatively, the use of cloud computing, femtocells and wireless access points can help to resolve the congestion problem.

**IT network management challenges**

The IT networks in place in some healthcare facilities may not support the level of data transfer that will be generated by e-health or the addition of vendor-specific programs. Open solutions could solve this problem.

…but what are the obstacles?

As with any business, there are obstacles which companies need to look out for if they are planning to expand into telemedicine and m-health.
Failing this, healthcare facilities and medical practices would have to upgrade their IT systems, which would generate additional costs.

IT departments will also have to manage more network-related issues in order to keep users motivated to use the system.

Data storage and management challenges
The huge amount of data generated will need to be stored and managed effectively and safely.

Responsibilities for it within healthcare facilities and doctor practices must be clearly determined.

Connectivity challenges
Wireless connectivity such as Wi-Fi (wireless fidelity) raises not only issues of safety and privacy but also of availability. Signal and therefore connection may be lost if access to the Wi-Fi network is restricted by inadequate environments (eg poor signal transmission due to location or unsuitable building architecture).

Lack of interoperability
One of the current and key issues with telemedicine is the coexistence of various platforms that do not communicate with each other, and the resulting interoperability issues.

The main healthcare stakeholders (healthcare providers, professionals, insurance companies, payers) are currently using different standards, making electronic communication between their different systems difficult if not impossible.

M-health and telemedicine can only be deployed fully if systems are interoperable, which can be achieved through the use of open standards for the recording and sharing of patients’ electronic data. It requires willingness and cooperation on the part of all industry players concerned (hardware and software manufacturers).

Exploiting telemedicine and m-health
Having discussed the potential market barriers, what should companies do to overcome these obstacles, exploit telemedicine and m-health opportunities and help the market grow?

Address reimbursement and cost issues
PwC’s HRI predicts that healthcare spending in Organisation for Economic Co-operation and Development countries will increase from 9.9% of GDP in 2010 to 14.4% in 2020. PwC also forecasts that healthcare spending in BRIC countries (Brazil, Russia, India and China) will rise, albeit at a much lower rate, from 5.4% of GDP in 2010 to 6.2% of GDP in 2020 on the back of their growing economies and improving health systems.

Cost and affordability will therefore remain a pressing issue in the future. This issue cannot be ignored by companies looking to establish themselves in the telemedicine and m-health market. For industrial players and government bodies, coming up with business models that focus on cost savings or revenue are crucial if m-health is to take off.

Given the keenness of some governments to promote e-health, it is highly unlikely that consumers and patients alone will bear the cost of telemedicine and m-health. Healthcare providers, insurance companies and payers will therefore be the main contributors. They will halt the growth of the telemedicine market if they limit the provision and reimbursement of telemedicine services. These organisations’ active involvement and commitment to providing and reimbursing telemedicine and m-health services will act as a signal for companies and organisations to start investing and innovating in the sector and for consumers to use the services.

In the US alone the Federal Communications Commission believes that $700bn can be saved over 15–25 years thanks to telemedicine. There is also anecdotal evidence that home-based treatment and early diagnosis can help to drive healthcare costs down. If the providers of the various e-health applications and technologies mentioned in this report can prove beyond doubt that their solutions help to reduce the cost of healthcare, telemedicine will become more attractive to payers, insurance companies and healthcare institutions alike and attract higher reimbursement rates.

Convince consumers about telemedicine
The proportion of people prepared to pay for telemedicine services is estimated to be 40–70%. Telemedicine requires a change of mentality and habits. People need to clearly understand what they could gain from using telemedicine services because, for telemedicine to take off, consumers and patients must fully adhere to it.

Assure healthcare professionals
The most common payment structure for healthcare systems in developed countries relies on payment per result. As healthcare providers become more efficient and effectively see fewer patients directly, their source of income will decrease, which is definitely a disincentive for them. Their effectiveness see fewer patients directly, their effect will be to reduce the cost of healthcare, telemedicine will become more attractive to payers, insurance companies and healthcare institutions alike and attract higher reimbursement rates.

Cost issues

- Equipment and services
- Charges for telemedicine and mHealth services

Organizational issues

- Surveillance of healthcare practices
- Limitations of ePrescribing

Technological issues

- Content
- Mobile infrastructure and networks
- IT network management
- Data storage and management
- Connectivity
- Inoperability
- Limitations of cloud computing

Legal and practical issues

- Confidentiality
- Standards of practice

Source: Business Insights

Figure 1. Challenges posed by telemedicine and health

— Equipment and services
— Charges for telemedicine and mHealth services

— Surveillance of healthcare practices
— Limitations of ePrescribing

— Content
— Mobile infrastructure and networks
— IT network management
— Data storage and management
— Connectivity
— Inoperability
— Limitations of cloud computing

— Confidentiality
— Standards of practice

Source: Business Insights
conditions themselves?
- Are patients qualified enough to substitute themselves for healthcare professionals?
- Are some healthcare professionals such as nurses at risk of ultimately becoming redundant?
- How will that affect healthcare shortages?

Collaborate to innovate
The financial crisis dampened for a while the plans of IT companies and medical equipment manufacturers to work together on supplying technology-ready products and services. The demand for innovation must be addressed if the industry is to grow through shared objectives and strategies.

Get the infrastructure right
The wide adoption of telemedicine relies heavily on having the right connectivity and infrastructure in place. This is where telecoms and IT companies come into play. Business opportunities exist, for example, in offering connectivity and data centre infrastructure and services to device manufacturers, and for service providers that offer home-based medical monitoring services directly to patients or caregivers.

Growing needs for data storage and data management in particular offer opportunities for ICT vendors and manufacturers that can act as integrators.

It is important to note that telemedicine and m-health applications require the transmission of a lot of data, which can be difficult to manage on 2G networks. However, with the continued deployment of 3G networks and the imminent arrival of 4G networks, more consumers will be able to enjoy telemedicine and m-health fully thanks to greater data transfer speeds.

Telemedicine will be able to move from SMS-based services to more advanced, two-way communication involving multimedia services.

Guarantee data security
Data transmission is at the heart of telemedicine and therefore reliable and secure wireless connections will be required to ensure the privacy of the data collected and downloaded. Data encryption must therefore be guaranteed for all telemedicine solutions provided, whether they are cloud-based or based on healthcare providers’ own servers.

New strategies for ICT and healthcare vendors
Business models for m-health need to aim at healthcare cost savings for healthcare providers and profit for industry players while contributing to overall better patient health.

One single company can hardly have the technological and healthcare expertise required to provide end-to-end solutions. Healthcare will therefore move towards integrated management and provision of healthcare.

Models to exploit m-health and telemedicine
While the efforts of bodies such as the European Commission, non-governmental organisations, academia, and government agencies have so far managed to take e-health forward, more initiatives are required for e-health to become a sustainable business model.

Understanding how all the elements of telemedicine and m-health interact is crucial for healthcare and ICT companies to be able to derive revenue from this market.

Health systems with a single point of contact are a good starting point
For industry players, the US is an attractive market owing to its traditionally lucrative deals and the abundance of intelligence on health. Countries with a national healthcare program, such as Canada or Great Britain, are also attractive markets for healthcare because of the single point of contact responsible for decision making.

Using a bottom-up approach in developing countries
Telemedicine applications such as home-based remote monitoring are gaining momentum in developed countries, but this application is less common in developing countries as it requires the right funding and infrastructure. Targeting more advanced applications of telemedicine immediately may work in richer countries, but a bottom up approach, starting from basic one-way communication with text-based solutions, will work better in developing countries before evolving to more complex two-way communication.

Basic one-way systems (where data is transmitted in only one direction), such as SMS-based m-health services, are simple to implement, cost efficient, and improve efficiencies and facilitating processes.

However, health and telemedicine become a more attractive proposition at higher volumes and levels of complexity for industry players such as network operators, device manufacturers, developers and service providers.

Pricing models for data storage and management
The sheer volume of transferred data that needs to be stored and managed poses a problem in terms of charge structure. The issue, as always, is fair usage and how to limit abnormal usage behaviour.

The possible pricing structures include:
- Charge per use;
- Charge per volume of data downloaded;
- Apply a flat fee;
- Charge a tiered fee.

Public–private partnerships
Public initiatives are currently driving the adoption of telemedicine and m-health. Public organisations also have a lot to gain from reducing healthcare costs and reducing any burden on public health.

Each of the stakeholders mentioned previously in this report stands to gain from the adoption of telemedicine and m-health.

Funding is a key issue in the adoption of m-health/e-health/telemedicine, especially while the market has not reached enough momentum. Public–private partnerships can benefit both parties by the public partner providing funding while the private partner provides the technological and/or healthcare know-how.

*This article is an edited extract from Trends in mHealth and telemedicine, a report authored by Emma Seka and published by Business Insights. For full details of this 100-page report as well as analyses of other healthcare markets, go to www.business-insights.com
Testing times ahead for medtech software and manufacturers

Medical device companies tend to be behind the curve in terms of developing and using sophisticated software in their products. Many other industries are far more advanced in this respect, says device industry and regulatory consultant Trevor Lewis. But while it is playing catch-up, the medtech sector also has to observe strict compliance to regulations that are evolving in tandem with the state of the art.

Interview by IBI principal analyst Ashley Yeo

“Could do better” might fittingly be the comment in the report on how well the global medical devices industry has risen to the challenge of developing and disseminating ICT-based products and decision-support software to users and patients.

So says Trevor Lewis, medical device industry and regulatory consultant at UK Medical Device Consultancy (MDC). “It is sad but true that typical software development tools used in the aerospace and automotive industries are far more sophisticated than in most of the device industry. Even the best medical device companies have room for improvement,” he says. “There are some good exceptions, but they are a small minority.” Device manufacturers need to look at the state of the art and view the issue from a total lifecycle approach, which is now an essential requirement for CE marking.

It doesn’t help that there is a shortage of skilled people available to address this problem – just as there are in many other areas of the industry, clinical evaluations and trials most notably.

Healthcare ICT has developed at such an extraordinary pace that the regulators – both competent authorities and notified bodies – find it a challenge to keep up. Indeed, developments often leave them behind.

“I don’t know any regulator that is comfortable in assessing sophisticated software-based products. Even simple IT systems are difficult and challenging to review with confidence,” says Mr Lewis.

This is partly because the technology is advancing at such speed, driven by competition among the major developers. Large-scale integrated systems development is being pushed by the big concerns, such as BT, Philips, Siemens, and GE Healthcare. There is also a range of other service providers in the fast-developing healthcare sector, such as a Samsung, Google Health, Facebook, YouTube, and a plethora of mobile phone applications providers.

The end products from these types of provider and from the peripheral areas in ICT are being developed apace all over the world. But they are often not being designed with regulations in mind.

“We are seeing an explosion of medical ICT applications, at a time when the interpretation of the governing regulations is changing.”

There has always been a need to regulate these devices. Mr Lewis asserts, but the sector is now beginning to see the first signs of devices that are not fully regulated being put into use. This worrying development is evident in Europe already, and will be soon become a focus of attention in the US.

Last month, the US FDA finalised a regulation for Medical Device Data Systems (certain software and hardware used with medical devices – www.clinica.co.uk, 16 February 2011), but that ruling does not apply to active patient monitoring or any product that is intended for a use beyond the those identified in it. An MDDS does not provide new or unique algorithms or functions, says Mr Lewis.

How has such a state of affairs come about? “The ageing population and the need to change the healthcare model by incorporating remote technologies and getting patients to take greater responsibility for themselves by using telehealth applications have forced the uptake of new technologies. “We are faced with the simple choice of adopting these systems, or being much poorer for not doing so.”

But there should be an unmoveable bottom line. “Such devices need to be safe and effective. They must also work reliably.” The original Medical Devices Directive (93/42/EEC) stated in article 12.1: “Devices incorporating electronic programmable systems must be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition (in the system), appropriate means should be adopted to eliminate or reduce as far as possible consequent risks.” This has been reinforced in the amending Directive 2007/47/EC.

Software can crash, which may not be too serious an issue if the system can be rebooted and put back online with no ill effect. “But for patients at home using, say, ventilators or dialysis machines, a system failure could produce catastrophic results,” Mr Lewis says: “For a lot of medical software, we are talking life and death issues – it is that serious.”

Thorough testing essential

Even in the area of diagnostics, wrong information can result in adverse incidents. The key is to ensure that software systems are thoroughly tested.

The essential measures that constitute best practice for software validation are: effective management and planning; ensuring all appropriate resources are in place that should include software tools and configuration control systems; definition of requirements; translation of requirements into specifications; risk management (software hazard analysis); translation and validation; test plans; test procedures; test cases; test results; test reports; and risk management (software hazard analysis).
of specification into programmss or code in a traceable manner; verification of programmes against specifications; release of verified software (configuration management); validation that the software does function as intended in its application environment; and change management.

These are the well-tried and trusted techniques for validating software. Mr Lewis recommends that every company developing software uses at least some of them: "For sophisticated systems, most techniques should be used to thoroughly test that the device software is robust." The techniques were listed in a specially-commissioned series of articles for Clinica by Mr Lewis in 2004 (go to www.clinica.co.uk). The essential messages in them remain valid. "Some companies need to re-read the clinical evaluation, EMC and safety testing articles," he recommends.

Well-known and used systems such as Microsoft Windows also crash from time to time, usually with few serious consequences. But such consumer systems are actually being tested by hundreds of millions of people in the world every day. With that kind of testing and feedback a reliable platform does eventually emerge. At the other end of the scale, many medical devices are used in relatively very low numbers and need to be prevented from crashing in the first place, the consequences of which are all too obvious.

Software has to be maintained and repaired. For high-risk software, in particular, this needs to be done appropriately and proportionately. On the other hand, if low-risk software – for, say, asthma regime compliance - crashes, this won’t likely cause serious harm. The therapy won’t need to be changed as a result. But if an implantable pacemaker is concerned, this would obviously be a more serious issue. "Just as for any other medical device, there is a risk profile in software."

Proportionate regulation

Any regulatory regime must be proportionate to the risk that the software represents. The trouble with large systems that intercommunicate is the potential for error propagation and viruses. These are the secondary effects caused by linking the systems together, and were unanticipated when the original directive was written.

Complete testing of all IT systems is theoretically possible, but the cost and time for such thorough testing often make it impractical.

"We’ll never be able to test every possible combination or connection. In some software systems, where the complexity means that mathematical abstractions and theory cannot be used, we have to adopt a realistic testing of the functionality of software."

So it is key to have an effective post-market surveillance system working. This has to be a team effort – involving both clinicians and the manufacturer – such user feedback will continually improve the product. "By testing, through use and finding fault, you are effectively developing a better piece of software over time."

Reuse and recycling

It is important for manufacturers to be aware that reuse and recycling of software is a good thing. Patients and users must also understand software that has been tried and tested provides a higher level of confidence concerning the safe and effective real world use of the product.

"A measure of how complicated this subject can be is that complex systems, like electronic patient records (EPRs), can consume literally billions of dollars of development funding and still not yield a robust solution. " Mr Lewis sees in this a salutary lesson: software is a major issue. "However, the way to proceed is with a risk-based approach, and with much care over interconnectivity and knowledge of how devices interact with the internet, cyberspace and other devices."

Don’t forget the user

Another issue is that of usability. This was a focus of a paper by David Ford, Swansea University’s director of health informatics, at the BioWales 2011 conference and exhibition.

Mr Lewis, also attending the event, stresses that software needs usability testing. "It’s not just a code in some abstract mathematical world. We need to know how it will interact with users, and people in the environment of the user. There may be young children in the vicinity, or the device may be being used by someone who is mentally impaired. The outcome could be attempted use of the device in a strange or random way,” he says.

"Manufacturers need to test for all these eventualities. Identification of potential hazards and a thorough risk analysis are just as important for software as for any other type of device.”

Deliberate misuse is a sinister but always possible eventuality. The case of Beverley Allitt, who in 1991 fatally poisoned four children and injured several others via infusion devices while working as a state-enrolled nurse (SEN), will spring readily to mind among UK readers. Unique identifiers or some kind of biometric controls in theory could indicate who operates what pump and where, when and how. Inadvertent or unintentional misuse is more common. But in both situations, there is a need for products to be robust.

The UK MHRA has examined infusion pumps in the past and ultimately this resulted in the National Patient Safety Agency infusion device toolkit being published. This is all the more necessary when we learn that some UK hospitals use more than 100 different types of infusion device, and not all of them are simple to operate. The US FDA has also examined the issue, given that these products tend to attract a relatively high number of adverse incidents. It has a specific web page on infusion pump software safety research, which includes useful further references.

A regulatory system in trouble?

A radical look at the entire device ecosystem is perhaps necessary. "To some outside observers we’re in a mess on the regulatory front in the EU,” says Mr Lewis. No one seems to be able to – or interested in – taking a holistic view of the entire system, wherein patient safety, clinical outcomes, cost containment and the viability of device innovators are all considered important to optimise.

Manufacturers need to be incentivised to comply better with regulations, and the regulators need to be more consultative and co-operative with manufacturers that do deliver compliant devices, while being harder on those that do not. ”The regulatory system works when used as intended,” stresses Mr Lewis. Efficient regulation of increasingly complex software is vital. Manufacturers have their role to play in this, and need to work with regulators to ensure proper control of all devices, especially high-risk products. Healthcare delivery is changing to suit a population that, eventually, will collectively see the benefits of being able to self treat at home for many common conditions, under remote clinician supervision.

The regulators have a difficult time ahead, in view of the onslaught of new ICT-based technologies, but keep up they must. "Manufacturers need to work with regulators to ensure their and the regulator needs are met, and that a holistic approach to the patient results in better, safer and more cost effective products that benefit us all,” says Mr Lewis.

* Contact Trevor Lewis at trevorlewis2@medicaldeviceconsultancy.co.uk.
E-health: ethical and data privacy challenges in the EU

E-health is a relatively new area of medical technology, and there is a need for clearer EU regulations governing its use. Brian Kelly, an associate in the Life Science Practice of UK law firm Covington & Burling, considers the regulatory framework for e-health, with a focus on the ethical and data privacy challenges.

E-health covers the interaction between patients and healthcare providers, institution-to-institution transmission of data, or peer-to-peer communication between patients and/or health professionals through information and communication technologies. Examples include health information networks, electronic health records, telemedicine services, wearable and portable systems that communicate health portals, and many other software-based tools that help disease prevention, diagnosis, treatment, health monitoring and lifestyle management. E-health also enables health service providers from different EU member states to work more closely together. If a particular treatment can be provided to a patient more effectively in another country, e-health systems make it simpler to organise and carry out treatment abroad.

However, the wider deployment of e-health, in particular in telemedicine and telemonitoring, raises new ethical and regulatory concerns. The lack of a clear regulatory framework for e-health products and services coupled with the need to ensure patient health information remains private and secure needs to be addressed to build trust and confidence in e-health systems.

**Regulatory framework**

**Health and information society services**

Telemedicine is both a health service and an information society service. Health services are generally governed at the member state level. However, the EU electronic Commerce Directive 2000/31/EC (E-commerce Directive) provides the legal framework for information society services, which include any service normally provided for remuneration, at a distance, by electronic means and at the individual request of a recipient of services. 'At a distance' means that the service is provided without the parties being in the same place at the same time. Services that are carved out of the E-commerce Directive include medical examinations or treatment at a doctor’s surgery using electronic equipment where the patient is physically present; and services that are not provided via electronic processing/inventory systems, including a “telephone/telefax consultation of a doctor”.

**Medical devices**

E-health products used for a medical purpose may fall under the definition of a medical device under the Medical Device Directive 93/42/EEC, as amended (MDD). Medical devices include software, instruments and appliances, including software intended to be used specifically for diagnostic and/or therapeutic purposes, and software necessary for a device’s proper application in diagnosis, prevention, monitoring, treatment or alleviation of disease.

E-health products that could fall under this definition include wireless monitoring devices for recording blood pressure, picture archiving and communications systems, and devices for calculation of anatomical sites of the body.

The European Commission has historically viewed software used for administration of general patient data – medical records, bookings and appointments – as being outside the scope of the MDD. However, a number of national regulators have revisited the issue of the borderline area between software and medical devices following amendments to the MDD that came into force in March 2010 and placed greater emphasis on use of software.

**Data protection and confidentiality**

E-health products and services are most likely to involve the processing of patient health information. The processing of such sensitive personal information is governed at the EU level under the Data Protection Directive 95/46/EC, as amended (Data Protection Directive) and the E-Privacy Directive 2002/58/EC, as amended (E-Privacy Directive). These directives lay down specific requirements to safeguard an individual’s rights to privacy and to ensure that communications and networks are secure. Indeed, the recently adopted directive on patients’ rights in cross-border healthcare makes clear that providers of cross-border e-health must comply with the Data Protection Directive.

In addition, EU member states have their own laws, regulations and guidance governing the processing of health information. For example, the Department of Health in the UK requires all e-health operators working within or for the National Health Service (NHS) to comply with the Department of Health’s Confidentiality Code of Practice and Guidelines on Information Security, which can require higher standards than those under EU law.

These codes and guidelines make clear that telemedicine consultations, emails and pictures sent electronically are likely to form part of a patient’s medical record, which would trigger separate rules governing record retention.

**Restrictions and requirements under the Data Protection Directive**

E-health operators are expected to comply with member state laws implementing the Data Protection Directive (ie under the UK Data Protection Act 1998). The most notable obligations are as follows:
• Legitimate purpose: Identifiable health information may only be processed if at least one of several conditions appearing in Article 8 of the Data Protection Directive is satisfied. For example, processing is permitted if it is required for the purposes of preventive medicine, medical diagnosis, the provision of care or treatment or the management of healthcare services, and where those data are processed by a health professional bound under national rules to the obligation of professional secrecy. Processing may also take place if the patient has given explicit consent or if it is necessary to protect the vital interests of the patient (usually life or death situations).

• Notice: In addition to the above, patients should be given information about the following, among other things: (i) the purposes for which their health information will be processed (eg, for diagnosis); (ii) disclosures of information to third parties (eg, other healthcare professionals responsible for managing the patient); and (iii) any transfers of personal information outside the EU, particularly disclosures to operations in the US (eg, if the data are stored on a US server or are accessed by maintenance operators based in the US). This information is necessary to satisfy the requirement of fair and lawful processing under the Data Protection Directive.

• Purpose limitation: Personal and health information collected via e-health systems should only be processed for the purpose of providing the e-health services (or other related purposes disclosed to patients) and should not be processed for any other purpose not disclosed to patients using the service. In particular, health information should not be sold or commercialised in any way without first informing individuals of this use of their personal and health information and obtaining their prior consent.

• Access rights: Under the Data Protection Directive, individuals have the right to request a copy of any personal information processed about them, a principle embodied in the new cross-border healthcare directive.

• Security: The Data Protection Directive specifies that appropriate technical and organisational measures be taken against unauthorised or unlawful processing of personal data and to protect personal data against accidental or unlawful loss, damage or destruction. While imposing a general security requirement, the Data Protection Directive does not mandate particular security measures for data at rest or in transit. As noted above, however, different EU member states often have their own security requirements that must be complied with. In the transfer context, there is a strong preference for applying reliable encryption techniques to data transferred over electronic networks and pathways. Patients should be informed, however, that no method of transmitting or storing electronic data is ever completely secure. When transmitting data electronically, e-health operators should therefore apply the "postcard test", ie, if you are uncomfortable sending particular information by postcard then sending this same information by email could also be problematic.

• International Transfers: To the extent that personal or health information is transmitted or accessible to persons outside the European Economic Area (EEA), then e-health operators would need to comply with European restrictions on cross-border data transfers. This may entail the use of data transfer contracts executed between the operator and parties located outside the EEA or obtaining the unambiguous consent of the patient to transfer their data to such foreign jurisdictions. However, some EEA member states preclude the actual transfer of certain types of patient data (UK NHS electronic medical records, for instance) from outside their jurisdictions, making international hosting of patient data outside the EEA difficult in some cases. For example, according to the UK Department of Health, contracts let by the NHS Connecting for Health agency, which is responsible for delivering the UK national IT programme, preclude the transfer of patient information outside the UK.

• Notification: e-health operators generally would need to notify the regulatory authority where the operator is based of their processing of personal data to (so e-health providers in the UK that process personal data would need to file a notification with the UK Information Commissioner’s Office). It is possible that in some countries operators may benefit from an exemption.

**Doctor-patient relationship**

The increasing use of telemedicine as a replacement for physical face-to-face consultations is becoming more acceptable provided patients are offered a physical examination where appropriate and patient privacy is safeguarded as described above. Indeed, some member states require healthcare professionals to offer a physical where appropriate; for instance, section 15 of the UK National Health Service (General Medical Service Contracts) Regulations 2004 states that doctors must be contractually obliged to offer NHS patients a physical examination where appropriate.

However, the use of cross-border e-health services raises additional concerns. For example, professional medical and ethical standards are not harmonised at the EU level, meaning that a doctor in one member state may be practising at a different professional and ethical standard to a doctor in another member state. There are also concerns over patient access to redress if treatment goes wrong and the conflict of jurisdiction issues that flow from cross-border treatment. The newly-adopted directive on cross-border healthcare hopes to address some of these issues.

E-health has huge potential to improve patient care but there are a number of regulatory and ethical challenges that need to be dealt with to increase patient and user confidence in the technologies. One of the fundamental challenges is ensuring that patient data remain confidential and secure. The Data Protection Directive provides a binding EU framework to safeguard patient privacy, and e-health operators should systematically assess the data privacy aspects whenever e-health services are provided. However, e-health operators need to be mindful of and compliant with national laws and regulations governing the specific processing of patient health information, which can require higher standards.

*Brian Kelly can be contacted at bkelly@cov.com*
Immunoassays has historically been one of the more rapidly-growing segments of the clinical diagnostics market. The sector expanded in 2009 in spite of the economic downturn and achieved significantly higher growth in 2010, and continues to represent an attractive market opportunity for suppliers.

The market includes a number of subsegments, including thyroid testing, infectious disease diagnostics, point-of-care (POC) rapid tests (mainly for infectious diseases and pregnancy), blood screening, tumour markers, fertility testing, drugs of abuse testing, serum protein analysis, anaemia testing, allergy testing, cardiac markers, therapeutic drug monitoring, and other tests including bone disease markers, cytokine tests, autoimmune disease testing, and other specialised immunassays.

High-growth subsegments include cardiac markers, infectious disease diagnostics, and tests for serum proteins and tumour markers. Low-growth subsegments include drugs of abuse testing, blood screening, allergy testing, and therapeutic drug monitoring. The market is continuing to expand due to the introduction of new tests, a recent example being the rapid adoption of certain new cardiac markers such as B-type natriuretic peptide (BNP) and troponin assays, as well as increased utilisation of tests such as those for vitamin D. New tests have not replaced older ones in most cases, either because the new test provides clinical information that was not previously available, or because clinicians tend to continue to use older tests even though newer ones may provide equivalent information.

Another important trend in immunodiagnostics is the consolidation of immunochemistry and chemistry testing on integrated system platforms. New applications under development within the immunodiagnostics segment include markers for stroke diagnosis and risk assessment, new tumour markers including pro-prostate-specific antigen (PSA) for prostate cancer and markers for breast cancer, advanced cardiac tests providing earlier detection of infarction, advanced risk markers for coronary artery disease, tests for sepsis and organ damage (eg, renal injury resulting from chemotherapy), and new POC infectious disease tests such as rapid HIV assays.

New immunodiagnostic products are also emerging, primarily as reference lab tests for use alongside targeted drugs to identify patients who express the drug’s target. The emerging field of proteomics promises to help further expand test menus in immunodiagnostics, perhaps based on multi-marker assay technology. However, some applications that may have been targets for immunoassay technology in the past are now being performed using molecular diagnostic techniques, which can, at least in some cases, provide more definitive clinical information than immunassays. In addition, technologies such as gas chromatography-mass spectrometry, which have historically been used primarily in life science research, are increasingly being employed for clinical testing in areas such as proteomics. These are technologically superior for analysing large panels of markers compared with immunassays.

Other products in the immuno-diagnostics segment include a number of general purpose open immunoassay analysers employing microplate enzyme-linked immunosorbent assay (ELISA) formats that are popular in Europe, as well as specialised microplate systems used in blood screening. There are also a very large number of rapid, non-instrumented tests, as well as a growing number of instrumented POC immunoassay systems. The latter can be used in a range of alternate site settings including the hospital bedside, the emergency room, the physician’s office and, increasingly, for self and home testing. Alere, formerly known as Inverness Medical, is now the fourth-largest supplier of immunodiagnostic products worldwide, with a wide array of manual and instrumented POC immunoassay tests. The firm had around a 10% share of the global immunodiagnostic products market in 2010.

Immunodiagnostic products

The immunodiagnostics segment covers a wide range of products for use in various settings including small laboratories, larger reference labs, and core labs for applications such as drugs of abuse testing, blood screening, and hormone testing. A key trend in the segment is the movement of testing to integrated chemistry/immunochemistry platforms as advances in technology have allowed a wide range of immunoassays to be performed on high-volume integrated
systems. Such systems provide significant benefit for users by eliminating the need to split samples to perform immunochemistry and chemistry tests, reducing labour requirements as well as the number of errors in sample processing. Speciality immunodiagnostic systems for applications such as protein analysis and allergy testing also comprise a significant segment of the market, as do systems for transfusion testing (screening of blood and blood products for infectious agents).

**General purpose systems**

These include stand-alone random access analysers as well as integrated chemistry/immunochemistry systems. The range of available products in the stand-alone analyser category has not undergone significant changes over the past five years, as suppliers have focused on developing integrated platforms and analysers capable of being interfaced in such platforms. The newest systems such as Roche’s COBAS e601 provide high sensitivity using assay technologies including electrochemiluminescence and magnetic particle separation to perform assays such as third-generation thyroid-stimulating hormone (TSH) tests, troponin and PSA, combined with high throughput of over 170 tests per hour.

Chemiluminescence detection is now the most widely used technology in immunodiagnostics because of its inherent sensitivity and rapid test turnaround time. Many systems, including Roche’s COBAS e601, Beckman Coulter’s UniCel, and Abbott’s c8200, employ magnetic particles to accomplish the separation step required in heterogeneous immunoassays. Heterogeneous techniques use a wash step to eliminate interfering substances, and typically provide higher sensitivity than homogeneous techniques.

Increasing test throughput is another trend in the immunodiagnostics segment, with some systems offering throughputs of up to 400 tests per hour. Another approach to handling higher-volume testing now being offered by a number of suppliers is to link multiple systems together in a workstation configuration, with up to four systems combined in one island of automation.

Some of the most successful products in the general purpose immunochemistry segment include Abbott’s AxSYM, Beckman’s Access, Bayer’s ADVIA Centaur, Siemens’ Immulite, Roche’s Elecsys, and bioMérieux’s Vidas.

Another characteristic of the general purpose immunodiagnostics segment is the increasing importance of certain high-value tests. An increasingly large proportion of the market is becoming attributable to only a few key tests such as PSA/free PSA, cardiac troponin, TSH, and BNP. These provide information that directly impacts patient management. New tests under development that are expected to drive growth in the market include stroke markers, new tumour markers, tests for earlier detection of acute coronary events, and tests used in the management of major chronic diseases such as heart failure, diabetes, and neurological disorders. In addition, there is continued growth in the infectious disease testing segment, as emerging infectious diseases continue to drive requirements for new tests.

**Speciality systems**

Speciality immunodiagnostic systems include products designed for allergy testing or protein analysis, or POC tests for analytes such as cardiac markers and the pregnancy marker beta human chorionic gonadotropin (hCG), and drugs of abuse. Examples of products in this category include Beckman Coulter’s IMMAGE, Dade Behring’s BN systems, and Pharmacia’s ImmunoCAP allergy testing system.

This segment is experiencing some erosion after the introduction of higher-volume, general purpose immunodiagnostic analysers that include assays such as protein, drugs of abuse, and allergy tests on their menu. Labs can in some cases eliminate workstations by transitioning to an integrated platform offering speciality tests alongside general purpose immunoassays. While in the past, speciality tests on general purpose platforms did not achieve equivalent performance because of technological limitations, newer general purpose systems have removed that barrier. For example, Siemens enhanced the capabilities of its general purpose Immulite analyser to allow allergy tests to be performed on that platform as opposed to its microplate allergy testing system, and has seen a continued increase in the percentage of sales attributable to its general purpose analysers.

However, other product groups within the speciality immunoassay category, notably dedicated systems for cardiac marker testing and tests such as beta-hCG that are used in POC settings, are experiencing rapid growth, offsetting the erosion within this segment and resulting in overall growth equivalent to that in the general purpose segment.

**Immunoassay-based blood screening systems**

The market for blood screening systems using immunoassay technologies is continuing to grow due to the addition of new analytes to the panel of screening tests. Examples of systems in this category include Abbott’s Prism and Commander, and Ortho’s Summit.

A related segment of the market, not included in the market figures for the immunoassay segment presented in this report, is made up of automated systems for blood typing. Products in this category for use in the hospital setting include the Ortho ProVue and Immucor’s Galileo, Galileo Echo and Neo.

Analysers in the blood screening segment are designed to perform high-volume testing, typically in a batch mode since there is not a requirement for stat testing in the blood bank and the panel of tests performed is well-defined. A typical screening panel includes tests for antibodies to HIV-1/2, human T-cell leukaemia virus, hepatitis C virus, hepatitis B surface antigen and core antigen, and tests for the parasite *Trypanosoma cruzi*, the causative agent of Chagas disease. Regulatory bodies such as the US FDA typically specify which tests must be performed on donated blood. As a result, the market is relatively stable unless the required test panel is changed, such as when a new infectious agent emerges that can be transmitted by blood transfusion (eg, *T cruzi*).

Recent trends include increasing levels of automation as the blood product testing segment becomes more consolidated, and the implementation of increasingly rigorous requirements for preventing specimen identification errors and ensuring
that proper quality control procedures are followed. One consequence of the increased focus on error prevention is the emergence of a growing market for informatics products in the blood bank, to ensure compliance with regulations and to automate documentation of the testing process.

Blood screening tests are highly regulated in most countries and must pass the most stringent regulatory approval process in order to be marketed. As a result, only three companies now dominate the segment. For blood typing, the requirements are somewhat different, since testing must be performed prior to giving blood or blood products to a patient to ensure that the correct blood type is transfused. Blood typing was one of the last areas of the clinical lab to become automated, since the test was usually read visually and required a high degree of technician expertise to ensure reliable results. However, Immucor succeeded in obtaining FDA approval for its automated blood typing system in the late 1990s, and has now been joined in the market by Ortho. Blood banks are now beginning to adopt automated blood typing systems due to labour shortages and continued increases in documentation requirements. Sales for Immucor, the leading supplier of automated blood typing systems, more than doubled from 2005 to 2009.

A major new development in the blood screening market is the emergence of nucleic acid testing to screen for infectious agents. Conventional immunoassay testing relies upon the donor developing an antibody response to an infectious agent such as hepatitis or HIV-1/2, creating a window during which the test will be falsely negative for newly-infected donors. Nucleic acid testing using target amplification technology allows direct detection of the virus, eliminating the need for antibodies to be generated in order to produce a positive result. Most of the blood supply in developed countries is now screened using nucleic acid testing in addition to the continued use of immunoassay-based screening. As a result of the high added cost to blood banks, and strong pressure from hospitals to avoid increases in the cost of blood products, prices for immunoassay products used in blood screening are expected to experience continued pressure. In addition, the number of blood donations has remained essentially flat over the past few years, limiting growth in the market.

**Market segmentation**

The global immunodiagnostics market totalled $12bn in 2010. The largest subsegment is the market for general purpose immunoassay systems, totalling $8.5bn including reagents, consumables, equipment and service in 2010. This segment includes both stand-alone immunoassay analysers as well as immunoassay tests performed on integrated chemistry/immunochemistry systems. The segment is forecast to grow at 7.4% per year on average over the 2010-2015 period. Factors responsible for growth in the general-purpose segment include the continued trend for speciality immunoassay tests to be converted to general-purpose testing platforms, strong growth in tests such as those for cardiac markers and infectious diseases, which are performed on general-purpose systems, and growth in the adoption of integrated chemistry/routine immunochemistry testing platforms.

The speciality immunoassay segment was estimated at $660m for 2010, making it the smallest segment. Growth is forecast at 6.9% per year over the 2010-2015 period, and will be driven by increases in test volume coupled with moderate pricing increases. Certain speciality tests such as high-sensitivity C-reactive protein assays and microalbumin assays are also expected to experience growth.

The blood screening segment totalled $1.153bn worldwide in 2010. Growth over the 2010-2015 period is forecast to average 2.2%, due to pricing pressures and an essentially stable level of blood donations. Some increases in volume may occur due to the addition of new analytes to the test menu, although most new screening tests for blood products (eg, a new screening test for West Nile virus) are implemented as nucleic acid tests rather than immunoassays. The implementation of nucleic acid testing has not, at least so far, resulted in a significant decline in immunoassay-based blood screening, in part because nucleic acid testing is only being performed for HIV and hepatitis C virus, and immunoassay tests for hepatitis B must still be performed. There was an impact on immunoassay-based screening when blood banks dropped HIV p24 antigen testing upon implementation of nucleic acid HIV testing, but that has been offset by the addition of new analytes to the screening menu such as T. cruzi.

The immunodiagnostics segment remains one of the most attractive of the clinical diagnostics market, particularly when the potential opportunities for certain new tests such as cardiac markers and tumour markers are considered. Overall growth is expected to be approximately the same as for the total clinical diagnostics market, but significant potential exists for market expansion as new tests such as stroke markers, sepsis markers, and markers for neurological disorders are introduced. The market for BNP alone, which now totals well over $200m, could easily reach $500m worldwide within the next five to seven years, and early markers for myocardial infarction may have a similar potential. Tests that represent significant areas of growth opportunity include:

- cardiovascular disease tests such as early markers of myocardial infarction, early markers of thrombosis, and stroke markers;
- risk assessment markers for cardiovascular disease (for testing of asymptomatic individuals) such as markers for vulnerable plaque;
- tumour markers for cancers such as breast, lung, and colorectal cancer;
- tests for neurological disorders; and
- tests for monitoring patient response to new drugs that target specific molecular entities, such as proteomic tests.

Innovations for improved internal wound healing and noninvasive diagnostic for pseudo-dementia disorder

This edition of Patent Watch looks at the most interesting medtech patent applications in January-February. They include cell-enhanced hernia/incision repair, a new method for diagnosing and monitoring a neurological condition often confused with dementia, and a radiation treated device to improve blood vessel wall healing. By Phil Greenfield

Electromedical and diagnostics

Normal pressure hydrocephalus (NPH) is a relatively unknown disease that is often mistakenly diagnosed as dementia, Alzheimer’s or Parkinson’s. This is because the symptoms, including disturbances in gait, confusion and urinary incontinence, are similar to those of dementia, plus the fact that NPH is a condition that mainly occurs in people over the age of 55. Studies have shown that up to 10% of dementia patients may actually be suffering from NPH. The condition is many times referred to as reversible or treatable dementia.

Diagnosis of NPH is usually first led by a lumbar puncture, followed by the evaluation of clinical response to removal of CSF. This can be followed by a CT, MRI, and continuous external lumbar CSF drainage for three or four days. Treatment is usually a shunt implant that diverts and regulates CSF pressure and flow, and often results in complete recovery.

WO2011003909 describes a non-invasive automated method which measures and regulates pressure and flow in the spinal canal in order to characterize individual patients’ cerebrospinal fluid dynamics to help diagnose NPH, and monitor the effectiveness of shunt treatment. The method comprises a disposable tube-set plate with computer-regulated solenoid pinch valves to control flow pressure and small pressure sensors allow for fully automatic control of the system.

Inventor Likvor is an Umeå, Sweden-based company which has developed an instrument to be used in neurological investigations. The CE-marked CELDA Instrument is the result of over 30 years of research at Umeå University and Umeå University Hospital assessing cerebrospinal fluid dynamics.

<table>
<thead>
<tr>
<th>Number and priority date</th>
<th>Title</th>
<th>Assignee</th>
<th>Description/application</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO2011022418 17 August 2009</td>
<td>Distributed external and internal wireless sensor systems for characterization of surface and subsurface biomedical structure and condition</td>
<td>The Regents of The University of California (US)</td>
<td>Systems and methods are disclosed that use wireless coupling of energy for operation of both external and internal devices, including external sensor arrays and implantable devices. The signals conveyed may be electronic, optical, acoustic, biomechanical, and others to provide in situ sensing and monitoring of internal anatomes and implants using a wireless, biocompatible electromagnetic powered sensor systems.</td>
</tr>
<tr>
<td>WO2011016712 4 August 2009</td>
<td>Vascular risk prediction using non-invasive optical technology</td>
<td>Universiti Kebangsaan Malaysia</td>
<td>A new method in vascular health assessment based on age and a non-invasively, optical biological signal aimed at vascular risk prediction. The invention employs photoplethysmogram (PPG) recording systems to record the PPG from a finger of a subject, using a finger sensor.</td>
</tr>
<tr>
<td>WO2011016035 3 August 2009</td>
<td>Electromagnetic sensor for use in measurements on a subject</td>
<td>Dune Medical Devices (Israel)</td>
<td>A sensor unit for tissue characterisation, which includes a near field electromagnetic sensor and a flexible signal transmission structure.</td>
</tr>
<tr>
<td>WO201109085 17 July 2009</td>
<td>Method and apparatus for assessment of sleep disorders</td>
<td>Oregon Health &amp; Science University (US)</td>
<td>Methods and apparatus for monitoring sleep in a home environment. Load cells placed under bed supports are coupled to a computing device that can process the load cell data to detect disordered breathing. A pattern recognition algorithm distinguishes between normal movements and movements associated with a sleep disorder.</td>
</tr>
<tr>
<td>WO2011003909 6 July 2009</td>
<td>Device and method for measuring and regulating cerebrospinal fluid parameters</td>
<td>Likvor (Sweden)</td>
<td>A method and device for measuring and regulating pressure and flow in the spinal canal, in order to characterise individual patient’s cerebrospinal fluid dynamics.</td>
</tr>
</tbody>
</table>
Orthopaedics

WO2011008150, filed by Sweden's Artimplant is an extension of the patents covering its Artelon technology, a biomaterial based on a polyurethane urea, which is used for reconstructing musculoskeletal tissue. The new patent application covers applications including tendon, fascia, periosteum, ligament and muscle reconstruction. The Artelon range is a degradable line of biomaterials that can be used as a scaffold for tissue growth and provide temporary support for healing tissue. Artimplant claims that the spacers can be used to treat osteoarthritis in the hands, feet and shoulders, and for other soft tissue injuries. The company has a non-exclusive agreement with US-based Small Bone Innovations. Artimplant’s strategy has been focused on marketing and its own sales force in the US, where it has recently employed more product specialists. Artimplant implemented staff cutbacks in Sweden during the autumn of 2010 equivalent to an annual saving of approximately SEK5m ($0.8m). 2010 sales were SEK18.5m and the company posted a loss of SEK22.4m. Artimplant’s recent rights issue was subscribed up to 189% and generated capital input for the company of SEK38.5m before issue costs.

WO2011005184 is one of a series of 15 worldwide patent applications for a new hip joint replacement from inventor Peter Forsell, under Milux Holdings. The device is claimed to reduce the risk of the hip joint dislocating when in use through a new design in which the femur head is retained in the medical device using clasps. Over the last 18 months, Milux has been filing patents for a wide range of medical devices and has been applying for trademarks such as Cardiacmaster, Arthromaster and Aneurysmmaster. Very little else is known about the company, but it appears Dr Forsell was previously involved with Obtech Medical, the Swiss company that marketed the Swedish Adjustable Gastric Band (SAGB), and which was acquired by Ethicon in 2002.

<table>
<thead>
<tr>
<th>Number and priority date</th>
<th>Title</th>
<th>Assignee</th>
<th>Description/application</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO2011022560 19 August 2009</td>
<td>Porous implant structures</td>
<td>Smith &amp; Nephew (US)</td>
<td>Porous biocompatible structures suitable for use as medical implants and methods for fabricating such structures. The structures may be fabricated using rapid manufacturing techniques. The struts and nodes can form cells which can be fused or sintered to at least one other cell to form a continuous reticulated structure for improved strength while providing the porosity needed for tissue and cell in-growth.</td>
</tr>
<tr>
<td>WO2011002511 30 June 2009</td>
<td>Multi-phasic implant device for the repair or replacement of cartilage tissue</td>
<td>Kensey Nash (US)</td>
<td>Tissue implants prepared for the repair of tissues, especially avascular tissues such as cartilage. An electric potential is applied capable of receiving and accumulating desirable factors or molecules from surrounding fluid when exposed to dynamic loading. The implant promotes tissue conduction and can be formed into a multi-phasic device that provides deep tissue mechanical stimulus by conduction of mechanical and fluid forces experienced at the surface of the implant.</td>
</tr>
<tr>
<td>WO2011008150 16 July 2009</td>
<td>Implant for soft tissue reconstruction</td>
<td>Artimplant (Sweden)</td>
<td>Implant for reconstructing tissue of the musculo-skeletal apparatus selected by the group consisting of tendon, fascia, periosteum, ligament, muscle, includes a porous matrix or scaffold of polymeric material having a tensile stiffness lower by 50 % or more than the tensile stiffness of the native tissue it is intended to reconstruct.</td>
</tr>
<tr>
<td>WO2011005933 10 July 2009</td>
<td>Devices and methods for tissue engineering</td>
<td>Bio2 Technologies (US)</td>
<td>A resorbable tissue scaffold fabricated from bioactive glass fibre, which forms a rigid three-dimensional porous matrix. The resorbable tissue scaffold supports tissue in-growth to provide osteoconductivity as a resorbable tissue scaffold, used for the repair of damaged and/or diseased bone tissue.</td>
</tr>
<tr>
<td>WO2011005184 10 July 2009 (one of 15 patents filed for this device)</td>
<td>Hip joint device</td>
<td>Milux Holding (Luxembourg)</td>
<td>A medical device for implantation in a hip joint, which is adapted to be fixated to the pelvic bone of the patient. The medical device is adapted to receive a caput femur (femur head) or its prosthetic replacement, and the device comprises at least one extending portion that clasps the spherical portion of the caput femur, such that said it is restrained in the medical device. Restraining the caput femur in the medical device reduces the risk that the hip joint dislocates when in use by the patient.</td>
</tr>
<tr>
<td>WO2011003002 2 July 2009</td>
<td>Systems and methods for zipknot ACL fixation</td>
<td>Medicinolodge (US)</td>
<td>A system and method for securing an ACL graft, which uses a “zipknot” fastener for faster, mlore durable suturing. The device comprises a line routed through a plate, the plate comprising an elongated body and a “dogbone” feature on one end. The line is routed to create a one-way slide so no knots are required, and comprises an adjustable loop that receives the graft.</td>
</tr>
</tbody>
</table>
Surgery

Repair of abdominal wall incisions not amenable to primary suture closure is sometimes performed using a synthetic mesh (such as polypropylene, prolene, polytetrafluoroethylene meshes) to reinforce the fascia and restore the abdominal wall. However, incision closure and treatment of abdominal wall defects remain difficult, particularly due to the complications resulting from synthetic mesh use. These complications include enteric fistulae formation and infection, which weaken the integrity of the incision closure.

WO2011002962 provides methods and devices for improved closure of surgical incisions and/or repair of abdominal wall defects, using an implantable device incorporating LifeCell’s (Branchburg, New Jersey) AlloDerm or Strattice Reconstructive Tissue Matrix, supports tissue regeneration by allowing rapid revascularisation, cell repopulation and white cell migration.

<table>
<thead>
<tr>
<th>Number and priority date</th>
<th>Title</th>
<th>Assignee</th>
<th>Description/application</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO2011022672 20 August 2009</td>
<td>Ultrasound-assisted gene transfer to salivary glands</td>
<td>Allegheny-Singer Research Institute (US)</td>
<td>Methods and compositions for delivery of genetic material (eg viral vectors) to salivary glands using ultrasound and polymer/lipid or gas microbubbles are described.</td>
</tr>
<tr>
<td>WO2011011234 23 July 2009</td>
<td>Endoscopic imaging system</td>
<td>Smith &amp; Nephew (US)</td>
<td>A cable-free hand-held endoscopic imaging system, designed to increase a surgeon’s ability to move, rotate, and aim the endoscope of an endoscopic imaging system during a procedure. The system includes an endoscope, a light source to transmit light through illumination channels in the endoscope, and an imaging unit to receive images of a region of interest that are formed at a tip of the endoscope that is inserted into the region. The components of the system are freely attachable and detachable from each other.</td>
</tr>
<tr>
<td>WO2011010229 20 July 2009</td>
<td>Surgical device</td>
<td>Adelman Research (Seychelles)</td>
<td>A minimally invasive surgical device for operations on the vertebrae, such as laminectomy, laminotomy, or laminoplasty, which is designed to reduce operation times and speed up patient recovery. The device comprises a cannula surrounding at least one lumen extending outside a patient’s body, to a tissue tip which is configured to be inserted into the patient and to rest over or against the treatment area. The tissue tip may be configured in different shapes to fit on to the tissue being treated. The edges of the tissue tip rest on the tissue adjacent to the area being treated. Surgical instruments, or implantable medical devices, can be received and guided by the lumen of the cannula.</td>
</tr>
<tr>
<td>WO2011002962 2 July 2009</td>
<td>Device and method for treatment of incision or hernia</td>
<td>Lifecell (US)</td>
<td>A device for treating an incision, hernia, or abdominal wall defect, comprising an elongated element and at least one sheet of porous biocompatible matrix.</td>
</tr>
<tr>
<td>WO2011022073 19 August 2009</td>
<td>Systems, methods, and devices for facilitating access to target anatomical sites or environments</td>
<td>Mirador Biomedical (US)</td>
<td>Methods and devices for detecting and facilitating positioning of a probe in a vascular tissue of a patient, such as a patient’s vein for central line or catheter placement. The device comprises a housing with a distal portion first port, which can be coupled to a probe and a proximal portion; and a sensing unit, a processing unit, and an output unit carried by the housing. The output unit is configured to output a reporting signal based on the determined physiologic parameter value such as pressure.</td>
</tr>
</tbody>
</table>

Cardiovascular and peripheral vascular

WO2011017031, from the University of California, describes a method of generating a “pro-healing” endovascular device, capable of speeding up the rate of endothelialisation following implant, and therefore prolonging the life of the implant. The invention describes irradiating a surface of the endovascular device with a high energy radiation (such as UV radiation) for a period of time to cause the surface to become a hydrophilic or super hydrophilic surface. A faster rate of endothelialisation and/or neointima coverage would enable blood-thinning medications to be withdrawn more quickly, and reduce the risk of spontaneous bleeding in organs such as brain and gastrointestinal tract. The device of the invention has been shown to increase the rate of endothelialisation as compared with an endovascular device without treatment by irradiation, for example, increased by 10%.
<table>
<thead>
<tr>
<th>Number and priority date</th>
<th>Title</th>
<th>Assignee</th>
<th>Description/application</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO2011017123 27 July 2009</td>
<td>Stent graft</td>
<td>Endologix (US)</td>
<td>A two-part endoluminal vascular prostheses and methods of placing the prostheses in the treatment of Type II endoleaks following aortic aneurysm and dissection treatments.</td>
</tr>
<tr>
<td>WO2011017031 27 July 2009</td>
<td>Prohealing endovascular devices</td>
<td>The Regents of The University of California (US)</td>
<td>A prohealing endovascular device, comprising a surface generated by a method comprising irradiating a surface of the endovascular device with a high energy radiation for a period of time to cause the surface to become a super hydrophilic surface. The high energy radiation can be any high energy radiation. In some embodiments, the high energy radiation is ultraviolet.</td>
</tr>
<tr>
<td>WO2011019401 12 August 2009</td>
<td>Cell coated implantable device</td>
<td>Duke University (UK)</td>
<td>A cell-coated implantable medical device where the blood-contacting surfaces are coated with endothelial progenitor cells (EPCs). Immune rejection can be avoided by using EPCs derived from a patient’s own blood.</td>
</tr>
<tr>
<td>WO2011019582 14 August 2009</td>
<td>Low profile prosthesis</td>
<td>Medtronic Vascular (US)</td>
<td>Enhancements to prostheses with a bare spring or crown stent structure, which improve attachment constructions with grafts or covered stents.</td>
</tr>
<tr>
<td>WO2011017103 27 July 2009</td>
<td>Dual endovascular filter and methods of use</td>
<td>Claret Medical (US)</td>
<td>An embolic filter device to capture and remove the emboli from the body.</td>
</tr>
</tbody>
</table>

Knowledge just got powerful

Get on-demand access to the latest devices and diagnostics research

We know you need to make intelligent decisions swiftly. That’s why we’ve developed a new home for Business Insights where you can get instant and unlimited access to strategic insights and reports on the medical devices and diagnostics industries.

Sign up for a free demo now at business-insights.com/about-interactive or call +44 207 551 9888
Philips to unveil Guardian for wireless hospital monitoring

Philips is to launch its new Guardian software, designed to simplify wireless patient monitoring in hospitals, this year. The firm’s marketing director for general care, Andreas Bindszus, spoke to Madeleine Armstrong about the advantages of the system, which automatically alerts clinicians when patients show signs of deterioration.

Around 40% of unexpected deaths in hospitalised patients occur in general wards. This is somewhat surprising as many of these patients are no longer acutely ill; they have been transferred to these wards from intensive care or emergency units because the obvious danger has passed.

A significant proportion of these deaths result from deterioration in the patient’s health that is not detected in time or dealt with appropriately. Many patients show recognisable signs in the hours before serious events like a cardiac arrest, such as impaired respiratory function, that could easily be identified, but they are missed.

One reason that hospitals fail to pick up on these signs is that the frequency of monitoring decreases once patients leave the intensive care unit. Even when vital signs are recorded and nurses notice that patients are deteriorating, they are often not trained or empowered to act on their observations.

Hospitals have tried to address the problem by creating rapid response teams: groups of specialised caregivers that respond swiftly when nurses notice possible signs of an impending serious adverse event and raise the alarm.

But this has raised issues of its own. "Clinicians typically don’t like to ask other clinicians for help," Andreas Bindszus, Philips’ marketing director, told Clínica. "So even if these teams are available, they don’t always get the calls." One reason for this is fear of getting it wrong. "If a nurse calls a doctor at night, there is always the worry that it may not have been necessary," he explained.

Philips aims to remove this uncertainty with an early warning system, known as modified early warning scoring (MEWS). Vital signs are monitored using the firm’s IntelliVue MP5 device, which has been CE marked for sale in Europe since 2006, and has included spot-checking capabilities since 2009. The monitor automatically compares the patient’s readings with a predefined set of values that are set by each hospital. It then calculates a score that indicates the patient’s status — for example, a score of 6 or more means the patient needs urgent attention, while a score of less than 2 means they fall into the normal range, and should continue to be monitored every few hours.

This has made the system less subjective for nurses, giving them clear guidelines about when to alert their colleagues about particular patients. "It could still be wrong, but the blame is no longer on the nurse, and that takes the fear away from these caregivers, allowing them to call for assistance," Mr Bindszus said.

### Wireless monitoring

Although this is an improvement over existing patient monitoring technology, the eventual aim is continuous monitoring of all patients in the hospital. This presents its own challenges because, unlike patients in the intensive care unit, those in the general ward can move around more easily, so cannot be hooked up to monitors.

Philips has therefore developed cableless sensors, which it launched in Europe in September and in the US in October 2010. The products received 510(k) clearance from the US FDA in August 2010, and are also CE marked.

One measures oxygen saturation and resembles a wristwatch, while the other measures blood pressure and is placed around the patient’s arm. "It’s like a traditional blood pressure cuff, but the difference is that it has the embedded electronics and the pump…to work as a self-standing device," Mr Bindszus explained.

This could expand the number of patients being monitored in the general ward, he hopes. "The typical general ward currently has about one monitor for every 10 patients. This is brought to patients to take a single measurement for each one every couple of hours, and that’s it. But we believe our cableless monitors will encourage clinicians to think about monitoring patients that they wouldn’t otherwise have been monitoring, because they don’t want to tangle them up in wires."

"We will be able to put the cableless monitors on patients who can stay mobile, walk around, meet their families. We’re talking about patients who are almost ready to go home, they’re not critically ill any more, but they’re still in the hospital for observation, and some of them still crash – and that often goes unnoticed, unless you have a monitor on the patient."

Currently, the sensors transmit their readings to the MP5 spot-check monitor, but Philips eventually hopes to bypass the device entirely, linking the cableless monitors directly to its new software system, Guardian. Launch is slated for mid-2011 in markets that have already embraced the concept of rapid response teams. "[By then] Guardian will have all the regulatory approvals necessary to launch it worldwide, but some markets are not there yet," Mr Bindszus said. "The idea of putting monitoring into a general floor depends very much on the individual countries. The UK, Australia, the US, the Netherlands and the Scandinavian countries have all started to implement rapid response systems, and could therefore use Guardian."

### Multi-purpose

The software serves three purposes, he explained: "The first is gathering the data that comes from the sensors. The cableless sensors do their job with only a tiny..."
auxiliary display, so clinicians can’t see the patients’ readings the way they do with traditional monitors. These vital signs will be transmitted to a central location, and that can be any PC running the Guardian software, for instance a PC in the nurses’ station.

“Number two, these devices are so small that they don’t have a real user interface. So if you want to change the settings, or change the repetition rate for blood pressure for example, it’s not very convenient to do this on the device itself. The Guardian software runs on a PC, and you can use it to change all the settings of the sensors.

“Guardian will also run the same early warning scoring mechanisms as the spot-check monitor,” Mr Bindszus continued. “The difference is that you don’t need a monitor with a patient anymore, now you can do this in a central location. And we don’t need a person sitting in front of the computer, monitoring patients’ data. For each patient the software builds up a record and looks at trends in their data, and identifies those patients who are deteriorating and going into a more critical situation. If it sees early indications of a patient going south, then it generates a warning that automatically goes to the pager of the nurse in charge of the patient that day.

“Because it’s an early warning system, that nurse has enough time to respond within the next half hour or so, and do some additional assessments that cannot be done with the wireless sensor, for example assessing the patient’s level of consciousness.”

The final purpose of Guardian is to connect with and feed the electronic records of patients’ data. “Not every institution has this, but those which do already enter everything into this electronic data record,” Mr Bindszus said. “And they absolutely want to make sure everything’s entered automatically into their master record, they don’t want a double entry. Guardian interfaces into the existing hospital information systems, using the same language that these systems speak, which is called HL7.”

The price of the system will vary depending on the number of patients being monitored and how easily the software can be integrated into existing hospital systems, he added. “The solutions we have calculated so far for some typical small- to large-site installations are around $7-18 per patient per day over three years, including sensor supplies over this period.”

“When asked how hospitals could justify the extra expense in the current economic climate, he replied: “We expect the system to increase quality of care and patient satisfaction. Both cannot really be measured in euros or dollars, but in terms of quality and satisfaction, both key metrics for hospitals today.”

“We expect that our system will reduce the average length of hospital stay”

“We also expect that our system will reduce the average length of hospital stay and the number of unplanned admissions to the intensive care unit, since it will reduce complications caused by a late response to a patient in trouble,” Mr Bindszus continued. “It is not so much that the cost of care per patient per day can be saved by reducing length of stay, but that this could increase bed capacity and throughput due to reduced use of ICU beds and shorter patient stays. This will increase hospital revenues without additional investment in space, beds and human resources.”

He is confident that this will save hospitals money in the long term: “That is where we expect the return on investment to come from, and we will carry out health economic studies to prove this.”

These are the first steps for Philips, but it is planning to expand its wireless monitoring capabilities. The sensors themselves will become even smaller over time, and the firm also aims to expand the parameters it can monitor wirelessly.

“Oxygen saturation and blood pressure are the first two clinical parameters that come to mind when you think of patient monitoring,” Mr Bindszus said. “But respiration is even more important. We have no appropriate technology to monitor respiration wirelessly now, and that is another area of research.

“Also, for the first time, we have enabled physicians on the general floor to put monitors on more patients,” he continued. “And this could lead to a number of false alarms – ideally not too many, but we already foresee that the next area of improvement will be to reduce this.”

As for its competitors, Mr Bindszus believes that Philips is way ahead. “More and more companies are addressing general wards, and recognising that there is more need for monitoring here, but they are approaching it from different angles,” he said.

“For example, some companies have solutions that just do pulse oximetry, while others have monitors that are mounted inside hospital beds. But with that approach, as soon as the patient leaves the bed, they’re not being monitored. There’s also a problem with bed management – these beds can go anywhere in the hospital, they don’t belong to a certain department.

Pulse oximetry involves measuring oxygen saturation of a patient’s blood noninvasively through the skin, for example via sensors placed on the finger or earlobe. Pulse oximeters employ two LEDs producing red or infrared light, which are absorbed to different degrees by oxygenated and deoxygenated haemoglobin (oxygenated haemoglobin absorbs infrared light and allows red light to pass through, while deoxygenated haemoglobin does the opposite). This allows pulse oximeters to calculate the level of oxygen saturation, by comparing the ratio of red to infrared light. Players in this market include Covidien, the industry leader with its Nellcor OxiMax devices, and Masimo, with its Rainbow SET technology.

“We think that Philips is in a unique position to bring everything together, because we have all the experience from patient monitoring, telemetry monitoring, running algorithms to look at vital signs and their combinations and trends, and the things that are hidden in these trends,” he said.

“I think what’s important about the Guardian solution is that it’s not isolated,” he concluded. “The software is the core, but it needs all the additional input: the measurements; the interaction with the nurses; the connection with the hospital information system. That’s important – it’s a pretty holistic solution.”
Cancer molecular diagnostics specialist Agendia has appointed David Macdonald chief operating officer. The company has also hired Mark Willig as executive vice-president of North American sales and Doug Bradley as vice-president of global marketing. Mr Macdonald has been working with Agendia for the past eight months in a consulting role; in his new position he will be responsible for lab operations, R&D, product support, IT and US human resources. Mr Macdonald has also worked for Quest Diagnostics, Nova Biomedical and AltheaDx. Mr Willig, who will oversee all sales activity in North America, has previously worked for microRNA specialist Exiqon and Thermo Fisher. Mr Bradley will manage all strategic and tactical marketing activities, and has experience at companies including Coherent Medical, Allergan and SenoRx. Agendia’s lead product, MammaPrint, analyses 70 genes to predict breast cancer recurrence.

Orthopaedic firm Orthofix International has promoted Brian McCollum to the post of chief financial officer. Mr McCollum has worked for the company for almost 10 years, and has been serving as interim CFO since January. Before joining Lewisville, Texas-based Orthofix, Mr McCollum was a senior audit associate with PriceWaterhouseCoopers. Last month, Orthofix reported a 3% increase in revenues for 2010, to $564.4m. Full-year net income was also up 31% to $39m.

Biomarker specialist NextGen Sciences (Ann Arbor, Michigan) has appointed Neal Siegel to the new role of director of assay development. Dr Siegel, who previously worked at Sword Diagnostics and Abbott Labs, will oversee assay delivery, validation and quality control at NextGen. The company has also appointed Glenn Barney vice-president of business development. Formerly of Decision Biomarkers, Mr Barney will help drive sales growth across all NextGen products. He will also lead the firm’s marketing activities, and will be joined by the new director of marketing.

Hiroshi Saito, who joins from internet and digital marketing agency Optiem. The new appointments come as NextGen prepares to launch two new biomarker assays markets in the first half of this year; one is a human plasma assay targeting several oncology disease areas, and the other is a human cerebrospinal fluid assay for central nervous system disorders.

EyeBrain has appointed Savita Bernal business developer for Northern Europe. She will be responsible for the development of commercial and scientific activities in the UK, Ireland and the Nordic countries. Ivry-sur-Seine, France-based EyeBrain develops medical devices for the early diagnosis of neurological diseases, and launched its eye-tracking system, the Mobile Eye Brain Tracker, in France, Belgium and Luxembourg since June 2010. The device, which permits early diagnosis of Parkinson’s disease and related conditions, is expected to be introduced to the UK and Irish markets in the first half of 2011, followed by the Nordic regions before the end of the year.
John Dwyer of Telcare

John Dwyer is the chairman of Telcare, a Bethesda, Maryland-based company that has developed what it believes is the world’s first “cellular-enabled glucose meter”. The company is awaiting FDA clearance and CE mark approval and expects to launch the product in the second quarter of 2011.

Clinica: Which areas within wireless healthcare do you see the fastest growth and the biggest opportunity?

John Dwyer: One of Albert Einstein’s classic axioms was: “Nothing happens until something moves.” This principle is very applicable to healthcare. Generally, we think the growth opportunities in wireless health are in those areas at the edge of the “cloud” and where data is locked within the “wired” healthcare system. Every day, billions of important clinical and logistical transactions are recorded on paper or in electronic environments which lack the ability to liberate the data and move it to other parts of the data supply chain where it is needed in order to render better care or make a healthcare system more efficient.

Home monitoring of blood glucose levels, blood pressure or weight are just three simple examples of clinical data that ideally would be recorded and made available in multiple locations, but this is not the case; the data are outside the “cloud.” We think capturing this data for large segments of the population and bringing it into the clinical data supply chain makes an important contribution to improving patient care and represents a very significant economic opportunity for wireless healthcare.

Another large opportunity for wireless healthcare is in detecting and transmitting data regarding unperformed actions. “Real-time” transmission of missed appointments, unfilled prescriptions, unreported lab results, or undelivered therapies and services can allow the system to react more quickly to omissions in care and to rebalance resources. Wireless technologies are well-suited for this growing market need, especially at the patient level.

Clinica: How does Telcare overcome these challenges?

JD: Telcare’s initial product is the first cellular-enabled blood glucose meter in the world. We developed this product first because there is general agreement that blood glucose data that is available in “real time” has value, and we designed the product with a price point that falls within most markets’ reimbursement structures for non-wireless meters. Candidly, we did not overcome the reimbursement challenge; we can generate a reasonable return within the existing market and expect to benefit as the market for wireless health continues to grow.

Clinica: You’ve held C-suite positions in several emerging growth companies. What is the best part of being in those roles?

JD: You become part of a team that really creates something. There are always new experiences, and the business stays fresh. It is fun. Our credo is “doing well while doing good.”

Clinica: And the hardest aspect of such a role?

JD: The singular sense of responsibility to the patients you serve and the shareholders that trusted you with their money.

Clinica: What advice would you give to early-stage healthcare companies trying to survive in this current climate?

JD: Focus on clear value propositions. Wireless health is uniquely capable of adding value to both patients and payers, simultaneously. Prioritise accordingly.

Mr Dwyer was talking to Tina Tan
Free Access

Request your free access today to see how RA Medtech can help you:

- Minimise compliance costs
- Mitigate risk
- Accelerate your time to market

An excellent tool which provides you, on a regular basis, with the hot items evolving in Regulatory Affairs.

Mireille Vanhoutte, Baxteronline

REQUEST YOUR FREE TRIAL TODAY
www.regulatoryaffairsmedtech.com/freetrial