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Ground-breaking UK devices initiative comes of age

UK industry set to embrace new future with HITF

The Device Evaluation Service (DES) of the UK's Medicines and Healthcare products Regulatory Agency (MHRA) is to be transferred to the NHS Purchasing and Supply Agency (PaSA), as part of a root-and-branch overhaul of medical technology's place in the UK healthcare industry.

As *Clinica* went to press, this was one of the main developments to emerge from the launch of the report of the Healthcare Industries Task Force (HITF), set up one year ago to develop a strategy to boost the sector's market access, R&D, regulation and export trade.

Referring to "deficiencies in the UK market and structural flaws in the NHS" identified by HITF, the ABHI had previously hinted at recommendations that could see the UK become a "world centre of excellence for medical device technology and accelerate adoption of new treatments".

But the prospects for the devices industry under HITF are no longer in the conditional tense. "The HITF policy proposals will speed up the rate at which the latest and best technology is made available in the UK," ABHI director general John Wilkinson told *Clinica*. The three main factors in this will be "improved device evaluation to accelerate uptake, stronger clinician involvement in procurement, and an improved environment for medical technology R&D," he explained.

The changes underway at PaSA and the MHRA are but a few of the developments that will dovetail into the HITF strategy. While the DES relocation, by April 2005, is central to HITF's market access stream, the changes for the MHRA are set to be more important under the regulatory stream (see also this issue, pp 4-8).

Early reaction from the diagnostics industry

The British In Vitro Diagnostics Association (BIVDA) welcomed the decision to transfer the DES to PaSA and hopes that the wider HITF strategy will adequately recognise the value of diagnostics in the healthcare system.

"I think initially there will be some suspicion, but we've had assurances that [the DES] will remain an independent service – a pure evaluation of devices – rather than be linked to pricing," BIVDA director general Doris-Ann Williams told *Clinica*. "And I think it will mean more investment to improve the service," she added.

"The aim is to have a once-only device evaluation service for the UK. I am not sure if, given the nature of the UK diagnostics market, that will be possible, but we would welcome it because when you have to perform evaluations over and over, from site to site, it does make things costly and time-consuming," Ms Williams explained.

The diagnostics industry's initial reaction to HITF was thus somewhat cautious. "I see this as only the beginning of the HITF dialogue and not an end product. There are many obstacles to overcome if our objectives as a group are to be achieved," said David Horne, managing director of diagnostics company Bio-Stat.

bernard.murphy@informa.com

• HITF: the broader picture – see next issue of *Clinica*.

HIGHLIGHTS OF 1133

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Clinica Head Office: Telephone House, 69-77 Paul Street, London EC2A 4LQ. Tel: + 44 20 7017 5000 (switchboard). Fax: +44 20 7017 6975. Email: clinica@pjbpubs.com Website: www.clinica.co.uk

US Office: Pharmabooks, 270 Madison Avenue, New York, NY 10016, US. Tel: +1 212 262 8230. Fax: +1 212 262 8234. Email: subsreps@pharmabooks.com

Japanese Sales Agent: T Hirata, Shiryo Kenkyujo, No 3-5-20-405, Sotokanda, Chiyoda-ku, Tokyo 101, Japan. Tel: +81 3 3258 9207. Fax: +81 3 3258 9209. Tlx: 2655207. Email: info@shiryoken.co.jp

EDITORIAL

EDITOR: Ashley Yeo (extn 6971)
DEPUTY: Bernard Murphy (6972)

SECTION EDITORS:
EUROPEAN REGULATORY AFFAIRS: Amanda Maxwell +44 20 8546 1518
US: Karen Riley +1 301 927 1485
SCIENCE & TECHNOLOGY: Neena Brizmohun (6974)
COMPANIES: Eleanor Malone (6976)
REPORTERS: Bernard Murphy
Tina Tan (4533) Daniel Barry (6978) Faraz Kermani
EDITORIAL ASSISTANT: Kellie Mundell (6977)
PRODUCTION: Anne Morrissey

PUBLISHER: PJB Publications, a trading division of T&F Informa plc

ADVERTISING

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Email: stephen.day@informa.com
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Maria Parfitt Tel: +44 20 7017 6800.
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EU competent authorities have final say on MDD review

The last week has seen further developments in the five-year review of the Medical Devices Directive (MDD), 93/42, following a closed meeting between the European Commission and competent authorities in The Hague, the Netherlands, on November 9-10.

As a result of progress made at that meeting, the European Commission's medical devices team is now polishing the proposed amendments to the Directive so that these can be passed to the Council of Ministers for a political agreement, once a new Commission team has been appointed.

The meeting provided an opportunity for each of the proposed amendments (see *Clinica* No 1128, pp 2-6) to be considered in turn. Written contributions from other stakeholders, including the European medical device industry association, Eucomed, were taken into account. The discussions focused on clinical evaluation, classification rules and the designation of notified bodies, among other themes.

However, the only major new item discussed at the meeting, *Clinica* understands, was whether to include clinical data information on the European database, Eudamed, and whether to include a reference to the Global Medical Device Nomenclature (GMDN) as the language of use for the database in the MDD, or simply to refer to accepted nomenclature.

Clinica understands that there is general support to centralise all medical device-related information on Eudamed, and therefore that this proposal has the backing of the Commission, but that it would be difficult to refer to the GMDN as mandatory, given that there are still outstanding copyright issues that need to be resolved.

It is unlikely that a political agreement will be reached before mid-January, given that the new Commission, once appointed, will have a series of other priorities to deal with. However, once this agreement has been reached, the text of the proposed amended Directive will then have to go for interservice consultation, where all interested directorate generals within the Commission will have an opportunity to comment on the proposed amendments.

This means that the text of the proposed amended Directive is unlikely to formally reach the Parliament and Council, where it will then start its lengthy journey to adoption, until April.

NEWS IN BRIEF

❑ *Unequal CAB count means US delay on MRA*

Following a long silence on the mutual recognition agreement (MRA) between the EU and the US, which most observers had expected would be officially adopted by now, it now seems that more observed audits will need to take place in the US before full implementation can take place. The indications are that the US now wants to ensure that it has as many conformity assessment bodies as the EU (currently it has three, compared to six in the EU). The speed at which the CABs can be recognised as ready for listing will depend on industry's willingness to invite potential conformity assessment bodies based in the US to take part in observed audits. In the past, companies were slow to put themselves forward, and it is unclear what the situation is now.

• More EU news on pp 10–11, and US news on pp 11–12

Industry slams German reform's impact on medtech aids quality

The German health reform law has effectively given the statutory health insurance funds (GKV) carte blanche to pressure prices and consequently endanger quality in the medical technical aids sector. This was the view expressed last week by the German industrial association for optical, medical and mechatronical technologies, Spectaris.

The law, which was introduced on January 1 2004, allows health insurance funds to issue tenders for medtech aids and then to sign contracts with those companies that are able to supply products in the lowest-third price bracket. Spectaris says that this will negatively impact the provision of quality devices to patients in need of medtech aids, such as respiratory therapy equipment, prostheses, wheelchairs and bandages.

Furthermore, it says that cutting GKV expenditure on medtech aids is merely a shortsighted, short-term solution to the financial problems of the funds. In the long term, it argues, the provision of lesser quality products and services will lead to far greater costs.

GKV expenditure on medtech aids during the first half of 2004 represented only 3.6% of the funds overall healthcare expenditure, or €2.5bn ($3.2bn). This figure has fallen by some 13%, compared with the same period last year. Certain manufacturers are even claiming reductions of up to 40% in specific sectors.

Klaus-Dieter Hagen, chairman of Spectaris' sector for rehabilitation medtech aids, says that it was naïve of the government to believe that quality could be maintained, while prices were forced down. And he claims that evidence for this negative trend is in plentiful supply. "It ranges from a reduction in available advice, to the provision of lower quality products, from a [forced] selection of the worst alternatives, to a refusal to provide care," he says.

Spectaris' member companies in the medtech aids division have called for quality to be maintained in any further restructuring of the sector. Following a series of successful negotiations with health insurance funds, they are currently working on a number of quality assessment criteria, incorporating manufacturer recommendations and quality standards.

NEWS IN BRIEF

❑ ***German reclassification not addressed in review***

Proposals from the German medical device regulatory authority to review the classification of a series of products over which it has safety concerns are not going to be addressed in the context of the review of the Medical Devices Directive (see *Clinica* No 1125, p 2). That became clear during the meeting between the European Commission and the competent authorities on November 9 and 10. But interestingly, it was the not the Commission but rather other member states who impressed on the Germans the need to use tools already available in the Directive to make a formal request for such changes, namely Article 9, Classification and Article 13, Decisions with regard to classification, derogation clause. There is the intention to expand both these articles in the context of the review for clarification purposes, but there is nothing to prevent an application through these articles now.

German medtech industry sees upturn in H2 2004

Despite a disappointing start to the year, member companies of the German medical devices industry association, BVMed, are predicting a respectable average turnover increase of 3.4% for 2004. According to a recently-compiled survey, some 40% of the association's membership is also expecting to see profitability improvements and to be able to consider increasing staff numbers, said BVMed director general Joachim Schmitt at a press seminar in Berlin last week.

All this is a lot different to the picture in early 2004, when turnover growth in the first half of the year struggled to reach 1.3%, compared with +3.3% in the corresponding period in 2003. One reason for the slow start to the current year was the government's healthcare reform law, which had a decidedly negative impact on sales of stoma and incontinence care products and other products within the medical technical aids sector. Here, sales fell by 1.5% in the first half of 2004.

The general slowdown in German medtech sales across the board last year saw the national device market grow by on 4.4%, 1.8% lower than the rates of growth in other key international markets, such as the US and Japan. Indeed, the world market last year was valued at €184bn ($223bn), with Germany accounting for €19bn out of a European total of €55bn, and the US leading the field, recording sales of €79bn. The fastest growing markets were China, Brazil and eastern Europe.

However, German medical devices firms remain upbeat about the future, claiming that theirs is still a growth sector and has major prospects, especially bearing in mind the country's ageing population, which will provide the impetus for more investment in the industry.

More dialogue with partners needed

Mr Schmitt has called for increased dialogue within the health service. Speaking at the press seminar, he said: "All partners must co-operate and take part in this new, modern and dynamic healthcare economy and exploit the growth potential of the healthcare sector." He urged a more market-led and competitive health service, and for the wider sector to embark on a deregulation offensive and adopt a results-based technology evaluation process for reimbursement, and new, flexible and optional financing models in the statutory health insurance system.

And BVMed chairman Anton Schmidt (Johnson & Johnson) said that more must be done to foster co-operation between the industry and practitioners/surgeons, as this had traditionally proven to be a motor of innovation for the sector. He recalled as examples the cross-sector collaborations that had spawned the Dräger-Roth anaesthesia apparatus (1903), PTCA balloon dilatation techniques (1977) and the Palmaz-Schatz coronary stent.

"These types of innovation are the driving force of the healthcare economy," he said. "The closer the co-operation between doctors and engineers from medical technology companies, the higher the level of innovation and, therefore, of economic success," he added.

Most medtech companies have by now set up procedures to harness any potential product developments between doctors and engineers, including co-operation with universities, and, later, the establishment of research centres housing scientists and industry experts.

Crisis brewing for devices representation at MHRA?

Nature of UK regulator changes: Is there no way back?

When the merger took place of the UK's Medical Devices Agency with the Medicine's Control Agency to form the Medicines and Healthcare products Regulatory Agency on April 1 2003, the medical device and diagnostics industries' concerns were focused mainly on the threat of medicines-type policies increasingly influencing the sector. Some 18 months down the line, the medical devices and diagnostics industies are facing a different set of concerns, brought about by factors beyond their control and linked to being part of a different culture – one that is being affected by increased suspicion about its workings, reports Amanda Maxwell

The medical devices industry seems to be in danger of being pushed into near oblivion if calls for investigations into the pharmaceutical part of the agency go ahead (see pp 6-7). With complaints that devices and diagnostics have already been "marginalised" following the merger of the MDA and MCA and that not enough resources are being made available within the MHRA for this sector, many in industry are concerned that its loss of independence will be hugely damaging if an investigation is carried out.

Indeed, not only are medical devices likely to be perceived as being linked with pharmaceuticals, and therefore possibly tarred by the same brush, should an inquiry go ahead as some MPs demand, but also the threat is all the greater because of the lack of leadership for devices at the agency, to help maintain the sector's independence and get its own messages across.

"...the question in everyone's mind will now be how possible it will be to ever get the agency back to the way it was in 'the good old days' of the openness in communication"

It is the lack of leadership for medical devices that has been the focus of considerable concern from the industry since Dr David Jefferys left the agency at the end of March this year. The British In Vitro Diagnostics Industry Association and the British Healthcare Trades Association are now renewing their calls for a new head of devices. But while they are doing so, the Association of British Healthcare Industries (ABHI), the largest of the three associations and initially the most vociferous in demanding a new authority figure for devices, says that it now accepts that a new leader will not be appointed in the short term and is determined to "move on" and work with the agency under the new framework.

Whether a new head of devices is appointed or not, the question in everyone's mind will now be how possible it will be to ever get the agency back to the way it was in "the good old days" of the openness in communication that existed with David Jefferys, and with Alan Kent before him. This now seems to be in very serious doubt despite the fact that this way of working was perceived by industry and regulators alike as positive and to the benefit of innovation and progress. And despite the fact that it helped the UK become a world-class medical devices regulator, setting examples that were admired and often copied in other markets.

It is in serious doubt because, if the regulation of devices and diagnostics is now seen by the public and politicians as being linked with pharmaceuticals, and if there is a whiff of suspicion about the impartiality of the pharma regulators, it is likely that all the staff at the MHRA will have to take steps to constantly protect themselves. The culture will inevitably have to be more official, more closely documented and less amenable to the type of open dialogue that has been a feature for the UK's medical devices sector for over a decade. It seems that the stage is now set for a complete culture change, and not one that will be welcomed by the medical devices and diagnostics industries.

UK medical device regulator without figure at helm as accusations fly

The medical devices division of the UK's Medicines and Healthcare products Regulatory Agency (MHRA) has been "sidelined since the merger [with the MCA] and may well have suffered from it". That was the view put forward by Dr Ian Gibson MP, during a debate at the House of Commons on the MHRA on November 10 2004.

But not only has it been sidelined, it has also been left without its own authority figure to cope with what could now be one of the most challenging eras ahead if issues raised during this debate lead to an inquiry of the MHRA.

While debate was heavily focused on concerns about the integrity of those working on the drug side of the agency, calls from MPs for an independent inquiry into the agency could threaten to further distort the focus away from medical devices, already rather weak, apparently, as civil servants become embroiled in efforts to salvage their reputations.

That is not to say that an enquiry of such a nature will go ahead, but at least the seeds have been sown on which to debate further. It will be difficult for ministers to deny allegations of lack of impartiality among regulators that were thrown up during the 90-minute long debate.

How the devices sector will manage this situation, especially given its lack of perceived separateness, now, from the pharma side, remains to be seen, but Mr Gibson raised the issue of what the government was going to do about the lack of a devices head, and the repercussions this is having on the medical devices sector.

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Dr Gibson said that there was "no independence" in the medical devices area, because of the fact that "a senior person has just left it".

And he demanded to know why no replacement has been named: "There is a problem as regards the two arms [of the MHRA] coming together and both parts having equal weight," he said. "It would be interesting to know why there is no head of devices services and diagnostics and what the agency's intentions are in that regard."

Argument for inquiry

It will be difficult for the government to dismiss the calls for an inquiry concerning the regulator, even if one is already going on into the workings of the industry. Labour MP Paul Flynn made a particularly impassioned plea for further investigation of the MHRA, accusing it of failing to carry out its regulatory responsibilities in a true spirit of independence. "This isn't a watchdog – it is a pussy cat which purrs in front of the industry and does what it is told," he said, going on to describe the agency as "at best ramshackle and ineffective, and at worst corrupt".

"...there was always the issue of: We have got to be very careful because the pharmaceutical companies will sue us..."

Mr Flynn said that it is difficult to believe that the pharma regulators can carry out their jobs independently given the long list of well-established relationships between the regulators and industry. The organisation has "an incestuous relationship with big pharma and a close association with the Association of the British Pharmaceutical Industry", he said. Indeed, he went on to say that "the whole body is part of the pharmaceutical industry, an industry that has a dreadful record of overselling its products...".

Even if the allegations of corruption are unfounded, there were still concerns that the MHRA could not respond independently because of the way in which the regulators feel obligated to the pharma industry, because it is the pharma industry which entirely funds the pharma side of the operations.

Liberal Democrat MP Paul Burstow referred to a comment that had been made by Richard Brook of the mental health charity, MIND, and who had "courageously resigned" as a lay member of the MHRA's expert group on the class of antidepressants that includes Prozac and Seroxat, "in disgust at its activities". Mr Brooks had said in his evidence to the Select Committee on the Safety of Medicines: "Every time we made difficult decisions there was always the issue of: 'We have got to be very careful because the pharmaceutical companies will sue us if we get this wrong...'. The MHRA officials were very mindful the whole time of that dimension, to my view, more than the dimension of public health and responsibility to the public."

Health minister response

When health minister Melanie Johnson responded on behalf of the government, she struggled to answer the many detailed points that had been made in the time available, battling against interruptions and offering no solutions to the need for increased independency in the devices sector.

She stressed that a significant proportion of the MHRA's senior scientific staff are, "of course, recruited from, or have a history in, the industry. That is necessary, as they make up the largest single pool of specialist advice for effective drug regulation", she said. But she did refer to last week's announcement by Lord Warner, parliamentary under-secretary of state for the Department of Health, concerning bringing UK policy into line with new EU legislation, which requires that experts should have no financial or other interest in the pharmaceutical industry that could affect their impartiality.

Prompt for better communications

One positive message that came out of the debate for both the drug and device sides of the agency was the perceived need, acknowledged by all those present, for better communication by the industry to stakeholders, the public and the press. It emerged that a communications director has now been appointed, and the MHRA has subsequently confirmed that Simon Gregor will take up this post on January 31 2004.

** Dr Gibson is also chair of the House of Commons Science and Technology Select Committee and only last week took the message of the benefits of medical technology to parliament (see* Clinica *No 1132, p 2).*

Conflicting industry views over need for devices head at UK's MHRA

Following Dr Ian Gibson's raising the issue of why there was no longer a head of the devices and diagnostics section at the Medicines and healthcare Products Regulatory Agency, Amanda Maxwell spoke to the Association of British Healthcare Industries (ABHI), the British In Vitro Diagnostics Association and the British Healthcare Trades Association to see how they are coping with the lack of authority figure for devices and found two surprisingly different views

The UK's in vitro diagnostics industry feels that there is both a lack of communication between the MHRA and the diagnostics industry, and a lack of understanding about the nature of the industry. "Our members feel that they often do not get an adequate response or that it often takes a long time to receive one," Doris-Ann Williams, director general of the British In Vitro Diagnostics Association, told *Clinica* during a conversation at BIVDA's offices in London following the Westminster Hall hearing called by Dr Ian Gibson MP (see this issue, pp 4–6).

Indeed, BIVDA feels that the numerous issues that have to be dealt with on the pharma side of the MHRA are keeping its management "very busy" with too little time to then focus on the diagnostics area. And Ms Williams is finding the stock response of the agency being under-resourced not only wearing, but also not entirely unconvincing, given the agency's 750 staff and budget of £65m ($118m). This compares with BIVDA's budget of under £350,000 and staff of just three.

There is no doubt in Ms Williams mind that the agency needs to have the management capability to respond more quickly and more appropriately to IVD issues. "Grey areas surrounding IVD issues have still not been addressed properly," she complained. And certainly, the MHRA is not as proactive in Europe when it comes to IVD regulatory issues as the Medical Devices Agency used to be, she added.

The same frustrations are being voiced by the British Healthcare Trades Association, which represents some 360 companies in the medical devices assistive technologies sector. "There is a feeling that medical devices are being marginalised under the new arrangement," Ray Hodgkinson, director general of the association, told *Clinica*. "We were not comfortable with the merger but we were given assurances that our representation would be upheld. This has not happened," he complained.

And he too, is worried about the profile of the MHRA devices side in Europe and internationally. "In terms of medical devices, the European contacts I meet at senior levels are expressing concern that the MHRA is not as present as it should be," he said. "I am also concerned that where it was once considered as a primary force on the international stage in terms of standards work, this is not so much now".

Uppermost in the minds of both trade associations is the need to appoint a head of the devices section to replace Dr David Jefferys who left on March 31 this year (see *Clinica* No 1101, p 7).

"The diagnostics industry does not feel that there is anyone at the MHRA at present with whom we can have the same relationship as we had with David," Ms Williams said. "Before, we could simply pick up the phone and discuss things with him or meet up. He was an official who acted as a liaison between the agency and the outside world. All the senior officials at the major companies knew him well enough to be able to approach him and settle many issues through informal/formal meetings," she noted.

Mr Hodgkinson was in agreement about the need for a devices head. "I am strongly of the view that medical devices does need a high-profile person to head up that division of the MHRA," Mr Hodgkinson said. "David Jefferys did that job particularly well," he added.

Ms Williams finds the officialdom that has replaced this familiar face often impersonal and impenetrable.

ABHI response

While the appointment of a devices authority figure at the MHRA in the post-merger era had been a key priority area for the Association of British Healthcare Industries, this is no longer the key issue, John Wilkinson, director general, and Mike Kreuzer, technical director, told *Clinica* during a telephone interview on November 12. The ABHI has now resolved to accept that this is not going to happen in the short-term, they said.

"We had been emphasising this for a long time, but we have reached a point where we feel that we have made progress in our dialogue with them and accept that they have made up their minds not to appoint a device section head for the moment," Mr Kreuzer said.

"The organisation itself is not necessarily that material," Mr Wilkinson noted. "What is important is the necessary skills and capabilities are in place to do what it required. This is the message that I have been putting forward to Kent Woods when we have met".

"There are excellent people who we deal with at the MHRA on a regular basis. But there is clearly some work to be done before the agency is in a position to have a team fully equipped for the job," he added.

The Health Industries Task Force Group (HITF), the joint industry/government initiative is the key element that has helped the ABHI have faith in the improvement in dialogue without the need necessarily for a new head of the devices section. "That process has been extremely important for us and commits them and us to an ongoing dialogue," Mr Kreuzer emphasised.

This does not mean that industry believes the MHRA devices sector will remain indefinitely without a figure at the helm. "This is an evolving organisation," Mr Wilkinson said. "Organisations change quite quickly, especially following a merger. It is just possible that things may be different 12-18 months downstream", he suggested.

With the publication of the HITF report, ABHI hopes that it will now be well placed in having an opportunity to influence the evolution of the agency.

Reading a statement prepared by ABHI exclusively for *Clinica,* Mr Kreuzer said: "ABHI recognises that there were complex issues involved in the merger of MDA and MCA. Ever since the announcement of the merger in 2002, ABHI has advocated the establishment of a separate section for device regulation within the new MHRA and this position was discussed during the HITF process. However, the central message emerging from HITF on regulatory matters is that

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the MHRA needs to engage with industry to build on the excellent relationship which existed in the past and to ensure that the UK continues to set the lead in the EU and overseas. It became evident that the priority was not only to ensure that there was a clear focus on device regulation but that adequate skills and resources were available to support it.

Should industry really accept the status quo?

Amanda Maxwell comments: While ABHI seems resigned to the current state of play, BIVDA is prepared to continue challenging the situation, my sympathies go to BIVDA, especially given my own experiences of frustration of not being able to either identify with or communicate with a key authority figure on device issues in a way that I have always been able to in the past, dating back to the days of Gordon Higson in the 1980s.

Indeed, when telephoning the MHRA to ask Kent Woods whether his organisation hoped to appoint a devices head in the short or medium term in researching this article, I met with diversionary tactics that I never faced with David Jefferys.

"Call the Department of Health's press department," Prof Woods' secretary told me. "Does this mean that I cannot pick up the telephone and speak directly to him?" I asked. "Not as things are at the moment," I was told, "although you may well be able to do that with the appointment of the new director of communications in the New Year."

Let us hope, then, that the new incumbent does not find himself overwhelmed in defending the pharma side of the agency against the type of accusations raised at the Houses of Parliament on November 10. Otherwise I fear that there is not much chance that even he will have time for the devices sector.

amanda.maxwell@informa.com

WAS DR JEFFERYS' DEPARTURE REALLY NECESSARY?

The departure of Dr David Jefferys from the MHRA at the end of March now seems hugely ironic in the light of allegations that are being made about regulators at the Medicines and Healthcare products Agency (MHRA), writes Amanda Maxwell.

Although nothing was said officially at the time or since, his departure from the post was more than likely linked to an investigation, completed in the second half of 2003, into claims that he had falsified research findings some 20 years ago while doing his MD thesis at the University of London (see Clinica *No 1101, p 7).*

Rumours surrounding the research findings only began to circulate when it became known that there was to be a merger between the MCA and the MDA, and that Dr Jefferys, with his early background in pharma and later transfer to devices, was thought to stand a good chance at securing the chief executive post that has since gone to Professor Kent Woods. The more than mildly curious would be forgiven for thinking that someone had it in for him.

The Department of Health has never published the outcome of this investigation, but whatever the truth may be, those accusations levelled at Dr Jefferys for an alleged misdemeanour in his student days seem rather tame in comparison now to those of corruption and subservience to the pharmaceutical industry that were being levelled at regulators within the MHRA during the House of Commons debate.

Indeed, the medical devices sector may well wish itself back in the days when it was independent from the MCA, and when the regulator had a proper identity, with Dr David Jefferys heading the Medical Devices Agency.

Dr Jefferys came from a pharma background, having worked for the MCA. But once at the MDA, he threw himself into the workings of the device sector with enthusiasm and great drive, and was readily available to discuss issues of concern to all stakeholders, including industry, and to be constantly present at meetings.

In the gap that has been created and maintained since he departed, the UK devices sector may be wondering if it is the innocent victim of a very strange sort of political correctness gone wrong.

NEWS IN BRIEF

❑ ***ABHI considers focus on neuroscience sector***

The Association of British Healthcare Industries (ABHI) is considering setting up a special interest section focusing on neuroscience issues. The ABHI has called on its members for expressions of interest, but this is also an opportunity for non-members to become involved in the UK's leading medical technology industry association. According to the ABHI, the new sub-group's leading roles would be to: represent the interests of the neurosciences sector of the ABHI; encourage smaller companies in this area to participate in ABHI activities; and provide a link between the sector and professional bodies. The ABHI contact is Judith Mellis (Judith.Mellis@abhi.org.uk). The ABHI has unveiled a new corporate identity to mark this week's launch of the Healthcare Industries Task Force report (see page 1).

❑ ***France to have second notified body from January***

France is to have a second notified body (NB) for medical devices and diagnostics. The health ministry has accredited the national testing laboratory, the Laboratoire Nationale d'Essais, to begin work as from January 1 2005, according to a Decision that appeared in the *Journal officiel* of November 14. The LNE has been accredited to test: active implantables against annexes II to V of the Active Implantable Medical Device Directive; all medical devices, including class I sterile and with a measuring function, against annexes II to VI of the Medical Devices Directive; and self-testing and Annex II diagnostic products (lists A and B) against annexes III to VII of the IVD Directive. G-Med is the other French NB.

❑ ***French tax form for manufacturers and distributors***

France has issued a decree on sourcing the form (see www.acoss.fr) to be used by manufacturers and distributors when making income declarations about contributions under national sickness insurance rules, the CNAMTS.

UK imaging/radiodiagnostics sector displays healthy growth

Over 1 million more imaging and radiodiagnostic examinations and tests were performed in England in 2003-04 than in the year before – the 4% increase to almost 31 million, suggests healthy growth for the sector across the UK, after a marginal increase the previous year.

Computed tomography (CT) and magnetic resonance imaging (MRI) showed the highest rates of growth at over 12% and 9%, respectively. The use of radioisotopes increased by almost 6% to over 580,000 tests. Fluoroscopy was the only technology area to decline, by 5.7%, to 1.22 million procedures. (For the totals and market evolution of each technology/procedure in each of the last two years, see table).

There was, however, a significant fall in the number of tests performed "with intervention" in 2003-04. The specific areas that most contributed to this are: MRI (-80%), from 10,657 to 2,119; radiographs with no fluoroscopy (-76%), from 161,674 to 39,402; and obstetric ultrasound (-69%), from 57,757 to 17,651.

There were two exceptions to the declines in this category: The use of radio-isotopes increased by a third (33.5%) to 20,594 procedures, while the number of fluoroscopy procedures increased (8%), from 290,336, to 313,341.

In turn, fluoroscopy was the only technology to fall in the "without intervention" statistics – from just over 1 million to 907,761 (-11%).

Technology	2002–03	2003–04	% change in procedures
CT	1,767,791	1,992,826	12.7
MRI	786,646	857,550	9
Obstetric ultrasound	2,008,455	2,055,438	2.3
Non-obstetric u/s	3,626,903	3,881,945	7
Radioisotopes	551,423	582,742	5.7
Radiographs (no fluoroscopy)	19,512,924	20,056,669	2.8
Fluoroscopy	1,295,639	1,221,102	–5.7
Totals:	**29,549,781**	**30,648,272**	**3.7**
without intervention	**28,826,821**	**30,116,395**	**4.5**
with intervention	**722,960**	**531,877**	**–26.4**

Source: DoH imaging and radiodiagnostic statistics, England 2002-04 (September 2003/October 2004)

Between 2001-02 and 2002-03, England's imaging and radiodiagnostic sector had expanded marginally, with the overall number of procedures increasing by 79,967, from 29,469,814 (+0.3%). Those performed with intervention rose by 15% from 626,134. There was a marginal fall, however, in the use of the technology without intervention, from 28,843,680 (-0.06%).

Radiation dosimetry in share of Scottish innovation £1m

Detector and Sensor Technologies is among the beneficiaries of this year's £1m ($1.86m) SMART:SCOTLAND product development award, with a novel radiotherapy dosimetry monitor.

The Glenrothes, Scotland-based company's project involves the "development of an improved radfet sensor and reader technology for radiotherapy dosimetry". The device consists of a miniaturised, silicon-based radiation sensor and dose monitoring system for use during cancer radiotherapy. "The development of an in vivo monitor will allow treatments to be more closely tailored to patients exact needs," said the Scottish Executive of the device.

The SMART scheme seeks to help new and existing small businesses (less than 50 employees) by funding the development (through technical feasibility studies) of "highly innovative and commercially viable products or processes". A further £3.15m is available under Scotland's SPUR scheme, which finances the projects to pre-production stage.

21 companies will receive a share of this year's awards, totalling just over £1m. The programme covers a range of sectors, including environmental, biotechnology, IT and healthcare applications.

NEWS IN BRIEF

❑ *Therapeutic R&D under UK Commons spotlight*

Therapeutic and fertility research are the subjects of two panel hearings being held by the House of Commons Select Committee for Science and Technology (STC) on November 24 2004, as part of its enquiry into human reproductive technologies and the law. The therapeutic research panel in this tenth oral evidence session will comprise: Professor Roger Pedersen, of the Medical Research Council's (MRC) Centre for Stem Cell Biology and Medicine (Cambridge); Professor Alison Murdoch, consultant gynaecologist and head of the Newcastle Fertility Centre; and Dr Robin Lovell-Badge, head of developmental genetics at the MRC's National Institute for Medical Research.

❑ *UK: final stage of Human Tissue Bill*

The UK's Human Tissue Bill has completed its passage through parliament and now awaits Royal Assent. It was passed by the House of Commons on November 10, after a debate (see *Clinica* Nos 1097, p 6 and 1105, p 8) that saw it through the House of Lords at its third reading.

❑ *More EU countries to adopt the euro*

Four out of the ten new EU member states plan to adopt the euro currency by 2007 and the remaining six by 2010. Estonia, Cyprus, Lithuania and Slovenia are the frontrunners, according to the European Commission's first report on the state of practical preparation for the euro in the new member states. There are still questions over how the new currency will be introduced in these countries – either all at once, or with a transition period. The Commission report notes that the current euro area countries (except Greece) had a transitional period of three years, but the lessons drawn since show that this is neither necessary nor advisable for the new countries. A short or immediate transition strengthens the case for starting preparations at an early stage in order to allow a full changeover on "E-day", it says.

December deadline for decision on animal tissue conundrum

The European Commission's working group on medical devices utilising animal tissues is due to meet in Luxembourg on December 13 to prepare a document on how competent authorities should deal with potentially unlawful products.

The document will determine what authorities should do about products that were already on the market on September 30 that have not yet been reassessed by a notified body under the terms of that Directive on medical devices utilising animal tissues (2003/32/EC), which was fully enforceable on October 1.

For the present, a temporary solution has been reached to ensure that such devices may remain on the market despite not being fully in compliance with the new Directive as long as manufacturers had ensured that they had sent their technical files addressing the new requirements to the notified bodies by October 1. This was necessary due to delays in setting up the regulatory structures necessary for implementing the Directive, in particular the official designation of the notified bodies that are competent to test these products (see *Clinica* No 1131, p 3).

The working group's document will be presented the next day to the European Commission's Medical Device Experts Group (MDEG) meeting, which is being held on December 14 and 15.

Agenda items

The MDEG meeting will also have on its agenda: a debate on in-house manufacturing; the joint implementation plan for the mutual recognition agreement with Australia; and progress reports from the Commission groups on clinical evaluation (the CETF), notified bodies (NBOG), market surveillance (MSOG) and software.

KEMA takes proactive stance on 2003/32 accreditation

Dutch notified body KEMA Quality began its animal tissue Directive (2003/32/EC) accreditation process some three years ago. It found that a good working relationship with the national competent authority led to a relatively smooth and swift conclusion, thereby enabling it to avoid the last-minute panic that has embroiled some NBs and tissue-containing devices as the Directive's effective date of October 1 loomed (see above and *Clinica* No 1131, p 3)

The new EU Directive on animal tissues, 2003/32/EC, came into effect on October 1, but not all companies operating in the EU with products containing animal tissues have been able to gain certification by the deadline that their products are in conformity. Not so for clients of Dutch notified body KEMA Quality (based in Arnhem, and with two offices in the US), considered to be one of the big four European NBs, alongside TÜV Munich, TÜV Rheinland and BSI.

KEMA resolved to take a proactive stance in order to gain rapid accreditation under the Directive, the company's cluster manager, medical, Martin de Bruin, told *Clinica*. It filed for accreditation in December 2003 and then worked closely with the national competent authority until it was audited in February 2004 and received accreditation mid-May.

The whole regulatory process took less than six months, but the important groundwork was done long before. "From the early stages of the discussions in Brussels with regard to 2003/32/EC, KEMA and Jos Kraus, the inspector at the competent authority (the ministry of health), discussed what was likely to happen once the Directive was in place," said Mr de Bruin.

"We built up our own systems and procedures to cope with what would happen," said Mr de Bruin, adding that a team approach between a project engineer, a certification manager, a product expert and an external consultant ensured a timely conclusion to the project.

Having been awarded the status, KEMA again moved swiftly to contact clients that have products incorporating animal tissue or its derivatives obtained from TSE-relevant species. Up to 35 of its clients have animal tissue-containing products. To these companies, it issued a guidance document detailing what information it needed to review devices under the new Directive.

Based on the responses it received from companies, KEMA either prepared summary evaluation reports (SERs) for the Dutch competent authority, which were in turn reviewed by the EU member states, or compiled an internal report, if, for example, EDQM certificates were available. Comments from the member states were received back at the beginning of September 2004, which prompted KEMA to make some minor changes to the to the SERs.

By September 30, the company had issued new certificates proving conformity to 2003/32 to over 90% of its applicable manufacturers. The company also reviews outsourced files from other notified bodies, it notes. So, for a short time, KEMA was in the enviable position of having been the first and only company audited under the Directive, as a result of the Netherlands being among the first EU states to transpose the TSE Directive.

KEMA Quality, a €50m ($91m) turnover company employing 450 staff, says its ability keep timelines agreed with the manufacturers and its policy of using one expert as the client interface throughout for the whole accreditation process kept clients satisfied. This member of staff also represents KEMA and all EU notified bodies in the TSE/BSE working group.

EC recommendations for EU devices industry in January

Next January will see broad political recommendations made for the EU's medical device industry on the basis of the European Commission's report on the competitiveness of the sector.

The next meeting of the Commission steering committee that is working on the report is expected late that month at which the recommendations should be agreed. That forum, will see an updated version of the text which was already assessed as being 70% ready by some of those present at a meeting that has just taken place on November 15. The most recent meeting provided the steering committee and stakeholders and opportunity to review comments on the first draft report.

Between now and January, there is due to be a major restructuring and re-editing of the document so that a near final document can be ready for the meeting in early 2005.

Economic and industrial study

The study aims to gather data in relation to economic and industrial features of the medical devices industry in Europe, the impact on health and public expenditure and the global competitiveness of the European medical devices industry.

E-labelling on EU agenda early next year

EU e-labelling issues may have to wait another couple of months before given a proper forum for debate. The first meeting of the European Commission's working group on e-labelling is unlikely to take place until February next year given how full the Commission's agenda is for the next two months.

Some progress has been made already, however, since the decision at the October 19 and 20 Medical Device Experts Group (MDEG) meeting to set up such as group: there has been a good response to the call for interested members.

Given the potentially controversial nature of this subject, with industry strongly in favour of e-labelling and a certain amount of the resistance among some competent authorities, the Commission intends to chair the first meeting.

There are already a number of documents that have been prepared by stakeholders (industry and authorities) on this subject, which should help progress, and the group's terms of reference will be agreed at the first meeting.

NEWS IN BRIEF

❑ ***Ireland confirms first case of vCJD***

Ireland's ministry of health and children has confirmed the country's first case of variant Creutzfeldt-Jakob disease. Health minister Mary Harney has met with chief medical officer Dr Jim Kiely and the chairman of the National CJD Advisory Committee, Professor William Hall, to discuss the "potential broader public health implications which may have arisen from this case". The young, male patient is being treated at a Dublin hospital. He was first suspected of having vCJD on October 21.

Spain moves to improve on mammography successes

The increased use of mammography by Spain's regional screening programmes has been seen to improve the rate of early diagnoses of breast cancer, which also explains the apparent rise in the incidence of the disease. So says the health ministry of the more than 15,000 new diagnoses being made annually. Earlier detection, it says, has also resulted in improved survival rates, currently at 70% of all diagnoses of breast carcinoma.

However, with around 6,000 deaths per year from the disease, the government has pledged to improve the quality of the tests used, continue to investigate ways of improving early detection and diagnosis of the disease, improve the service involving familial (genetic predisposition) cases, and encourage more women to accept the invitation to be screened.

"Earlier diagnoses, combined with the scientific and technical advances, have also resulted in greater use of less-invasive surgical procedures and supporting therapies, which has also contributed to improving survival," said the health ministry, which says it is working in close collaboration with the regional health authorities on the said priority areas.

California makes itself US stem cell point of reference

The state of California is poised to become the epicentre for embryonic stem cell research after voters agreed to a $3bn bond initiative on November 3 to fund studies in this promising medical area.

Under the initiative, the state is authorised to sell 10-year tax-exempt bonds and use the proceeds to fund $295m in annual grants for stem cell research conducted within California.

The amount far surpasses total federal funding and is expected to have a profound effect on the development of this nascent medical area. As David Greenwood, executive vice-president of Menlo Park-based Geron, explained to the *San Diego Union Tribune*: "The money dwarfs what any other political entity in the world is spending."

Last year, the US government spent $25m on embryonic stem cell research and $190m on adult stem cell research. Only a limited number of stem cell lines have been sanctioned for federally-funded research out of deference to the religious right. Of the 22 cells currently available, all are considered tainted because they were grown in mouse feeder cells.

But California's funds would not contain such limitations. "Other states are worried about losing their biotech braintrust to California," state senator Deborah Ortiz told the *Oakland Tribune*.

Already, the CEO of Massachusetts-based Advanced Cell Technology has moved to California and disclosed that it is currently looking for possible laboratory sites in the state.

Meanwhile, the vast University of California system is currently discussing how it should organise itself to take advantage of the money. The initiative established a new entity, the California Institute for Regenerative Medicine, to decide how to distribute the funds. The institute will be ruled by a 24-member board that will include four representatives from the biotechnology industry.

Cost pressures may force Congress to review Medicare spending

The new US Congress may be tempted to dip into the Medicare and Medicaid budgets next year as it looks for ways of staunching the growing federal budget deficit. The two programmes provide the main "pots of money" available to lawmakers as they look for ways to achieve President Bush's goal of cutting the deficit in half by 2009, a key Republican aide said last week.

The President's budget deficit goal is all the more difficult, given the war in Iraq and his plan for further tax cuts, the aide told a reimbursement conference last week sponsored by the Medical Device Manufacturers Association (MDMA). A Democratic aide concurred. "We probably won't be able to expand coverage options a heck of a lot and cuts might be on the table," the aide said.

A recent report by the consulting firm of PricewaterhouseCoopers points out that the last time the nation faced a large budget deficit Congress passed the Balanced Budget Act of 1997, which sharply curtailed Medicare spending and created the outpatient prospective payment system. In today's dollars, a similar level of reduction in the Medicare programme would amount to a cut about $450bn over the next 10 years. It predicts that the Medicare increases contained in the 2003 MMA "may become unsustainable".

None of this is good news for the device industry, which has been on the front lines arguing to wary Medicare officials about the benefits of covering costly high-technology products. Moreover, AdvaMed for one, is hoping to lobby for higher reimbursement for in vitro diagnostic products next year.

The federal budget deficit has increased in each of the last four years and could exceed $450bn by next year, according to some estimates. Medicare spending is currently growing at about 8.3%, but the growth rate will escalate to 15.4% in 2006 when beneficiaries will be able to enrol in the health plan's new drug plans. Medicaid, the state and federal health plan for the poor, has also been increasing by 11% in the last two years.

US: IDE does not necessarily equal national coverage

An FDA investigational device exemption for a product does not automatically guarantee nationwide coverage for the product, a local Medicare carrier warned last week. Saty Satya-Murti, Medicare medical director for Blue Cross and Blue shield of Kansas, says there are times when local carriers choose not to cover such investigational products.

Device companies have been fighting for years to secure Medicare coverage of as much of their clinical trial costs as possible.

Last year's Medicare prescription drug bill mandated that Medicare pick up routine clinical care associated with clinical trials involving breakthrough products.

But Congress did not cover routine patient costs incurred during clinical trials for so-called category B devices, which are subject to a 1985 memorandum of understanding between the FDA and the Centers for Medicare & Medicaid Services (CMS).

That accord leaves it up to Medicare carriers as to whether to cover the product or not, but is silent about routine costs. Some local carriers will automatically approve coverage but Dr Satya-Murti said he and others look at each trial on a case-by-case basis to determine whether the study offers actual merit for Medicare beneficiaries.

Coverage might be denied if there are flaws in the study design, such as ineffective control groups, inadequate primary endpoints or questions about compensation beyond Medicare's own potential contribution, he said. However, as frustrating as it is for device companies, more uniformity might be even worse.

The medical director said he would rather have coverage decisions for investigational devices made at the national level, which might further limit the number of studies being done. Meanwhile, companies seeking national coverage are well advised to have their clinical trials published in peer-reviewed literature first, a CMS coverage expert warned at the same conference.

Marcel Salive, director of the division of medical and surgical services in the agency's coverage and analysis group, notes that many studies are discussed at scientific conferences but never appear in print.

But CMS simply cannot give the same credence to these findings, he said.

CRP test outside Medicare cardiovascular screening coverage

Medicare officials have decided that three common lipid tests will fulfil a new cardiovascular screening benefit for the health plan's elderly and disabled beneficiaries. The three tests are for total cholesterol, cholesterol for high-density lipoproteins and a triglyceride test, the Centers for Medicare & Medicaid Services (CMS) declared in its physician payment rule for 2005, which was published in the *Federal Register* on November 15.

But any other cardiovascular screening tests must first clear the agency's national coverage process before Medicare will pay for it, the agency said. Some experts asked CMS to cover the highly-sensitive C-reactive protein (CRP) test.

The test has received so much publicity in recent years that many individuals now demand it. But a 2003 consensus panel sponsored by the American Heart Association and the Centers for Disease Control and Prevention (CDC) found that, while the presence of CRP appears to be associated with an increased risk for coronary heart disease, sudden death and peripheral arterial disease, it is not an effective screening tool. It is more useful when a physician is undecided about a course of treatment for a patient who is considered at intermediate risk of heart disease, they said.

CMS agreed, concluding that the evidence was insufficient to cover CRP for screening. It also rejected recommendations that it cover a 12-lead electrocardiogram, tests for carotid artery disease, blood pressure screening and a non invasive arterial test known as the ankle-brachial blood pressure test that combines an ordinary blood pressure cuff and a Doppler ultrasonic sensor to detect the blood pressure in the ankle.

karen.riley@pjbpubs.com

GHTF shapes clinical evidence and other new documents

The precise aims of the new study group on clinical evidence at the Global Harmonisation Task Force (GHTF) have emerged with the publication last week of the minutes of the June 28-29 GHTF meeting.

The new Study Group 5 will focus on global convergence in the area of clinical evidence, and its work is intended to take to a global level the type of studies already underway in the EU to clarify exactly what manufacturers' obligations are in this respect (see *Clinica* No 1115, p 12).

The immediate goals of SG5 will be to:

- harmonise definitions of terms;
- review existing GHTF documents on classification, conformity assessment procedures and risk management and applicable ISO/ICH documents, and to ensure that terminology is consistent and interfaces are clear;
- harmonise guidance on how to conduct and document clinical evaluations; and
- harmonise content and format for clinical investigation reports.

In a second phase, the study group will focus on harmonised principles to determine when a clinical investigation, as opposed to other forms of clinical evidence, is necessary.

TGA's Harris chairs SG5

Graeme Harris, of Australia's Therapeutics Goods Administration, was invited to be chair of the new study group.

The meeting on June 28–29 also provided an opportunity for the existing four study groups to report on their progress.

SG1

This study group reported steady progress with its conformity assessment document and said that a document could be ready within one year for advancement as a proposed document. The GHTF Steering Committee (SC) agreed to advance SG1's revised final document on labelling for medical devices (SG1/N043R6), to the proposed document stage and to post the document on the GHTF website for comments, which happened just over a week after the meeting.

It also underlined the priority given to ongoing work at the SG1 and agreed to postpone a new decision on the work item proposal on the Content and Format of Registration and Listing Information for Medical Devices until the next SC meeting in May 2005.

In June, SG1 was at the stage of analysing comments on a series of documents that had been posted on its website last December on: summary technical documentation for demonstrating conformity to the essential principles of safety and performance on medical devices; the principles of medical device classification; an information document concerning the definition of the term "medical device"; on essential principles of safety and performance of medical devices (including IVDs); and on the role of standards in the assessment of medical devices (including IVDs).

It then planned to concentrate on modifying existing documents to introduce specific requirements for IVDs.

SG2

The SC agreed to advance the document on Application Requirements for Participation in the GHTF National Competent Authority Report Exchange Programme, NCAR SG2 N38R14, to the proposed document stage, and post it on the website for comments, which occurred about a week later. The SC expressed its support for changes introduced to the document, allowing for a wide participation of non-founding members in the exchange programme.

SG3

The main focus of Study Group 3 had been risk management, and the work that it has done on risk management as part of the quality management system document, posted as a proposed document (SG3/N15R6) in January 2004. The SC noted that the document was due to be presented at its next meeting.

SG4

This SC confirmed the high importance of the SG4 work on Part 2: Regulatory Auditing Strategy, but also emphasised the importance of Part 3: Regulatory Audit Reports. It requested that SG4 and SG3, with which SG3 is working in close co-operation with regard to the integration of auditing in regard to risk management, give priority to work on the audit reports.

New work items

Three new work items were discussed at the meeting: design for patient safety; and medical software. Design for patient safety has been identified by all founding members as increasingly important and, at the conclusion of a debate on this issue, the SC agreed to record current activities in each region and to continue discussions at its next meeting.

As to software, the different regions agreed to exchange information, to allow SC members to draw on the experience of others when addressing this issue in their own regulatory system.

Separately, the SC chair agreed to organise a special (electronic) meeting of the SC in the second half of November to review comments on the review of the GHTF procedural rules. These relate to: roles and responsibilities; guiding principles and operating procedures.

There was also a very interesting discussion following up on the high level workshop on international standards for medical technologies in February 2004. One of the main items that emerged from this meeting was the need for clarification of the legal status of the maintenance agency of the Global Medical Devices Nomenclature (GMDN) and of copyright issues.

HIV in Russia "seriously underestimated", warns expert

The number of HIV infections in Russia has increased 10% so far this year, surpassing the 300,000 mark, according to official figures released last week. But after announcing that 30,000 new diagnoses had been recorded between January and the end of October, the head of the health ministry's Federal AIDS Center, Vadim Pokrovsky, warned that the real figure was likely to be at least three times that number, reports the Interfax news agency.

"In the first ten months of 2004 alone, the number of registered HIV patients grew to 300,000 from 270,000, or more than by 10%. These are official data. To get the real number of those who contracted [HIV], this figure should be multiplied at least by 3," Mr Pokrovsky is reported as saying, adding: "The most realistic figure is between 1 and 1.5 million."

This appears to demolish even the widest-ranging expert estimates of the disease across the entire Russian federation. According to a WHO/UNAIDS report published in July 2004, based on a 2003 assessment, HIV infections could number between 420,000 and 1.4 million.

By 2008, Russia will have to spend at least $1.2bn per year (at current costs) just to treat HIV/AIDS patients, according to a report by Transatlantic Partners Against AIDS (September 2004). However, Russia's 2004 federal budget for AIDS was "just $4m", it claims. It says that $97m has been earmarked under federal and regional funding during 2002-06.

NEWS IN BRIEF

❑ ***IEC and ISO boost information platform***
The International Electrotechnical Commission (IEC) and the International Organization for Standardization (ISO) have launched a website for their joint information centre. The site (www.standardsinfo.net) features general information on the roles of the two bodies and their influence on the facilitation of world trade. The site also provides standards catalogues, details of work under development and a dedicated enquiry service.

❑ ***Kazakhstan's "major victory" in joining IEC***
Kazakhstan has joined the International Electrotechnical Commission (IEC) as Associate Member, in what has been welcomed as a "major victory" for this community of 63 member states. The central Asian country, the largest former Soviet republic, can apply to become a Participating Member on up to four technical committees, with a right to vote on the technical work they produce. Until now, it had been part of the IEC's Affiliate Country Programme, which was set up in 2001 with the aim of involving newly-industrialised nations. Kazakhstan has a population of 15 million and borders China, Russia and fellow former Soviet republics Turkmenistan, Uzbekistan and Kyrgyzstan.

❑ ***Sudan renews medtech prospects***
International healthcare efforts in the Darfur region of Sudan are set to resume, after the government signed a series of security and humanitarian access agreements yesterday. The move is in response to widespread condemnation of the severe social instability in the region. The situation has essentially obviated the calls made in July to meet shortfalls in medical supplies and diagnostic services and hospital infrastructures (see *Clinica* No 1117, p 13).

Mercosur sets A&E and ICU standards

The Mercosur trading bloc's common market group (GMC) approved a series of resolutions establishing healthcare delivery standards across its member states in the areas of A&E and intensive care. The four healthcare-related resolutions approved at the GMC's latest meeting, held on October 6-8, in Brasilia, Brazil, include Resolution GMC 25/04 on the Common requirements for the approval of mobile A&E care units and Resolution GMC 28/04 on the Common requirements for adult intensive care units (ICUs).

Another healthcare-related Resolution (GMC/DT 23/04), no details of which have yet been published, is still the subject of an internal consultation in Brazil, says the GMC meeting report. Brazil is due to announce the results of this consultation (Draft Resolution 02/00) ahead of the next meeting of the GMC, but it is not clear whether it will be made public. The next meeting is scheduled to take place on November 25-26, in Belo Horizonte, Brazil.

Mexico and Chile sign manufacturing and R&D deal

Chile has welcomed as bringing "many more industrial and technological opportunities" the signing of a convention with Mexico for co-operation in areas that span biomedical manufacturing, healthcare R&D and service development. A specific plan of action is to be drawn up "within a short timeframe" by their respective health ministers and co-signatories, Pedro García Apillaga and Julio Frenk Mora.

The convention formalises a series of agreements reached in September. The importance of the initiative is evident in the wording of the joint declaration signed then by the two state presidents, Ricardo Lagos and Vicente Fox, pledging to "promote a strategic and global association in all areas of their bilateral relations".

While seeking to boost co-operation on an industrial level, the convention provides an opportunity to refocus on the application of medical technology for the benefit of the population, said Chilean minister, Dr García Apillaga.

COMPANY NEWS IN BRIEF

❑ ***BD invests $50m in Columbus expansion***
Becton Dickinson is to inject $50m into its Columbus, Ohio operations, adding two new manufacturing lines for prefilled syringes in response to growing demand BD told *Clinica*. The expansion, which also includes a new sterilisation building, will create 75 new jobs over the next 18 months. The company expects to complete one production line by early 2005 and the second in 2006.

❑ ***Stratagene to face PCR patent suit***
Applera has filed suit against research and immunodiagnostic tools manufacturer Stratagene for alleged infringement of its '934 patent. The products involved in the dispute are instruments used to perform real-time PCR. La Jolla, California-based Stratagene is already licensed to manufacture, use and sell PCR thermal cyclers originally developed by Applied BioSystems, one of Applera's two main business groups.

Haemonetics confirms under investigation in Italy

US company Haemonetics has confirmed to *Clinica* that it is under investigation in Italy as part of a criminal probe into equipment supply contracts at Niguarda Cà Grande Hospital, Milan. The automated blood processing system maker says its audit committee began an internal investigation several weeks ago, but that it is too soon to report any findings or corrective actions.

"The Italian authorities have given us no information. There have been no accusations, no formal inquiries, nothing like that, so we don't have any definitive information on the scope of the investigation," Haemonetics spokesperson Julie Fallon said. She confirmed that a former sales agent of the company has been arrested, but could not say whether his arrest related to his activities while working for the Braintree, Massachusetts-based company.

According to reports in the Italian media, representatives for Haemonetics, GTI and Immucor are under investigation for bribing Dr Federico Mercuriali, head of the immunohaematology department at Niguarda Cà Grande Hospital, to swing supply contracts for blood processing equipment in their favour. The probe is understood to be looking at least as far back as 2001. Dr Mercuriali, who committed suicide in early October after being placed under house arrest, allegedly paid the money into a Swiss bank account.

As a result of the investigations, Immucor's CEO, Dr Gioacchino De Chirico, has already had to stand down temporarily from his duties (see *Clinica* No 1131, p 16). He headed the company's Italian operations at the time it made a €13,500 ($17,000) payment to Dr Mercuriali, and also signed off the accounts as CEO. The invoice breached US laws because it did not specify the recipient or the services rendered, but the company insists it was an innocent mistake and that the payment was for a conference on its Galileo automated system that Dr Mercuriali chaired.

Although Immucor has publicly disclosed limited details of the matter, Haemonetics said it was under no obligation to do so in the US, and GTI was unobtainable for comment.

Another major US company that supplies similar equipment to the Italian market is Ortho-Clinical Diagnostics, a unit of Johnson & Johnson. OCD is not under investigation, and Willie Burns, vice-president for Europe, Middle East, Africa & Asia Pacific, told Clinica the company was "very confident that none of its business practices contravenes good business practice or international, US or local European laws". The company's Italian sales are around €70m, on worldwide sales in excess of $1bn.

NEWS IN BRIEF

❑ ***Roche says Biosite infringes two patents***

Roche Diagnostics has filed two patent infringement complaints against Biosite in a district court in Indiana. San Diego-based Biosite says the allegations, which refer to a device for separating plasma or serum from whole blood and analysing it and biosensing meter technology for use during the process, are without merit, and that it will contest the claims. Biosite recently reported a 43% increase in revenues to $61m and a 61% rise in net income to $10m as sales of its cardiovascular and drug screening products continued to expand.

Boston builds DES business with bioresorbable stent

Having successfully taken on the drug-eluting stent (DES) market with Taxus Express2, Boston Scientific is wasting no time in reinforcing its arsenal with a new-generation DES. The company has made an equity investment in REVA Medical, as well as securing an exclusive option to buy the private, San Diego-based developer of bioresorbable stents. Details of the agreement were not disclosed.

REVA's stents, made from tyrosine-derived polycarbonate co-polymers, are designed to perform comparably to metallic DESs and then be resorbed by the body once the artery has healed. The stent's slide-and-lock design gives the polymers the required strength to maintain structural integrity. REVA is developing an uncoated version of its stent as well as one coated with paclitaxel, the active agent used in Boston's Taxus Express2 DES.

According to Boston, some clinicians believe that bioresorbable stents enable them to treat multiple lesions in one patient as well as a wider range of vascular diseases. The company decided to invest in REVA as it believes the latter "has a better chance of solving the challenge of combining drug elution with a bioresorbable polymer stent platform than any other programme we've seen".

The rise and rise of the DES

Boston's stent business has been growing at an accelerated rate since the approval of its Taxus Express2 DES in the first quarter this year. Despite a summer tainted by recalls of certain units of its Taxus stents, the company recorded strong financial results for its third quarter. Revenues during this period reached $1.5bn, a 69% increase from the same quarter last year.

Net income doubled to $258m from $124m the previous year.

According to the company, demand for the Taxus Express2 DES continues to rise, albeit at the expense of its bare metal counterpart which has seen a decline in sales. Boston estimates that as of the end of the third quarter, around 85% of the stents used in interventional procedures have converted from bare metal systems to DESs.

Fischer Imaging let off hook in SEC inquiry

The US Securities and Exchange Commission has concluded its 16-month investigation into Fischer Imaging's accounting practices. While no civil money penalties were dealt to the Denver, Colorado-based company by the Commission, Fischer agreed to entry of an order that it cease and desist from violating certain provisions of the federal securities laws.

The SEC launched the inquiry in June 2003 after the company decided to restate its financial results for the years between 2000 and 2003.

The decision followed an internal investigation revealing that the company had breached federal accounting regulations by booking sales of products before customers had taken full delivery (see *Clinica* No 1062, p 13).

The company completed restatement of its financial results earlier this year and filed audited financial statements for the period in question with the Commission.

AED segment developments

Access CardioSystems closes amid defibrillator faults

A company that boasted of the comparatively low price of its automated external defibrillators (AEDs) has abruptly ceased operations after serious problems with its devices necessitated a worldwide recall.

Privately owned Access CardioSystems, of Concord, Massachusetts, said it was recalling all of its Access AEDs following reports of two types of defect. In some cases, the devices have turned on unexpectedly, and the on/off switch has ceased to work. In other instances, the AED's shock delivery circuit has failed. There were 33 complaints associated with the on/off problem, and 11 of "a catastrophic failure of the shock delivery circuit".

Although Access CardioSystems said initial investigations indicated the two types of failure were restricted to specific lots of its product, the company's cessation of business represents a serious issue for users of all of its devices. This is because they will be unable to order replacement disposable battery packs and electrode sets for their devices. AEDs are used by hospitals and emergency response agencies, and are increasingly being placed in public areas like airports and shopping centres.

Previous reports suggest more than 15,000 Access devices are in use around the world. It appears that the company is not offering any support for its customers, although *Clinica* was unable to obtain precise details because the company is not responding to enquiries. In the recall notice, it advises customers to discontinue use of Access AEDs when their disposables run out. "Customers should consider replacing the AEDs as soon as possible. It is your responsibility to equip yourself with AEDs that meet your medical needs," the recall notice states. Users with affected lot numbers are advised to remove the devices from service immediately.

Access CardioSystems was founded four years ago by physician Dr David Barash and medical device industry veteran Randall Fincke, and received FDA 510(k) marketing clearance two years later for its Access AEDs. Its devices were marketed as cheaper and lighter than many competing products. Other companies that make AEDs include Medtronic, Welch Allyn, Zoll Medical, Philips Medical Systems and Cardiac Science.

GE deal opens N Am AED market to Cardiac Science

Cardiac Science is looking forward to heightened interest in its automated external defibrillators (AEDs) from US and Canadian hospital customers following the signing of a new distribution agreement with medical products giant GE Healthcare. Under the deal, GE's hospital sales force will market the Irvine, California firm's devices in the first quarter of 2005. Cardiac Science's own reps will support the effort.

Included in the deal is Cardiac Science's Powerheart AED G3 PRO, a high-end AED designed for use by medical and emergency rescue professionals that received FDA clearance in August. GE will also sell the company's Powerheart AED G3 and its Powerheart CRM, a single device combining external defibrillation and therapeutic monitoring.

"To date, we have had little, if any, distribution capability in the US and Canadian hospital markets," said Cardiac Science's chairman and CEO, Raymond Cohen. "With GE as our distribution partner, we not only open up a new important market but are also provided with immediate credibility and access."

GE already markets Cardiac Science's G3 PRO outside North America under its own GE Responder AED PRO brand name.

According to market research by Frost & Sullivan, the worldwide AED market could be worth more than $650m in revenues by 2006.

NEWS IN BRIEF

❑ ***ATS to co-promote CryoCath AF ablation tech***

ATS Medical has signed an agreement to co-promote cryoablation products to treat atrial fibrillation made by Montreal, Canada-based CryoCath Technologies. While the co-promotion deal covers the US market, ATS will also assume exclusive distribution rights in the rest of the world. Minneapolis, Minnesota-based ATS Medical already has 30 sales people targeting over 300 US hospitals with the company's mechanical heart valves. While other cardiac ablation systems use heat to treat cardiac arrhythmias, cryoablation involves targeted freezing to create lesions on the heart. Separately, CryoCath received premarket application (PMA) supplement approval for Freezor Max, a new, more powerful version of its Freezor catheter device line.

Medtronic extends glaucoma line with new aqueous stent

Medtronic has bought the intellectual property rights to an investigational device for treating glaucoma, the CellPlant Aqueous Stent, from Wound Healing of Oklahoma Inc. Details of the transaction were not disclosed.

The acquisition represents a timely purchase as surgical procedures become increasingly prevalent as an alternative option to drugs for glaucoma management, says Medtronic. The glaucoma stent is designed to drain excess fluid and reduce pressure in the eye. It is implanted during a standard trabeculectomy, the second most common ophthalmic surgery worldwide after cataract removal. The device is made of a polymer with enhanced biocompatibility, which is designed to prevent cell adhesion and create a more effective, permanent passage for fluid outflow from the eye. The stent also eliminates the need for a filtering bleb, a permanent blister surgically created to enable drainage postoperatively.

Medtronic will begin clinical trials of the device after gaining FDA study approval. If successful, the CellPlant stent will enhance Medtronic Ophthalmic's current glaucoma product line, which includes the Tono-Pen XL portable applanation tonometer and ENDOLaser, an endoscopic laser treatment to reduce production of aqueous fluid.

Glaucoma is the second leading cause of blindness, with around 4.5 million people having lost their sight from the condition, according to the World Health Organization.

ClearStream floats on AIM, raising €7m

Irish company ClearStream Technologies has raised €7m ($9m) through a flotation on London's Alternative Investment Market (AIM). The Enniscorthy, County Wexford firm intends to invest the proceeds in R&D to build its pipeline of coronary, peripheral and carotid angioplasty products. It will also make a number of senior appointments.

Following the fundraising, management retains 21% of the company's stock, and its original venture capital investors hold 30%. Subscribers to the flotation included UK-based financial institutions and private investors.

The flotation comes just a few months after the Nasdaq debut of ClearStream's former parent company, AngioDynamics (Queensbury, New York), which focuses on peripheral vascular intervention products.

NEWS IN BRIEF

❑ ***Meridian to buy diagnostic bio component company***
Meridian Bioscience of Cincinnati, Ohio, has agreed to acquire all outstanding capital stock of OEM Concepts, a developer of biological components used in diagnostic tests. These monoclonal antibodies, which generated over $4m in revenues for Toms River, New Jersey-based OEM, are an important component in diagnostic tools for infectious diseases and for monitoring metabolic disorders, pregnancy and cardiac disease. The transaction, which involves a mix of cash and milestone payments, is expected to close within 60-90 days.

Integra to acquire foot implant maker Newdeal

Integra LifeSciences, of Plainsboro, New Jersey, is to pay €38.5m ($49.8m) in cash to acquire French group Newdeal. The deal will bring Integra a range of implants for foot and ankle surgery targeting a market worth about $500m worldwide.

The companies plan to combine Newdeal's know-how in orthopaedic implants with Integra's regeneration technology, which it uses in marketed products to treat chronic and traumatic wounds of the foot and ankle.

Greater European presence

Furthermore, the deal will expand Integra's direct sales force in Europe. Lyon-based Newdeal has an in-house sales force in France, Belgium and the Netherlands. Its products are sold in other countries, including the US, through distributors. Newdeal's management are to join Integra's leadership team, and the company's name will remain unchanged.

As a result of the deal, which Integra expects to close in January 2005, the company has upped its 2005 revenue projection from $270-280m to $290-300m. Newdeal's latest full-year sales were €13.8m, and its business has historically grown at 20% a year.

Integra recently reported third-quarter revenues of $59m, up by 26%, and highlighted strong growth in regeneration and wound dressing products. However, the company slipped into the red with a net loss of $7.6m against previous-year income of $6.8m, a major factor in this being charges related to the extension of president and CEO Stuart Essig's contract.

pSivida clinches first Japanese deal for BioSilicon

pSivida has partnered with Tokyo-based trading giant Itochu to develop and commercialise products derived from the Australian company's BioSilicon platform.

Under the agreement, the two firms will identify opportunities for licensing deals, direct investment, distribution agreements and development programmes for BioSilicon in Japan and other significant Asian markets, including Singapore, Korea, China and Hong Kong.

Itochu and Perth-based pSivida will focus initially on the existing range of BioSilicon products. This includes the lead brachytherapy technology, BrachySil, which recently demonstrated promising results for treating liver cancer in a phase IIa trial (see *Clinica* No 1129, p 20). The agreement also provides for the development of ingestible BioSilicon in the area of food technology.

pSivida's managing director, Gavin Rezos, anticipates that the products developed through this partnership would be ready for commercialisation in Japan within two years. According to Mr Rezos, Japan represents a fast-growing market for BioSilicon products in drug delivery, brachytherapy and diagnostics, as well as in non-core areas of tissue engineering, wound management and orthopaedics. "The Japanese market is growing for the same reasons as in Europe and the US," he says.

€50.2m S&S deal will give Whatman 16% market share

Whatman's planned purchase of Germany-based Schleicher & Schuell for £34.6m ($63.8m) will give the UK separations company a 16% share of the global lab sciences sector, making it the clear number three behind Millipore and Pall. The integration of Dassel-based S&S will increase Whatman's employee base by some 400 to over 1,110 and expand its sales by around 40%, the combined unit expecting sales in 2005 of some £116m, including £34m from S&S.

S&S's position in Germany will give Maidstone, Kent-based Whatman a stronger presence in Europe's largest market and will complement Whatman's presence in the UK and elsewhere in the EU. In the US, the enlarged group will benefit from S&S's presence in the US bioscience and medtech sectors and that of Whatman in lab sciences. S&S also has emerging bioscience technologies that have rapid growth potential, and which, with Whatman's FTA technology for DNA storage and analysis, gives the group strong medium-term growth prospects.

Revenue synergies will be available as of 2005 and cost synergies of £8m will have filtered down by 2007. Whatman chairman Bob Thian said: "This transaction has a compelling strategic logic. There is an excellent commercial and geographic fit between the two companies. S&S brings some very interesting new technologies." Whatman's shares rose by 22% on the news. Shareholder approval is expected on November 30.

MonoGen signs specimen automation distribution deal

MonoGen, a privately held company focusing on laboratory automation, has secured a distribution deal with Cardinal Health. The Dublin, Ohio-based healthcare product and service provider will sell MonoGen's new MonoPrep system, which automates the preparation of patient samples prior to cell-based diagnosis.

"Specimen automation is a new and fast-growing capability for the pathology lab. We're getting in at the front end of what could be an entirely new platform in diagnostics," commented Mark McLoughlin, vice-president and general manager of scientific products distribution at Cardinal Health.

The current system is for a range of general cytology applications. MonoGen is preparing a second system that will target women's health, for which the Vernon Hills, Illinois firm expects to apply for FDA marketing approval later this year.

NEWS IN BRIEF

❑ ***Expansion for DiaSys in Latin America***

Diagnostic test maker DiaSys is building its business in Latin America with the recent signing of two new distribution deals. Costa Rica's biggest clinical diagnostic products distributor, Tecnodiagnostica, and Venezuelan firm Repreclin will distribute DiaSys products in their respective markets. The Waterbury, Connecticut-based firm sees a particularly good opportunity for its parasite and urine testing products in these markets.

Cyberonics sales hit by FDA rejection

Cyberonics' summer of discontent has taken its toll as the company recorded a $2m loss in net earnings for the second quarter, a contrast to last year's performance when the company netted a profit of nearly $4m during the same period. Second-quarter revenues also took a 13% fall from the previous year's level to $25.4m.

The company has so far incurred a total net loss of $4.6m since the start of the new fiscal year, partly because of increased spending on regulatory activities related to its application to market its Vagus Nerve Stimulation device for depression. However, the US FDA dealt Cyberonics a hard blow in August when it rejected the company's application on the grounds of insufficient data (see *Clinica* No 1121, p 1).

Robert Cummins, Cyberonics' CEO and chairman, says that the quarterly results were in line with the company's revised guidance and that they had achieved their sales objective "in spite of the considerable distraction" caused by the non-approval letter from the FDA.

Shaken but undeterred, the company submitted additional data to the FDA through a PMA supplement amendment in September and is now expecting to receive a decision from the FDA by the end of January 2005, says Mr Cummins.

In the meantime, financial recovery seems unlikely in the short term as the company predicted flat sales of around $25m for the third quarter and a bigger loss in earnings of $3.3m.

Ceapro en route to diabetes test launch

Ceapro is to see in the new year with the Canadian launch of its AccuScreen Type 2 diabetes and prediabetes test.

The test involves the patient consuming 10 specially calibrated wafers – each containing standardised amounts of carbohydrate, fat and protein – then measuring their blood glucose levels with a handheld glucometer 45 minutes later. According to Ceapro, the AccuScreen provides faster and more accurate results than currently available diabetes tests. Its accuracy is more than 85%. In addition, it is the only diagnostic tool available for testing prediabetes, or impaired glucose tolerance, a condition in which the patient has elevated levels of glucose but is not clinically diagnosed with diabetes. Early intervention at this stage could prevent or delay the onset of diabetes.

AccuScreen will be marketed through pharmacies and healthcare providers and is designed for home use as well as in clinics. Edmonton, Canada-based Ceapro adds that it has plans to introduce the test in the US, Japan, South America and the UK.

The Canadian Diabetes Association says there could be up to 1 million undiagnosed diabetics in the country, as well as 2 million who know they have the disease. In the US, meanwhile, there are 18.2 million diabetics, of whom 5.2 million are unaware of their condition, according to the US National Institute of Diabetes and Digestive and Kidney Diseases. It is believed that around 16 million people in the US have prediabetes.

TriPath identifies biomarkers for cervical cancer screener

TriPath Imaging has identified a number of biomarkers it believes will help improve the detection of cervical dysplasia and cancer. The company hopes to develop a formulation of the markers for use with its cervical cancer screening test, SurePath. Clinical trials are planned to begin next year.

Research, presented at this month's American Society of Cytopathology meeting, in Chicago, showed that formulation of the combined biomarkers was 93% sensitive and 92% specific in identifying biopsy-confirmed moderate to severe cervical dysplasia. Levels of the biomarkers' expression also indicated the risk of developing cancer. "Our studies indicate that these research biomarkers are over-expressed in biopsy-confirmed high-grade cervical disease cells and are minimally expressed in normal proliferating cells and low-grade cervical dysplasia," said Douglas Malinowski, TriPath's chief scientific officer. The company would not disclose the combination the biomarkers took, but did tell *Clinica* it included MCM2, MCM7, topoisomerase II, P16 and intergrin Beta 6.

The formulation is currently being developed for use with the company's SurePath liquid-based Pap test. "Patient samples would be collected in the SurePath test pack, as they are today. Unstained slides could then be prepared, and then stained with proprietary TriPath reagents using specific biomarkers in an easy-to-use immunocytochemistry assay. Slide interpretation will then be based on both biomarker reactivity and cellular morphology," said Paul Sohmer, chairman, president and CEO of TriPath.

"We expect to initiate a clinical trial in 2005 that could support an application for US FDA premarket approval," he added.

The combination of biomarkers is not just confined to cervical cancer. TriPath expects to initiate research on other cancers as well. "Over-expression of these biomarkers has been associated with several other types of cancers, including oesophageal, lung, colon and breast cancers," said Dr Sohmer.

Smart stethoscope "listens in" on kidney stone break-up

Using a small stethoscope-like device placed near to the patient, doctors can now hear when a kidney stone has been successfully treated with lithotripsy, UK researchers claim. Further therapy can then be administered according to the feedback received. The developers of the device hope the product will help reduce the number of patients who require re-treatment for their kidney stones - currently 50% - which is often time consuming and costly.

The "smart stethoscope" works similarly to a normal stethoscope, picking up sounds reverberated from the kidney stones, and transmitting the signal back to the user for interpretation. "When the stone is intact you hear a 'tick' and when the stone becomes fragmented you hear a 'tock'," described Tim Leighton at the Institute of Sound and Vibration at Southampton University. "The device just sits there and listens," said Dr Leighton. "It allows doctors to determine if they are giving too much or too little therapy, tailoring the dosage accordingly."

Developed in collaboration with Dr Andrew Coleman of the Guy's and St Thomas' NHS Foundation Trust, the smart stethoscope has already been tested in over 50 patients, with a commercialisation agreement currently under negotiations, Dr Leighton told *Clinica*. "The trials worked very well. In the 12 cases where our mark 3 version of the product was used, doctors observed 100% effectiveness with the device."

Kidney stones are crystalline structures that form on the kidney's inner lining. Shockwave lithotripsy is the most common treatment given and involves delivering high frequency sound waves to break the kidney stone into fragments small enough to be passed out via the urinary tract.

Development of the smart stethoscope was part-funded by the UK EPSRC (The Engineering and Physical Sciences Research Council), but after reaching the clinical data limit allowed by the funding agency, Dr Leighton and his team are now seeking additional sources of finance. Dr Leighton said the device might also have some application in lithotripsy-assisted bone healing, but added that this route required further examination.

bioMérieux puts Novel's TB test on 12-month trial

French firm bioMérieux is funding a 12-month trial to test the efficacy of Novel Diagnostics' antibody technology for TB detection, PlasmAcute. A product could be commercially available next year if the collaboration proves successful, Novel Diagnostics told *Clinica*.

Novel will run the two-stage TB trial in Paris, with the company aiming to implement PlasmAcute in over 1,000 TB patients during the course of the year. According to the Bergen, Norway-based company, PlasmAcute is the first and fastest diagnostic available for "acute" TB, and is able to detect the TB bacterium from as early as three days after infection. "We can take a sample from a prick of blood and give you an answer in two hours", said David Parker, Novel's chief scientific officer. Such a feature is particularly important for contagious diseases, such as TB, where one of the aims is to reduce the spread of infection.

Traditional tests work by detecting antibodies once they reach a critical level in blood serum. However, these can take up to 10-12 days to obtain. Novel's approach is to track the antibodies to their source: B lymphocyte (B cells), detectable at 3-4 days. These cells then differentiate into the plasma cells that emit the antibodies. "What we do is break into the cell and take the antibodies before they reach the end of the production line."

"bioMérieux has given itself 12 months to make up its mind on PlasmAcute, but I expect the company to have made a decision by the end of phase one [planned to be completed by January]," Dr Parker added. "After that, bioMérieux could have a product out within six months."

Dr Parker said Novel had "hit the jackpot" in its deal with bioMérieux, but added that it has been in contact with other manufacturers regarding further applications of PlasmAcute. "We are talking to a number of other companies about our technology," he said, noting that the cost of the test would depend upon the terms of the manufacturing agreement.

Evidence mounts for Evalve's mitral regurgitation clip

Paving the way for percutaneous cardiac valve repair, a tiny metallic clip that is deployed to the heart via a catheter to treat mitral regurgitation is continuing to show promise in a feasibility trial.

The device, made by Redwood City, California firm Evalve, is building a favourable safety and feasibility profile as the phase I stage of the study – called EVEREST I – nears its completion, reported trial investigators from the Hospital of the University of Pennsylvania, in Philadelphia.

Evalve's clip works by grasping both valve leaflets and fastening them together to reduce mitral regurgitation, which occurs when the valve fails to close properly, allowing blood to leak back into the left atrium. Importantly, the device provides doctors treating the disorder with a less invasive modification of an already proven and established surgical technique, called "edge-to-edge" repair. Because the procedure is less invasive than surgery, it is expected to reduce morbidity, mortality, patient pain, recovery time and the length of time a patient has to stay in the hospital.

The product made the headlines in March this year, when an assessment of the first 10 patients in EVEREST I showed the device to be technically possible and, in certain cases, successful at reducing mitral regurgitation (see *Clinica* No 1103, p 17). To date, a total of 24 patients with mitral regurgitation have received the clip as part of the multicentre trial, which is being conducted under a US FDA-approved investigational device exemption. At last week's American Heart Association (AHA) meeting, in New Orleans, the Pennsylvania team revealed positive results from their assessment of 15 patients to undergo the procedure.

Successful valve coaptation was obtained in all patients, the researchers said. Clip implantation with an immediate reduction in mitral regurgitation was accomplished in 12 patients (80%). Success was achieved in 70% of the first 10 patients and 100% of the next five patients after the protocol was modified to allow placement of two clips (two patients). There were no procedural complications. At a 30-day follow-up, there was a partial clip detachment in one patient who underwent successful elective surgical repair, but no other major adverse events occurred. The mean time to implant the device time fell from 219 minutes in the first six single-clip cases to 153 minutes in the second six cases. All patients were discharged home at a mean of 1.8 days post-procedure.

The study, led by Howard Herrmann, concluded that the percutaneous approach for mitral regurgitation was feasible and safe. In addition, procedural time was reduced through experience and technique improvements, and the option to use two clips increased efficacy. Further study of the technique in a phase II study is warranted, the researchers said, noting that such a trial may be initiated later this year.

In May this year, it was announced that Guidant had invested $15m in Evalve (see *Clinica* No 1109, p 15). Guidant also committed to investing a further $15m based on milestones. The investment was part of a $35m financing round including existing venture capital investors.

American Heart Association®

Breaking news from the annual AHA meeting in New Orleans by Neena Brizmohun.
See issue 1132, p 21 for first report and next week's *Clinica* for more coverage.

"Rescue" angioplasty proves best for failed thrombolysis

In what promises to have an impact on clinical practice for heart attack cases, a UK study has found that "rescue" angioplasty is the best strategy for patients in whom thrombolysis therapy has failed.

Thrombolysis fails to reopen blocked arteries in up to 40% of heart attack cases treated within 12 hours of their onset, said study investigator, Anthony Gershlick, of the University of Leicester. While some doctors attempt to improve vessel patency by using another boost of thrombolytics, many have intuitively used rescue angioplasty to reopen the vessels, despite a lack of scientific evidence that the latter approach provides any benefit.

In a trial called REACT (REscue Angioplasty versus Conservative therapy or repeat Thrombolysis), Dr Gershlick and colleagues sought to examine the usefulness of rescue angioplasty for failed thrombolysis.

Some 427 patients with acute heart attack who had failed to respond to an initial dose of thrombolytics were randomised to either one of three groups: repeat thrombolysis, conservative treatment (using heparin), or rescue angioplasty. The primary endpoint of the trial was a composite of death, another acute heart attack, severe heart failure or stroke.

At a six-month follow-up, the incidence of any event was reduced by around 50% in the rescue angioplasty patients, compared with either repeat thrombolysis or conservative therapy groups. The survival rate for rescue angioplasty was 84.6%, versus 68.7% for repeat thrombolysis and 70.1% for the conservative approach. There was also benefit associated with rescue angioplasty in terms of the need for further revascularisation. "Patients in the rescue angioplasty arm needed much less repeat procedures than those who were randomised to the conservative or thrombolysis arm," Dr Gershlick said in a presentation of the findings at this month's American Heart Association meeting in New Orleans.

The REACT trial demonstrates for the first time that following failed lysis, rescue angioplasty provides the best clinical outcomes, Dr Gershlick continued. "I think that the findings will make a difference to medical practice."

Biosensors International gets DES study boost

In what could intensify competition in the drug-eluting stent (DES) arena, Singapore firm Biosensors International has released positive results from a first-in-man trial of its BioMatrix device.

Six-month follow-up data from the company's STEALTH study of the Biolimus A9-eluting coronary artery stent showed that the device was safe and significantly reduced neointimal hyperplasia - the process leading to restenosis or reblocking of an artery.

The findings, presented last week at the American Heart Association meeting in New Orleans, promise to create new rivalry in the DES market, which is currently dominated by Boston Scientific and Johnson & Johnson.

BioMatrix comprises Biosensor's bare metal S-Stent and releases its drug component from a bioabsorbable PLA polymer coating. "Currently approved drug-eluting stents use a permanent polymer coating to release the anti-stenosis drug. After drug release, the permanent polymer remains inside the patient's coronary artery for life," said STEALTH investigator Alexandre Abizaid, of the Instituto Dante Pazzanese of Cardiology in São Paulo, Brazil. Because BioMatrix uses a bioabsorbable coating that during drug release dissolves into natural products that are excreted by the body, the device may offer potential advantages over permanent stent coatings by eliminating concerns over long-term structural failure or chronic inflammatory effects of the polymer, Dr Abizaid postulated.

Biolimus A9 is in the "limus" family of anti-restenosis compounds and is similar to the drugs being used by J&J and two other companies yet to enter the DES market, Guidant and Medtronic. "It is a new rapamycin derivative pharmaceutical that is being developed to improve upon the pharmacokinetic properties of the 'limuses' for implantable 'on-stent' medical device coating applications," said Dr Abizaid. However, he admitted that it was still unknown whether structural changes to the rapamycin molecule would lead to improved efficacy, particularly in high-risk subgroups.

The STEALTH study was a 120-patient, double-blinded, randomised trial conducted at heart centres in Germany and Brazil. It was designed to demonstrate the safety and efficacy of BioMatrix in de novo coronary lesions.

At the six-month follow-up, angiographic analysis indicated a low restenosis rate (3.9%) in the DES group, compared with the bare-metal stent control group (7.7%). There was also a decreased late loss - thickness of the scar tissue that forms inside the stent - in the DES group (0.26mm), versus the control group (0.74mm). No restenosis occurred at the proximal or distal edges of the stent in either group. Intravascular ultrasound analysis showed that the percentage neointimal volume - a measure of the total volume of scar tissue formed inside a stent - was significantly lower in the DES group (2.6%), compared with the control group (23.5%).

The incidence of late acquired incomplete stent apposition was low in both groups (3%) and compared favourably with other currently marketed DES products, said Biosensors.

Commenting on the study, US analyst Glenn Reicin from Morgan Stanley said the results were "impressive, especially when one considers that patients in the trial were slightly more challenging than other comparable first-in-man studies, with slightly more diabetics and patients with longer lesions". He added that the company planned to initiate a first-in-man study in the US in the first half of 2005, with a pivotal trial following in the first half of 2006, a move that "would potentially put them in the US market in 2008". Mr Reicin continued: "Biosensors could be one of several new DES players to get approval in Europe in 2005 and 2006, making things generally more difficult for J&J and Boston Scientific."

ICDs are cost-effective in landmark heart failure trial

Eight months after showing that a large group of heart failure patients can live longer if they receive an implantable cardioverter-defibrillator (ICD), a landmark study has now revealed that treatment with the device is also cost-effective.

The cost of using ICD therapy to add one year of life for patients with moderate heart failure and poor heart pumping action is $33,192, according to an economics analysis of data from the trial, called SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial). The cost is well within the $50,000 range typically considered to represent a cost-effective therapy.

"The conclusion from this cost analysis is clear: implantable defibrillators represent an economically attractive way to save lives in many people who have moderate, stable heart failure due to a damaged heart muscle," said study investigator Daniel Mark, of the Duke Clinical Research Institute, in Durham, North Carolina. "It is highly unusual and very exciting that we have a therapy that provides such a significant impact on saving lives and does it efficiently from an economic standpoint."

Noting that ICD therapy comprises less than 1% of the Centers for Medicare & Medicaid (CMS) annual budget, ICD manufacturer Medtronic, said that the analysis demonstrated that the treatment was "an appropriate and valuable use of healthcare dollars".

The findings, presented at this month's American Heart Association meeting, in New Orleans, also support CMS' decision in September this year to expand Medicare's coverage of ICDs in the heart failure population (see *Clinica* No 1126, p 11). The agency's verdict was based largely on findings from SCD-HeFT, which, in March showed that ICDs reduced death by 23% in the group of heart failure patients studied in the trial, compared to those who did not receive defibrillators (see *Clinica* No 1099, p 1). At the time, CMS claimed its ruling was likely to increase the number of beneficiaries who might qualify for the device by about one third, or 500,000 patients.

SCD-HeFT was a randomised, placebo-controlled, three-arm study examining the use of ICD therapy and anti-arrhythmic drug therapy in 2,521 patients with moderate heart failure and impaired pumping function of the left ventricle. One-third of the patients enrolled in the study received an ICD provided by Medtronic, which helped fund the US National Institutes of Health-sponsored trial.

AHA conference report by neena.brizmohun@informa.com

Blood test may determine risk of stillbirth

A blood test performed in the early stages of pregnancy could help identify women at high risk of stillbirth.

So says a UK study published in the *Journal of the American Medical Association* (November 10), which showed that women with low levels of the pregnancy-associated plasma protein A (PAPP-A) during the first 10 weeks after conception, were 40 times more likely to have a stillbirth as a result of placental dysfunction. The research examined the records of nearly 8,000 women who had given birth in Scotland from 1998 to 2000. These were then divided into five further subgroups based on their level of PAPP-A in the first trimester. A low PAPP-A level increased the risk of all-cause stillborn (up 9.2-fold), stillbirth due to abruption (58-fold) and stillbirth due to placental dysfunction (46-fold). Lead study author, Professor Gordon Smith from the University of Cambridge, said a test to measure blood levels of PAPP-A could be available within the next 5-10 years.

NEWS IN BRIEF

❑ ***CMA Microdialysis gets CE marking for ISCUS***
Swedish firm CMA Microdialysis has CE marked for sale in Europe its portable, bedside analyser, ISCUS. The device monitors the tissue biochemistry of vital organs by measuring levels of glucose, lactate, pyruvate and glycerol collected from a microdialysis catheter. ISCUS was designed for use in the intensive care setting, the Stockholm-based company says.

Early data back CryoLife's spinal disc repair tech

Pre-clinical data, presented at this month's IN SPINE Medtech conference in Dallas, Texas, has supported the potential role of CryoLife's BioDisc spinal disc nucleus system in restoring structural integrity to damaged vertebra.

The study compared the mechanical properties of intact normal calf spinal segments, denucleated calf spinal segments, and BioDisc-repaired calf spinal segments. The findings showed that the denucleated calf spinal segments resulted in a significant drop in stability, compared with the normal and BioDisc-repaired spinal segments. The BioDisc also withstood over 10 million cycles of compression, demonstrating the product's level of durability, the Kennesaw, Georgia company noted. Under high levels of stress, spinal discs may weaken, and then rupture, causing the inner part of the disc, called the nucleus pulposus, to become displaced. The BioDisc is designed to fill the gap left by the nucleus pulposus using a protein-based hydrogel, a material already approved for use as a surgical adhesive in the US and Europe.

NEWS IN BRIEF

❑ ***Exactech gains US nod for shoulder prosthetic***
Orthopaedic device manufacturer Exactech, has received US FDA 510(k) market clearance for its Equinoxe shoulder system. The company said that the prosthetic represents the next generation in complex shoulder fracture treatments, and should be available for sale in a full market release, early next year. Equinoxe combines robustness with complex anatomic precision to provide doctors with intraoperative flexibility. It is estimated that up to 25,000 shoulder arthroplasty procedures are carried out each year in the US, generating around $100m in revenue per year, said the Gainesville, Florida firm.

❑ ***Medtronic steams ahead with carotid stenting trial***
Medtronic has begun the third in a series of studies to evaluate its system of devices to treat blockages in the carotid arteries that can lead to ischaemic strokes. The MAVErIC III clinical trial will gather data for submission to US regulatory authorities to evaluate the safety and efficacy of a combination of the firm's Interceptor PLUS carotid filter system and Exponent self-expanding carotid stent. It has already enrolled the first patient and will include 413 high-risk patients at 35 centres in North America. According to the American Heart Association, carotid stenting is expected to grow from about 17,000 procedures this year to more than 125,000 worldwide in 2008, Medtronic said.

❑ ***BD's glucose tests cleared for additional test sites***
Becton Dickinson has gained US go-ahead to expand the number of sites on the body on which it can use its blood glucose monitors – the BD logic and the Paradigm Link. Previously the products were only recommended for fingertip testing, however, repetitive injection can often make the site uncomfortable and inconvenient. The device can now be used on the palm and forearm. The Franklin Lakes, New Jersey company says that while other meters on the market have been cleared for alternate site testing, BD is now one of only a few that can claim that palm testing is equivalent to fingertip testing for blood glucose monitoring systems.

COMPANIES MENTIONED IN THIS ISSUE

PEOPLE

❑ Durham, UK-based imaging tools supplier **Bede** has named *John Smith* as global operations director. He has also been appointed a full member of the executive committee. Mr Smith previously held positions with DEC, Compaq, Applied Materials and, most recently, Celerity Systems.

PEOPLE

❑ *Stephen Campbell* has been named chairman of the **Medical Industry Association of Australia** (MIAA). He has been a member of the board since 2000, and is the general manager of the healthcare division of Kimberly-Clark Australia. The MIAA represents the Australian device and diagnostics industry. Current issues for the board include the new IVD legislation, and legislation governing the establishment of the new Trans Tasman joint regulatory agency.

❑ Medical imaging product manufacturer **Guerbet** (Solihull, UK) has appointed *Ginette Camps-Walsh* as UK general manager. She will be responsible for all aspects of marketing, sales, customer service and distribution. Prior to this appointment, Ms Camps-Walsh served as a general manager for a supplier of GI contrast agents and interventional radiology products. Her background includes R&D in immunodiagnostics with Amersham.

❑ *Wolfhart Hauser* has been appointed CEO of international testing, inspection and certification organisation **Intertek** (Leatherhead, Surrey, UK). Dr Hauser is a former head of German testing firm TÜV Süd. He has served as a non-executive member of Intertek's board since October 2002.

❑ **PhotoCure ASA** (Oslo, Norway), a developer of medical device and pharmaceutical products for the photodynamic treatment of cancer, has appointed three new senior executives and made two promotions. *Grete Hogstad* has been named vice-president of sales and marketing, effective February 1 2005; *Pål Bråthen* has been appointed vice-president of business development; and *Christian Fekete* has been named CFO. Vice-president of research and development *Kjetil Hestdal* has been promoted to COO, and finally, *Hilde Morris*, former vice-president of strategic marketing, will become vice-president of research and development.

❑ **Trinity Health** has selected a new president and CEO. *Joseph Swedish* will begin his new role on January 1 2005. He has served in the same capacity for Centura Health since 1999. Trinity Health is a 45-hospital Catholic, not-for-profit healthcare organisation based in Novi, Michigan.

❑ Medical aesthetic device manufacturer **Syneron Medical** (Yokneam, Israel) has appointed *Dan Suesskind* and *Michael Anghel* to its board of directors, serving as both independent directors, and as external directors (for Israeli law purposes). Mr Suesskind is CFO of Teva Pharmaceutical Industries, a generic drug company. Dr Anghel is president and CEO of the Israel Capital Markets and Investments Corporation.

❑ **InterGenetics** (Oklahoma City, Oklahoma), a company focused on cancer genetics, prevention, diagnostics and therapeutics, has elected *Donald Capra* to its board of directors. Dr Capra is president of the Oklahoma Medical Research Foundation. The firm has also appointed *Gene Rainbolt*, chairman of BancFirst, to its board.

❑ Mountain View, California-based **RITA Medical Systems** has announced the election of *Thomas Dugan* to its board of directors, effective immediately. Mr Dugan had previously served as president of Inter Vascular, a subsidiary of Datascope, and has also served for Tyco Healthcare. He fills the seat created by John Gilbert's resignation last month.

send people announcements to: kellie.mundell@informa.com

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