MEDICAL DEVICE DAILY™

THE DAILY MEDICAL TECHNOLOGY NEWS SOURCE

MONDAY, OCTOBER 3, 2016 VOLUME 20, NO. 191

MICROCHIP-BASED DIAGNOSTICS

Contract awarded to advance analysis for antimicrobial resistance, influenza

By Amanda Pedersen, Senior Staff Writer

About 15 years ago Chris Toumazou imagined that if the electronics industry could scale down electronic circuits so that they were smaller, faster, and cheaper to produce – paving the way for consumer-based products like mobile phones and tablets – it might be possible to apply microchips to the health care industry.

Inspired by that idea, Toumazou, a professor at Imperial College London, invented a way of detecting protons released during DNA synthesis to enable DNA sequence detection using a standard silicon-chip based transistor. This optics-free, label-free method shifted DNA sequencing from specialized, expensive genome centers into the mainstream of local labs and primary care clinics. Now, the company that Toumazou

See DNA, page 4

DISRUPTIVE TO TAVR

First bioabsorbable heart valves implanted as Xeltis tests technology

By John Brosky, Contributing Writer

PARIS – The first artificial heart valves to use a bioabsorbable, synthetic material for valve leaflets were implanted in three pediatric patients this summer as part of a first-in-man clinical trial for Xeltis AG based in Zurich, Switzerland.

The company reported the world-first news at the meeting of the European Association for Cardio-Thoracic Surgery (EACTS) being

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REGULATORY

Attorney says Yates memo's effect mostly on relations with corporate employees

By Mark McCarty, Regulatory Editor

The memo regarding prosecution of False Claims Act violations by deputy attorney general Sally Qullian Yates is roughly a year old, and a couple of cases have come through demonstrating that individual culpability is indeed the focus of federal prosecutors. However, an attorney told *Medical Device Daily* that

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Australia's R&D tax incentive could hurt small med-tech and biotech companies

By Tamra Sami, Contributing Writer

PERTH, Australia – The Australian government's release of the Review of the R&D Tax Incentive met a mixed response from the biopharma and med-tech communities operating in the country.

If the recommendations outlined in the report are implemented as proposed, they would have a "very bad impact" on early-stage companies in the med-tech and

See Tax, page 7

FASTER VIEWING OF IMAGES

Canadian company to show off improved version of minimally invasive radiology device

By David Godkin, Staff Writer

A Vancouver, B.C.-based med-tech company is set to launch the second iteration of a Human Machine Interaction (HMI) device designed to streamline surgical workflows and provide a faster and more efficient way to read

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IN THIS ISSUE

NEUROLOGY EXTRA

Executive Editor Holland Johnson and Senior Science Editor Anette Breindl on one of med-tech's key sectors

Read this week's Monday Special

OTHER NEWS TO NOTE

Greiner Bio-One North America Inc., of Monroe, N.C., is helping to sponsor a National Institutes of Health-funded collaborative effort between Scripps Florida, Cold Springs Harbor Laboratory (CSHL) and **Nano3-D Biosciences Inc**., of Houston, Texas, to advance high-throughput screening (HTS) 3D spheroid based technology aimed at early drug discovery and clinical cancer biology. This work will involve the development of 3D spheroid technologies into 384-well and 1,536-well formats that are automation amenable for HTS drug screening.

Medtronic plc, of Dublin, Ireland, said two previously communicated global voluntary recalls related to Framingham, Mass. Heartware International Inc's HVAD System have been classified as Class 1 by the FDA. Class 1 recalls describe situations where there is reasonable risk of serious adverse health consequences or death. In a safety notification letter distributed globally in May and June 2016, Heartware notified physicians regarding potential damage to controllers from exposure to moisture through loose power and data connectors. In the U.S., all clinician notifications have been acknowledged, and globally 99 percent of clinician notifications have been acknowledged. Hospital clinicians were advised to inspect patients` HVAD Heartware Controllers for loose connectors at patients` regularly scheduled appointments and to replace affected controllers with a new controller at the clinicians` discretion. Clinicians also were advised to remind patients about the safe use of the HVAD System, particularly with regard to moisture and proper connection to power and data sources. Damage to the controllers from this issue could cause loss of communication between the controller and monitor, reduced ability to detect alarms or interruption of circulatory support due to pump stop, which could lead to serious injury or death. Medtronic first reported it would acquire Heartware in June. (See, *Medical Device Daily*, June 28, 2016.)

MEDICAL DEVICE DAILY

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BUSINESS OFFICE

Donald R. Johnston (Senior Director, Current Awareness), Penney Holland (Web Production Manager)

10 BIGGEST U.S. WINNERS FOR THE WEEK

By Percent		By Dollars	
Stereotaxis	35.94	Intuitive Surgical	14.61
Bovie Medical	23.46	Abiomed	5.06
Accuray	12.54	Athenahealth	2.29
Transenterix	9.74	Zimmer Biomet	1.69
Mazor Robotics	5.33	Thermo Fisher Sci	1.40
Abiomed	4.10	Idexx Laboratories	1.37
Strata Skin Sciences	3.92	Varian Medical	1.36
Spectranetics	3.51	Mazor Robotics	1.31
Cardiovascular Syst	3.22	Hill-Rom Holdings	1.20
RTI Surgical	2.62	Bovie Medical	0.99

10 BIGGEST U.S. LOSERS FOR THE WEEK

By Percent		By Dollars	
Echo Therapeutics	-47.95	C.R. Bard	-5.63
Delcath Systems	-34.87	Teleflex	-3.50
Titan Medical	-23.61	Cantel Medical	-3.15
Sunshine Heart	-22.22	Cynosure	-1.99
Biolase	-9.33	The Cooper Cos	-1.71
Tearlab	-8.54	Henry Schein	-1.47
Fluidigm	-6.53	Stryker	-1.35
Novocure	-6.46	Vascular Solutions	-1.33
Dehaier Medical	-5.92	Penumbra	-1.33
Cantel Medical	-3.88	Delcath Systems	-1.33

MDD STOCK REPORT FOR PUBLIC MED-TECH COMPANIES

COMPANY	SYMBOL	CLOSE 9/23	CLOSE 9/30	%CHANGE WK	%CHANGE YTD	VOL (000)
Abbott Laboratories	ABT	42.19	42.29	0.24	-6.06	31519
Abiomed	ABMD	123.53	128.59	4.10	36.83	2196
Accuray	ARAY	5.66	6.37	12.54	-16.15	4583
Agilent Technologies	A	46.61	47.09	1.03	11.48	9355
Alere	ALR	43.24	43.24	0.00	10.62	2280
Align Technology	ALGN	94.13	93.76	-0.39	42.95	2551
Allscripts Healthcare	MDRX	13.25	13.17	-0.60	-13.85	9137
Athenahealth	ATHN	123.83	126.12	1.85	-23.07	1226
Baxter International	BAX	47.49	47.6	0.23	24.48	15665
BD	BDX	179.5	179.73	0.13	16.49	3671
Biolase	BIOL	1.93	1.75	-9.33	129.46	312
Boston Scientific	BSX	23.71	23.8	0.38	28.58	42141
Bovie Medical	BVX	4.22	5.21	23.46	100.95	1483
C.R. Bard	BCR	229.91	224.28	-2.45	21.36	2571
Cantel Medical	CMN	81.13	77.98	-3.88	30.56	1209
Cardiovascular Syst	CSII	23	23.74	3.22	52.12	1935
Checkcap	CHEK	2.05	1.98	-3.41	8.47	140
Conmed	CNMD	39.83	40.05	0.55	-9.58	593
Cynosure	CYNO	52.93	50.94	-3.76	18.49	942
Dehaier Medical	DHRM	1.6901	1.59	-5.92	-25.28	20
Delcath Systems	DCTH	3.8	2.475	-34.87	-52.50	464
Dentsply Internat	XRAY	59.36	59.43	0.12	-2.45	6699
Echo Therapeutics	ECTE	0.73	0.38	-47.95	-48.59	376
Edwards Lifesci	EW	119.77	120.56	0.66	51.65	4323
Endologix	ELGX	12.74	12.8	0.47	28.69	3154
Fluidigm	FLDM	8.57	8.01	-6.53	-20.72	503
Haemonetics	HAE	37.48	36.21	-3.39	16.25	1496
Halyard	HYH	33.96	34.66	2.06	1.65	1605
Henry Schein	HSIC	164.45	162.98	-0.89	3.96	2131
Hill-Rom Holdings	HRC	60.78	61.98	1.97	26.47	1888
Hologic	HOLX	38.45	38.83	0.99	-0.62	9220
iCAD	ICAD	5.19	5.2	0.19	0.39	200
ICU Medical	ICUI	126.34	126.38	0.03	12.02	538
Idexx Laboratories	IDXX	111.36	112.73	1.23	52.72	1658
Inogen	INGN	61.04	59.9	-1.87	52.26	841
Intersect ENT	XENT	15.78	15.84	0.38	-29.87	793
Intuitive Surgical	ISRG	710.22	724.83	2.06	29.98	1372
Invuity	IVTY	13.44	13.72	2.08	52.38	334
Iridex	IRIX	14.73	14.49	-1.63	58.56	72
Labcorp	LH	137.39	137.48	0.07	11.12	2927
Livanova	LIVN	61.03	60.11	-1.51	2.80	1778
Luminex	LMNX	22.79	22.72	-0.31	6.55	800
Masimo	MASI	59.77	59.49	-0.47	43.99	1114
Mazor Robotics	MZOR	24.56	25.87	5.33	141.73	588
Medtronic	MDT	87.71	86.4	-1.49	14.07	19564
Meridian Bioscience	VIVO	19.77	19.29	-2.43	-3.65	852
Novocure	NVCR	9.13	8.54	-6.46	-59.17	1055
Nuvasive	NUVA	66.77	66.66	-0.16	23.40	2418
Nxstage Medical	NXTM	24.78	24.99	0.85	13.10	1942
Orthofix Internat	OFIX	43.56	42.77	-1.81	11.09	499
Pavmed Inc.	PAVM	14	14	0.00	180.00	3
Penumbra	PEN	77.32	75.99	-1.72	43.69	839
Quest Diagnostics	DGX	85.44	84.63	-0.95	20.10	4171
Quidel	QDEL	22.71	22.09	-2.73	7.12	751
RTI Surgical	RTIX	3.05	3.13	2.62	-23.17	557
Senseonics Holdings	SENS	3.97	3.9	-1.76	22.15	464
Smith & Nephew	SNN	33.35	32.78	-1.71	-6.32	3706
Spectranetics	SPNC	24.24	25.09	3.51	60.96	1604
St. Jude Medical	STJ	79.64	79.76	0.15	28.93	10288
Stereotaxis	STXS	0.64	0.87	35.94	-13.91	508
Steris	STE	73.12	73.1	-0.03	-2.95	2383
Strata Skin Sciences	SSKN	0.51	0.53	3.92	-54.05	33138
Stryker	SYK	117.76	116.41	-1.15	26.71	5264
Sunshine Heart	SSH	0.72	0.56	-22.22	-46.67	588
Syneron Medical	ELOS	6.98	7.16	2.58	-9.47	371
Tearlab	TEAR	0.7107	0.65	-8.54	-48.87	470
Teleflex	TFX	171.55	168.05	-2.04	30.48	1981
The Cooper Cos	COO	180.97	179.26	-0.94	34.87	3541
Thermo Fisher Sci	TMO	157.66	159.06	0.89	11.15	7754
Titan Medical	TITXF	0.36	0.275	-23.61	-52.00	2870
Transenterix	TRXC	1.54	1.69	9.74	-37.90	4270
Varian Medical	VAR	98.17	99.53	1.39	21.50	3168
Vascular Solutions	VASC	49.56	48.23	-2.68	44.11	414
Wright Medical	WMGI	24.4	24.53	0.53	0.91	4807
Zeltiq Aesthetics	ZLTQ	40.24	39.22	-2.53	41.04	3075
Zimmer Biomet	ZBH	128.33	130.02	1.32	25.10	4878

NOTES

Trading volumes for Nasdaq, Amex and NYSE are recorded as the total number of shares traded (in thousands) on a weekly basis (cumulative Monday through Friday); the weekly and YTD % changes are from IPO completion, where applicable.

Average Percent Change Week: -0.50%
Range: -47.95% to +35.94%; Number Of Companies: 76
(not market weighted)

Average Percent Change YTD: +16.52%
Range: -59.17% to +180.00%; Number Of Companies: 76
(not market weighted)

DNA

Continued from page 1

founded as a spin-out from Imperial College, DNA Electronics Ltd. (DNAe) is in the late stages of developing a point-of-need solution for rapid DNA analysis – and the platform has attracted the attention of the U.S. government.

The Biomedical Advanced Research and Development Authority (BARDA) awarded the London-based company a contract worth up to $51.9 million to develop its DNA sequencing platform for the rapid diagnosis of antimicrobial resistant infections and influenza. DNAe said the contract will support the development and validation of its Genalysis platform, as well as a series of applications for FDA clearance.

As the father of a boy who lost his kidneys at a young age due to a genetic predisposition, Toumazou told *Medical Device Daily* that early detection is something he has long been passionate about.

"You wonder, if we detected it early enough, maybe we couldn't have prevented it, but we could have managed it better," he said.

According to the company, the platform will combine the ability to sequence the DNA of the infectious organism, in a sealed microchip-based system, direct from a clinical specimen, with analysis that enables actionable identification of the disease agent within a few hours. The first product will be a rapid blood-to-result diagnostic system aimed at bloodstream infections that lead to sepsis.

DNAe said the new system is already in late stage development and testing and is expected to be ready to launch in 2018.

The collaboration with BARDA demonstrates the suitability of DNAe's next-generation sequencing platform to address a range of clinical needs, Toumazou said, as demonstrated by the application in antimicrobial resistance and influenza testing, where there is a very high unmet need."

When a doctor prescribes a patient a drug, such as an antibiotic, for instance, making sure that person can metabolize that drug quickly becomes critical, Toumazou said. Blood tests can take up to three days to answer those questions, and by that time the antimicrobial-resistant bug has mutated so many times that it's too late, he said.

The Genalysis platform is designed to return results within a couple of hours to guide treatment decisions before it's too late.

The company is also leveraging technology from Nanomr Inc., an Albuquerque, N.M.-based company DNAe acquired in January 2015 for that developed a system for rapid isolation of rare cells in the bloodstream. The acquired technology is designed to target multiple rare cell types such as those contained in bacteria and fungi from bloodstream infections at levels of 1 cell/mL or lower in less than 30 minutes, making it the ideal sample preparation technology for DNAe's rapid point-of-need diagnostic tests, the company said.

By combining the two systems, Toumazou said, "we go straight from sample to result almost on a desktop" simply by taking a blood sample and putting it into something that looks like a mother board of a computer with a microchip, he said.

BARDA had a hand in moving along the development of the automated sample preparation system as well, with a $21.5 million contract awarded to Nanomr in 2014.

Sam Reed, president of DNAe's Washington-based office, who is leading the sequencing program, said the platform can be operated by users who are not specially-trained in sequencing, enabling it to be used in a wide range of near-to-patient environments where sequencing has not been possible before. "Unlike existing sequencing devices, the platform operates 'push button' directly from raw clinical specimens such as blood or swabs, delivering a clinically-relevant report for the physician," Reed said. **//**

REGULATORY FRONT

Epic Research & Diagnostics of Scottsdale, Ariz. has won a *de novo* declaration by the FDA for the company's Clearview system, described by the agency as an evoked photon image capture device. The agency announced Sept. 30 that the sponsor had filed the request in January 2015 for the device, which is not a diagnostic system and hence is deemed a class I device. The system is intended to obtain data from the fingertips for the purpose of evaluating general health.

PRODUCT BRIEFS

San Diego-based **EMR Direct** released its Interoperability Engine 2017 for its health information service provider services. New functions in the release allow vendors to deploy public Application Programming Interfaces (APIs), enabling patients to access their electronic health data using the Health Level Seven International (HL7) Fast Healthcare Interoperability Resources (FHIR) standard. The company said it will also offer an application platform, Healthtogo, to connect with public application access APIs. FHIR is a draft standard describing data formats and elements and an API for exchanging electronic health records. The standard was created by the HL7 health care standards organization.

TAVR

Continued from page 1

held Oct 1 to 5, 2016 in Barcelona, Spain.

The advanced polymer used for the pulmonary heart valves is expected to degrade over one year, progressively being replaced by human cells to form natural valve leaflets.

If successful, the Xeltis Endogenous Tissue Restoration (ETR) technology could prove highly disruptive for transcatheter aortic heart replacement (TAVR) valves with leaflets that are fabricated with animal or human tissue.

"Today's standard of care in heart valve replacement are leaflets made of homograft or bovine jugular vein material and both have limitations in availability," Xeltis CEO Laurent Grandidier told *Medical Device Daily*.

"Our pulmonary valves are made of a bioabsorbable polymer that we can produce in large quantities in precise sizing without supply constraints," he said, adding that the company is already conducting pre-clinical studies for a TAVR device.

"There are a dozen sheep walking around with our valves," Grandidier said.

The durability of animal tissue leaflets has emerged as the final barrier for TAVR in overtaking surgery as the standard of care for replacing native aortic heart valves that are failing.

TAVR sales are soaring with a consensus among industry analysts that the market will swell at 14 percent compound annual growth to reach $5 billion worldwide by 2020.

The three children receiving the novel pulmonary valve are the first of 12 patients Xeltis expects to enroll before the end of the year for its Xplore-1 safety and feasibility clinical trial.

Grandidier is confident he will be able to report preliminary results for Xplore-1 at next year's EACTS meeting.

If successful the Xplore-1 trial will be rolled into an expanded pivotal trial to support a CE Mark submission.

In March 2016, Xeltis received a humanitarian use device (HUD) designation for the bioabsorbable pulmonary valve from the U.S. FDA, which Grandidier said opens the door for a formal investigational device exemption (IDE) clinical trial.

"Our strategy is for parallel regulatory pathways in Europe and the U.S.," he said.

The pulmonary valves are the first product for commercialization to spin out of the Xeltis ETR technology platform.

The pediatric pulmonary valves were surgically implanted to correct a congenital malformation by reconstructing the right ventricular outflow tract using a tube inside of which are three valve leaflets.

The three children were discharged from hospitals in Krakow, Poland and Budapest, Hungary after open heart surgery procedures conducted in July and August 2016.

The Chief Development Officer at Xeltis, Eliane Schutte said there is an enormous clinical need in this space as currently children receive pulmonary valves that fail faster than either patients, parents or physicians would want.

"These patients receive conventional tissue valves that degenerate, that have a limited useful life. And the exact size required is never available, resulting in long waiting periods. Consequently these patients face the possibility of having open heart surgery up to five times during their life, and face each time the risks of that procedure," she said.

The degeneration of valve leaflets has become critical for continued growth in TAVR as cardiologists seek to implant the prostheses in patients at a lower risk for surgery during which valves with a demonstrated durability of 25 years and greater are implanted.

In May 2016 at EuroPCR, the annual meeting of interventional cardiologists, a preliminary but highly explosive report found up to 50 percent of implanted valves were degenerating after eight years. (See *Medical Device Daily*, May 18, 2016.)

The controversy is divisive because where cardiologists agree there is insufficient data on TAVR leaflet durability, some say this is a reason to continue toward lower risk patients while others, including the editor of the Journal Eurointervention, call for a halt until the durability question is answered. (See *Medical Device Daily*, Sept. 20, 2016.)

"There is not a binary outcome where either the valve works or it does not," said Grandidier. "The valve may work fine for a few years, but then the patient finds he or she is not able to exercise and progressively becomes confined to the home for years."

"What we hope to implant is a bioabsorbable heart valve that allows the body to heal itself. It is porous so that the body can pervade the support structure with its own cells to recreate its own tissue. This removes problems with current devices, which is long-term, chronic heart risk," he said.

Made of delicate animal tissue, the leaflets of all current TAVR devices must be crushed to fit in the narrow catheter that enables the percutaneous implantation through the femoral artery and, as a result, may compromise leaflet integrity.

The Xeltis ETR polymer can be compressed more than animal tissue, according to Grandidier.

"IIn TAVR the profile of a device has become very important. We are building a lot of data regarding how much smaller devices could be using our techology," he said.

"There are also enormous manufacturability benefits for ETR in using an unlimited supply of polymers versus the sourcing of animal tissue, as well as eliminating a potential reaction of the human body to the presence of chemicals used to treat those animal tissues," said Grandidier.

"Next year at EuroPCR we will have data to share," he said.

Xeltis has a full schedule at EACTS 2016 in Barcelona.

The head of the Budapest's Children Heart Centre will discuss the first implantations of the bioabsorbable pulmonary heart valve.

The company will present two-year follow-up data from a feasibility trial on its bioabsorbable patch and shunt used in corrective surgery

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Memo

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the effect of the memo is less on the size of monetary penalties and more on the legal relationships between a corporation and its executives and employees.

Much of the thinking about the Yates memo in the weeks following its publication was that the memo – which emphasizes individual accountability and expands the amount of information companies would have to disclose in order to win any prosecutorial discretion for cooperation – applied substantial pressure on attorney-client privilege. Companies had also been advised in the weeks following to revisit their directors and officers liability insurance policies as well, given the prospect that the memo would drive more officers and employees to retain their own counsel separate from that of the employer. (See *Medical Device Daily*, Nov. 9, 2016.)

Deputy assistant attorney general Jonathan Olin addressed the memo at a meeting last year held by the Food and Drug Law Institute in which he advised that companies might rid themselves of the idea that prosecutions under the False Claims Act (FCA) are more than just the cost of doing business. He emphasized that prosecutors will give weight to companies that identify any individuals culpable for the presumed violative conduct, stating, "individual accountability is at the heart of our strategy." (See *Medical Device Daily*, Dec. 10, 2015.)

The case of North American Health Care demonstrates one direct effect of the Yates memo. DoJ announced Sept. 19, 2016, that it had settled with NAHC over allegations the company had induced the filing of false claims for rehabilitation services, and the company parted ways with more than $28 million to settle the case. However, two executives with NAHC had to surrender a total $1.5 million, thus affirming the individual culpability provisions of the Yates memo.

Doug Sprague, a former prosecutor and a partner in the San Francisco office of Covington, told *Medical Device Daily* that federal prosecutors "do have a great deal of discretion generally speaking" about how they prosecute cases. He said the memo does not handcuff a federal prosecutor's discretion, remarking that the memo serves primarily as "a great reminder to prosecutors and their supervisors that they need to be focused from the outset on individual accountability."

By some accounts, DoJ prefers that cases against corporations and its officers and employees come to a more or less simultaneous conclusion, but Sprague said this is no apparent source of tension between a corporation and any individuals caught up in an investigation. On the other hand, he said, "there is increased discussion of and sensitivity to an individual's need to consult with separate counsel, which increases [legal] costs for the company for sure."

Sprague said employment contracts ordinarily include legal liability insurance, but noted that prosecutors should not see such policies as indicators of lack of cooperation. "I would certainly hope not ... as it's frequently contractually required," Sprague commented, although he said, "once [an individual is] charged or convicted, there may be different provisions regarding" legal fees in those insurance policies.

On the other hand, Sprague said a government attorney might have a different perspective on corporate payment for an individual's legal costs when such payment is not part of the employment agreement.

"I don't think it has a day-to-day effect" on relations between employers and their executives and employees, Sprague said of the memo, but when a subpoena arrives, "there is at least the potential that the Yates memo can affect that relationship because the company is feeling more pressure to cooperate with DoJ." He pointed out that corporations will nearly always default to a vigorous internal investigation, but individuals may in some situations be motivated to not provide certain information, or as previously noted, to hire separate counsel.

An individual's retention of their own legal counsel could delay or add cost to corporation's internal investigation, Sprague said, adding that there will be times when anyone who has engaged in questionable or flatly illegal conduct may be more motivated to point the finger at the company or other employees.

Sprague said there has always a tension between voluntary disclosure and full cooperation on the one hand, and attorney-client privilege on the other. He said the Yates memo does not require anyone to waive privilege, but he observed that companies do hear the message that cooperation is enhanced by at least considering waiving privilege, which he said is "another thing that may pit the interest of the company against the individual."

Companies probably do not have to rewrite or adjust the broad outlines of their employees' contracts as a response to the Yates memo, but Sprague remarked that compliance and ethics practices have become an area of "increased focus and a higher priority for companies because the memo is another of many incentives" to do so. Companies will have to ensure that their compliance and ethics staff have the needed resources, and ethics programs have to be up to date.

Nonetheless, Sprague said a few more years may have to pass before the effect of the Yates memo can be fully appreciated. Where the department's emphasis on corporate cooperation is concerned, the question at present is still, "was it really a change, or was it just another reminder?"

"I think the jury is still out on the long-term impact" of the memo, Sprague concluded. **//**

Tax

Continued from page 1

biotech sector, AusBiotech CEO Glenn Cross told *Medical Device Daily*. He said the $2 million cap that would be placed on small- to medium-sized entities would be particularly devastating.

"This sends a bad message to the investment community," Cross added. "The people who invest in companies and would conduct trials in Australia are mostly SMEs, and it doesn't make sense internationally."

Under the current R&D tax incentive plan, there is no cap for SMEs. The R&D tax benefit currently provides a refundable 43.5 percent tax offset for companies with turnover less than A$20 million, and a non-refundable 38.5 percent tax offset for other companies.

Additional tax breaks are offered for profitable companies with a tax liability to induce greater R&D investment.

To boost innovation and strengthen R&D in Australia, the government established a separate agency in December called Innovation Australia to map out an innovation strategy for the years ahead.

As part of that effort, the agency was tasked with forming a review panel to look for ways to improve the effectiveness of the R&D tax incentive program and to sharpen its focus on encouraging additional R&D in the country.

"The medical research sector has not been matched by translational excellence," Innovation Australia Chairman Bill Ferris told *Medical Device Daily* in an interview. He said that Australia punches above its weight when it comes to medical research, but it "runs the risk of squandering this exceptional capability" by not being able to attract and keep innovation in the country.

The R&D tax incentive is aimed at improving both the quality and quantity of R&D investment in Australia and accounts for roughly A$3 billion in annual government support, according to the report, which was released Sept. 28.

Authored by Bill Ferris, Alan Finkel, chief scientist; and John Fraser, secretary to the treasury, the panel found the R&D tax incentive program falls short when it comes to encouraging additional R&D and spillover benefits to the community. The panel received 92 submissions from industry stakeholders.

The report provides six major recommendations to improve the overall effectiveness of the R&D program and keep it sustainable:

• Retain the current definition of eligible activities and expenses under the law, but develop new guidance to give greater clarity to the scope of eligible activities;

• Introduce a collaboration premium of up to 20 percent for the non-refundable tax offset to provide additional support for collaborative R&D expenditures undertaken with publicly funded organizations;

• Introduce a cap of A$2 million to the annual cash refund payable under the R&D tax incentive, with remaining offsets treated as a non-refundable tax offset that could be carried forward to use against future taxable income;

• Introduce an intensity threshold in the order of 1 percent to 2 percent for recipients of the non-refundable component of the R&D tax incentive such that only R&D expenditures in excess of the threshold attracts a benefit;

• If an R&D intensity threshold is introduced, increase the expenditure threshold to A$200 million so that large R&D-intensive companies retain an incentive to increase R&D in Australia; and

• The government should investigate options for improving administration of the R&D tax incentive program and improve transparency by publishing names of the companies claiming the tax incentive and the amount of the R&D expenditure claimed.

FOCUS ON SMES

The report notes that the R&D incentive needs to home in on "high-potential entrants," such as early-stage companies that often operate at a loss. Placing limits on the refundable amount could help ensure that the level of support for these loss-making companies is "appropriate."

On a positive note, the report suggests that the government consider quarterly payments of expected annual refunds to help companies address cash flow issues while they are actively involved in R&D activities, rather than waiting until year end. The report acknowledges that young SMEs often find it more difficult to raise capital than mature companies, so they should remain a target group for the refundability element of the R&D tax incentive.

AusBiotech's Cross said the report bodes well for larger companies because it plays up to the higher end by increasing the expenditure claim threshold to A$200 million from the current A$100 million threshold. The expenditure-claim threshold limits the cost-to-revenue of the program but also removes the incentive for companies to undertake additional R&D beyond that threshold.

The report authors point out that by focusing on the "higher-value" larger R&D companies, the country is more likely to profit from spillover effects, such as partnering opportunities and additional investment in Australia as result of that spillover effect.

Andrea Kunca, co-lead of the Medical Technology Association of Australia (MTAA) said that the association was pleased that the review "acknowledged the need for extra incentives for collaboration and commercialization between academics and publicly funded research organizations.

"This backs our Medical Technology Blueprint report released last year which recommended the need for closer collaboration between governments, academia and industry to drive commercial outcomes, she said.

The report concludes that the size of the tax benefit should be sufficient enough to induce more R&D and to provide stability to keep companies engaged in long-term investments. It

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Radiology

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radiology images. NZ Technologies Inc. CEO Nima Ziraknejad began developing Touchless Interaction with PACS in Sterile Operations (TIPSO) three years ago to save interventional radiologists and surgeons the walk from the OR to an outer room to view radiology images.

"TIPSO not only eliminates scrubbing in and out, but also reduces the amount of radiation exposure to the patients. That's huge," Ziraknejad told *Medical Device Daily*. "At the same time it preserves the cognitive focus of the surgeon and enables him to use softer hand movements to interact with the radiology images."

TWO VIEWS ARE BETTER THAN ONE

To gain a precise view of the patient's anatomy, surgeons use TIPSO's two interactional modes: the first is a menu of icons projected from a self-contained, 3-D sensing unit at ceiling height onto the drape covering the patient. The surgeon scrolls through the menu to pre-existing images of the body targeted for surgery. By touching the icon the surgeon can zoom in or out of each image or pan around for a more precise view.

The second mode allows surgeons to perform similar tasks, but with a simple finger motion hovering above an "air pad," placed on the drape; this eliminates direct contact with the patient and the potential for in-surgery contamination. Ziraknejad said TIPSO also saves valuable OR time. "According to research done at Vancouver General Hospital (VGH), TIPSO reduced the surgeon's time in the OR from 10 to 15 percent," he said.

That seems to accord with the experience of John Chung, an interventional radiologist at VGH. He told *Medical Device Daily* he "constantly refers to imaging to find the blood vessels you need to find" during Yttrium-90 radioembolization, a minimally invasive, but very complicated procedure for treating liver cancer. "In one case where I would usually have scrubbed in and out ten to fifteen times, I stayed on inside the room using Tipso and did it twice. Invariably that's a time saver."

EVEN BETTER THINGS TO COME

Any surgeon will tell you elbow room in a busy operation room is at a premium. With that in mind, NZ Technologies will launch its second iteration of TIPSO at the Radiological Society of North America's annual meeting in Chicago in November. "TIPSO2 will have new HMI features and is much smaller," said Ziraknejad, making it even less intrusive than the original. Equally important, said Dr. Chung, he will no longer have to switch back and forth between the two interactional modes during surgery.

"They're combining the two so that there are certain really good qualities in the air pad mode that will be present at the same time as features in the projection mode…I haven't tried it yet, but I'm quite happy and excited to do that to see how things go."

Like Tipso, the projection and air pad modes in TIPSO2 will draw on CT, X-ray and other images contained in the hospital's PACS (Picture Archiving and Communication System). These feed images to the surgical unit's display monitors.

Designated a Class 1 device in the U.S. but not in Canada, Tipso was financed by grants of approximately one million dollars from the Canadian government, C$300,000 by Ziraknejad himself and angel investments earlier this year of approximately C$400,000. Previously, Ziraknejad had contemplated selling the device outright to hospitals, but changed the capital cost model to a subscription fee.

"So we provide both the hardware and software. But instead of charging C$69,000, you only have to give us an annual subscription fee of $12,000. And at any time you can stop the subscription." //

TAVR

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for pediatric cardiovascular patients, data that was essential for advancing to approval for use of the pulmonary valves.

And a panel that includes a Nobel prize laureate, cardiac surgeons and Xeltis' Chief Technology Officer and co-founder Martijn Cox will discuss how bioabsorbable heart valves could redefine cardiovascular interventions.In December 2015, Xeltis closed a series B financing round raising $32 million.

"We are very well funded with a committed group of investors and while we are having discussions regarding our options moving forward, we do not have financing concerns," said Grandidier. //

Tax

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warned the government that reducing the current rates any further would only deter investment.

Medicines Australia, which represents multinational pharmaceutical companies operating in Australia, said its members invest around $1 billion a year in R&D in the country.

"With global demand for new medicines expected to double over the next decade, Australia stands at the cusp of exciting opportunities in medical research and development," spokesman James Boyce said in a statement. "Making the most of this opportunity will help drive economic growth, deliver more high-skilled STEM jobs and provide Australians with improved access to medicines and health innovation.

Boyce said the association would review the document further and would consult with its members before submitting comments. Comments will be accepted on the report until Oct. 28. More discussions will then be held with industry to map out the path forward. //

NEUROLOGY EXTRA

Keeping you up to date on recent developments in neurology

By Holland Johnson, Executive Editor and Anette Breindl, Senior Science Editor

Missing link found in the development of bioelectronic neuroprosthetics

New research, led by the University of Southampton, has demonstrated that a nanoscale device, called a memristor, could be the missing link in the development of implants that use electrical signals from the brain to help treat medical conditions. Monitoring neuronal cell activity is fundamental to neuroscience and the development of neuroprosthetics - biomedically engineered devices that are driven by neural activity. However, a persistent problem is the device being able to process the neural data in real-time, which imposes restrictive requirements on bandwidth, energy and computation capacity. In a new study, published in *Nature Communications*, the researchers showed that memristors could provide real-time processing of neuronal signals (spiking events) leading to efficient data compression and the potential to develop more precise and affordable neuroprosthetics and bioelectronic medicines. Memristors are electrical components that limit or regulate the flow of electrical current in a circuit and can remember the amount of charge that was flowing through it and retain the data, even when the power is turned off. The research team developed a nanoscale Memristive Integrating Sensor (MIS) into which they fed a series of voltage-time samples, which replicated neuronal electrical activity. Acting like synapses in the brain, the metal-oxide MIS was able to encode and compress (up to 200 times) neuronal spiking activity recorded by multi-electrode arrays. Besides addressing the bandwidth constraints, this approach was also very power efficient - the power needed per recording channel was up to 100 times less when compared to current best practice.

A worm holds the key to treating epilepsy

Current methods to control epilepsy are not only inefficient but haven't improved in more than 150 years when the first anticonvulsant drug was developed. Researchers from Boca Raton, Fla.-based Florida Atlantic University, in collaboration with The Scripps Research Institute, have opened up the possibilities for rapid drug screens to treat seizures in the near future by developing the smallest whole-animal electroconvulsive seizure model using a microscopic nematode worm. Electroshock is one of the most common experimental models of acute and chronic seizure in mammals to study epilepsy. The researchers have been able to demonstrate, that just like rodents and even fruit flies, the tiny 1 millimeter *C.elegans* worm also can undergo an electroconvulsive seizure. The study, "Modulating Behavior in C.elegans Using Electroshock and Antiepileptic Drugs," published in *PLOS One*, has led the researchers to build on the current animal models for inducing seizures via electroconvulsion in the genetically modifiable *C.elegans* that only has 302 brain cells called neurons. *C.elegans* has been used for decades as a model animal to study the genetic and molecular underpinnings of neurological disorders through a number of techniques including bio imaging, electrophysiology and behavior. For the study, researchers treated the worms with several antiepileptic drugs approved for human use, which improved recovery from electroshock seizures worsened by genetic or pharmacological pro-convulsants Because this new method is rapid, inexpensive and has shown relevance with existing antiepileptic drugs, the *C.elegans* electroshock assay developed at FAU has the potential to become an efficient screening tool for human seizure therapeutics.

New hope in fight against aggressive and often hard to treat brain tumor

Researchers from the U.K.-based University of Southampton have discovered a potential way of stopping one of the most aggressive types of brain tumor from spreading, which could lead the way to better patient survival. Glioblastoma is one of the most common types of malignant brain tumors in adults. They are fast growing and can spread easily. The tumor has threadlike tendrils that extend into other parts of the brain making it difficult to remove it all. Although there have been great advances made in the treatment of Leukaemia's and other cancers, little is known about how Glioblastomas are formed and how these tumors infiltrate the brain tissue. Published in *Molecular Neurobiology*, the study researchers, analyzed how enzymes called ADAMs affect the movement and function of the human tumor cells. The findings suggest that if you are able to block specific enzymes called ADAM10 and ADAM17 the tumor stops growing and spreading. It also moves the cancer cells away from the place where they were growing which could allow them to be removed through traditional cancer treatments such as radiotherapy, chemotherapy or surgery.

How Parkinson's protein gets around

Fibrils of misfolded alpha-synuclein used (lymphocyte-activation gene 3) LAG3 to spread from neuron to neuron in animal models of Parkinson's disease. It has become increasingly clear that misfolded alpha-synuclein aggregates into fibrils, and that such fibrils can spread and seed fibrils in a way that is reminiscent of infection. Researchers from Johns Hopkins University have shown that the receptor that mediated travel from cells to cell was the LAG3 receptor. Mice with Parkinson's diseases that lacked LAG3 were

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"substantially" slower to lose dopaminergic neurons and develop symptoms. "The identification of LAG3 as a receptor that binds [a-synuclein fibrils] provides a target for developing therapeutics designed to slow the progression of PD and related alpha-synucleinopathies," the authors concluded. Their work appeared in the Sept. 30, 2016, issue of *Science*.

Quanterix and Immunarray team up address neurodegenerative disease

Lexington, Mass.-based **Quanterix Corp.**, a company digitizing biomarker analysis to accurately measure change for precision health, today announced it is making a strategic investment in Rehovot, Israel-based Immunarray Ltd., a molecular diagnostics company advancing the development of multi-marker tests for complex diseases. As part of the deal, Immunarray gains access to Quanterix Simoa technology. Both companies are pioneering new approaches to medical diagnoses in complementary areas of neurological disease, focusing on the identification and analysis of molecular biomarkers in the blood. With this agreement, Quanterix and Immunarray will work together to continue advancing research and technology in order to provide an accurate method for detecting mild to moderate traumatic brain injury in the future. Also, Quanterix will add select Immunarray markers to its multiplexing panel for the neurology research market. These additions provide researchers with the ability to measure multiple proteins simultaneously at the single molecule level using Quanterix' Simoa technology.