Agency for Science, Technology and Research SINGAPORE

MINISTRY OF HEALTH SINGAPORE

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SINGAPORE RAMPS UP BIOMEDICAL SCIENCES EFFORT WITH INJECTION OF S$36M INTO MEDICAL TECHNOLOGY RESEARCH

A*STAR collaborates with CIMIT to enhance the environment for growing the medical technology industry as part of the drive to transform Singapore into a knowledge-based innovation-driven economy

Local doctors, BMS scientists and engineers given the boost to create engineering solutions to medical problems

1. The Agency for Science, Technology and Research (A*STAR) announced at the 14th Biomedical Sciences International Advisory Council (BMS IAC) meeting today that $36m would be pumped into new programmes to give Singapore's growing medical technology industry a greater push. The new programmes include the collaboration between A*STAR and CIMIT (Center for Integration of Medicine and Innovative Technology) in Boston, USA, and A*STAR's Biomedical Engineering Programme. The programmes were endorsed by the BMS IAC chaired by Sir Richard Sykes, also the Chair of NHS London. Information about the medical technology industry in Singapore is at Annex A.

A*STAR-CIMIT COLLABORATION

2. Under the A*STAR-CIMIT collaboration, engineers, clinicians and/or BMS scientists in Singapore will be able to work with clinicians in Boston to come up with engineering solutions that have clinical and market relevance. This alliance is part of A*STAR's goal in fostering a vibrant medical technology innovation ecosystem in Singapore. It will not only create greater opportunities for impactful innovations in the area of medical technology but more pertinently, it will also provide an environment conducive to training innovators for the growing medical technology industry in Singapore.

3. A win-win relationship, this A*STAR-CIMIT collaboration will result in the co-development of intellectual property between A*STAR, the universities, hospitals and CIMIT in time to come. Some other foreseeable outcomes that this collaboration will bring to the growing medical technology industry, which already had an output of S$3 billion and employed more than 8,000 people in Singapore in 2008, include the

creation of more high-level and high-skill jobs in the market, the creation of value to large medical technology companies in Singapore, and the gearing effect with local manufacturers as part of the supply chain. More information about the collaboration is at Annex B.

BIOMEDICAL ENGINEERING PROGRAMME

4. Under the Biomedical Engineering Programme, grants have been awarded to eight new research projects helmed collaboratively by research engineers at A*STAR and clinicians in local hospitals, and involving researchers from the universities and hospitals. These projects aim to develop and provide cost-effective, innovative and clinically impactful solutions for healthcare systems. With the active participation of clinicians who understand the needs of their patients, these projects will be highly relevant to patients and meet their needs. The intention is for these innovations to eventually be developed for the local, regional and international markets. More information on medical technology projects is at Annex C.

ARTSBCI

5. One of the research projects under the Biomedical Engineering Programme is the ArtsBCI (Advanced rehabilitation therapy for stroke based on Brain-Computer Interface) led by Dr Guan Cuntai from the Institute for Infocomm Research (I^2R) and Dr Karen Chua from Tan Tock Seng Hospital (TTSH), in collaboration with Dr Ang Beng Ti from National Neuroscience Institute (NNI). This project makes use of the novel and award-winning technology of the Brain Computer Interface (BCI) also developed by Dr Guan, and improves on it to achieve a holistic and comprehensive system for advanced rehabilitation therapy for stroke patients.

6. ArtsBCI comprises components for hospital as well as home use. The component for home use, namely the portable ArtsBCI, will enable stroke patients to employ a holistic and personalised rehabilitation regime as and when they need it. ArtsBCI will be the first system to make use of a brain computer interface and robotics to detect brain signals as well as end effectors to allow stroke patients to have the ability to perform multimodal movement rehabilitation exercises, eg, the movement of the shoulder, elbow, wrist, hand and fingers. In addition, it will also address swallowing dysfunctions in patients – a common problem after a stroke. Such rehabilitation will also allow patients to rebuild the motor neuron networks so necessary for their own movement in a comparatively shorter period of time. The project is now in its early stage of research.

7. The relevance of ArtsBCI to Singapore is high given the fact that there is an estimated prevalence rate of 4% of stroke cases in Singapore, and where about 50% of people who survive a stroke have to live with moderate to severe disabilities in movement, cognition and speech, which greatly affect their daily living and quality of life. The situation in other countries is not too different from that of Singapore. In the United States, stroke is the No. 1 case of severe or long-term disability. About 15m people suffer from stroke every year around the world. At least one-third of them will require rehabilitation from disabilities after a stroke.

AGLAIA

8. Another project under the Biomedical Engineering Programme is AGLAIA (Automatic GLaucoma Diagnosis and Its Genetic Association Study through Medical Image InformAtics). When it is developed, AGLAIA will be the first of its kind of software system that will be able to detect and diagnose glaucoma in the general populace in a cost-effective and efficient manner. This is especially relevant because glaucoma is a major blinding disease which affects more than 60m people worldwide, with a further 100m who are glaucoma suspects. It has significant impact on vision, quality of life and adds a substantial cost of treatment to the health care system. In Singapore alone, 3% of people older than 40 years of age have glaucoma, with more than 90% of these cases often going undiagnosed. Glaucoma also has a strong genetic basis, and people with a family history of glaucoma have four times higher risk of glaucoma.

9. A collaborative research project led by Dr Jimmy Liu from I^2R and Prof Wong Tien Yin from Singapore Eye Research Institute (SERI), AGLAIA is an improvement over the ongoing project of ARGALI (an Automatic cup-to-disc Ratio measurement system for Glaucoma AnaLysIs), which is also developed by I^2R and SERI. ARGALI uses a specialised image processing software to analyse photos taken of the retina to detect glaucoma. The improved version of AGLAIA aims to be a more robust system that will capture more parameters indicative of early glaucoma damage in the eye. This technology will be especially welcome because glaucoma in its early stage is hard to detect since patients with early glaucoma generally do not exhibit any symptoms. With AGLAIA, patients in the early stages of glaucoma may be diagnosed easily, thus allowing for early treatment which could prevent any further progression of this disease.

10. AGLAIA will also be able to explore the genetic factors related to glaucoma through an integrative genome-wide association study approach using information collected from 15,000 participants through various eye cohort studies performed in Singapore and Australia. This will help to identify certain genetic factors that could possibly be associated with the onset of glaucoma. Currently, AGLAIA is also in its early stage of research.

11. Said Mr Lim Chuan Poh, Chairman of A*STAR and Co-Chair of the BMS Executive Committee, “Our Biomedical Sciences Initiative has been intended to impact four major industrial sectors of pharmaceuticals, biotechnology, medical technology and health care services. Given what we have done to build up our biomedical capabilities in the last eight years, we are now in a better position to leverage on our strengths in engineering to integrate both the capabilities to boost the medical technology industry. This will not only attract more medical technology companies to anchor their activities here, but will also open up more employment opportunities for Singaporeans in this space. The companies are also interested to be here because of our conducive business environment and very importantly, the growing Asian market and the need to better customise their products and services to this market.”

12. Said Ms Yong Ying-I, Permanent Secretary of Health and Co-Chair of BMS Executive Committee, "I am glad that our BMS journey has brought clinicians and engineers closer together to improve health for the general population, and with the view to keeping healthcare costs affordable. This also speaks volumes of our capability in knowledge creation, which is a key to anchoring MNCs and industry in Singapore."

PROGRESS OF BMS EFFORTS

13. The BMS IAC commended Singapore's BMS efforts in the area of Translational and Clinical Research (TCR), which have facilitated close collaboration between basic scientists and clinicians to translate research findings into medically relevant applications that benefit patients. The on-going systemic study of screening for gastric cancer under the Gastric Cancer TCR Flagship Programme has recruited more than 2,400 high-risk individuals[1] as of Sep 2009. To date, the screening detected early gastric cancer in 10 of them. This study created new knowledge that could potentially impact early detection and treatment for gastric cancer, a major killer in Singapore and the region, which is curable if detected early. The Eye Disease TCR Flagship Programme has filed two patents to date. While only less than two years into their funding, the TCR Flagship Programmes have demonstrated great promise from combining the clinical strengths and multidisciplinary research expertise of Singapore's hospitals, specialty centres, universities and research institutes.

14. Following the announcement at the BMS IAC press conference in 2008, progress has been made in enhancing the infrastructure for clinical research and clinical trials. Two Investigational Medicine Units (IMUs) have been established at the NUHS and the SingHealth Campuses to develop investigational medicine capabilities and support for early phase clinical trials, and the Singapore Clinical Research Institute (SCRI) was set up to develop the infrastructure, core support and scientific leadership of Singapore for clinical research with a current focus on late Phase 2 and 3 trials to strategically dovetail and complement the two IMUs. As of Sep 2009, the two IMUs are running 46 on-going clinical trials while SCRI is running 26 on-going trials and other research projects.

15. In terms of economic outcomes, the manufacturing output for BMS was S$19 billion in 2008, up from S$6.3 billion in 2000. Employment has also more than doubled to about 12,500 jobs in 2008 from under 6,000 jobs in 2000. Today, over 100 global biomedical sciences companies have leveraged Singapore's world-class manufacturing capabilities, excellent clinical and scientific infrastructure, connectivity to Asian markets and pro-business environment to carry out strategic business operations ranging from regional headquarters, to cutting-edge research and manufacturing. These include companies such as Abbott, Roche, GlaxoSmithKline, Merck, Novartis, Pfizer, Schering-Plough, Wyeth, Siemens and Becton-Dickson. In addition, Singapore also secured six major biologics investments over the last few years totaling about S$2.5 billion from Roche, Lonza, GlaxoSmithKline, Novartis and Baxter, which could potentially create about 1,300 new jobs. Building upon this

[1] All recruited individuals will be followed for a period of five years.

success, A*STAR's Singapore Stem Cell Consortium, BTI and EDB engaged Lonza in further discussions which culminated in the recent establishment of a Cell Therapy Manufacturing Facility in Singapore, the first one set up by Lonza outside the US and Europe. More information on the updates of the BMS effort is at Annex D.

16. Said Sir Richard Sykes, "I have been with the BMS IAC since its inception and I believe that Singapore's commitment to research in the biomedical sciences is unique on the global stage. Firstly, because Singapore is able to take a long-term view – which is essential in order to build up a successful research enterprise – and secondly, because of Singapore's highly pragmatic and sensible focus on investing in research areas and capabilities that will create economic value for the country as well as improve healthcare outcomes for patients. Each year, the IAC has seen Singapore make great strides towards achieving these twin goals and there is clear and compelling evidence that the BMS industries are responding to these initiatives in a very positive way. In addition, the progress made in biomedical and clinical research, coupled with Singapore's existing strengths in engineering, has now created an exciting opportunity for Singapore to increase its contributions in the area of medical technology, and this will consolidate Singapore's position as an outstanding biomedical sciences and healthcare hub."

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Encl:
Annex A- Information sheet on Medical Technology Industry
*Annex B- Information sheet on A*STAR-CIMIT Collaboration*
Annex C- Information sheet on the Biomedical Engineering Programme
Annex D- Information sheet on the Biomedical Sciences Initiative

For queries and clarifications, please contact:

Evelyn Ho
Deputy Director, Corporate Communications
Agency for Science, Technology and Research
Tel: 6826 6273 (O); 9682 6922 (Hp)
Email: evelyn_ho@a-star.edu.sg

Joshua Woo
Assistant Head, Corporate Communications
Agency for Science, Technology and Research
Tel: 6826 6442 (O); 9616 1682 (Hp)
Email: joshua_woo@a-star.edu.sg

Yeo Wen Qing
Ministry of Health
Corporate Communications Division
Tel: 9642 4567 (Hp)
Email: yeo_wen_qing@moh.gov.sg

Annex A

INFORMATION SHEET
ABOUT THE MEDTECH INDUSTRY IN SINGAPORE

The medical technology (MedTech) sector is part of Singapore's burgeoning biomedical sciences industry. In 2008, the MedTech sector's manufacturing output was about S$3 billion and employed more than 8,200 people.

Today, 25 global medical technology companies have invested in commercial-scale manufacturing plants in Singapore. They develop and manufacture a wide range of medical products, such as contact lenses, scientific analytical equipment, implantables, syringes, stents, catheters and hearing aids as well as research instruments. Today, Singapore is a global leader in medical technology manufacturing and accounts for 10% of the global supply of contact lens, half of the world's thermal cyclers and more than 50% of the world's microarray.

Singapore also hosts leading medtech companies' R&D centres for innovation in Asia.They include *Fluidigm* and *Hill-Rom* that set up their first Asian R&D facility here for research instrumentation and electronic systems in hospital beds respectively. In addition, *Qiagen* opened a molecular diagnostics R&D centre in Singapore in partnership with *Bio*One Capital*, while *PerkinElmer* opened its Centre of Excellence that will serve as the base for its R&D in research instruments and diagnostics for Asia. In October 2009, 3M opened its first drug delivery R&D centre in Asia Pacific.

Leading medical technology companies that have set up commercial-scale manufacturing facilities here include *Affymetrix, Baxter, Becton Dickinson, Bio-Rad, Biosensors, Clearlab, CIBA Vision, Edwards Lifesciences, Fluidigm, Illumina, JMS, Life Technologies, MDS Sciex, , ResMed, Siemens Medical Instruments, Waters,* and *West Pharma*.

MedTech Projects involving A*STAR, hospitals and universities

Medical technology research is characterised by cross-disciplinary research collaboration among clinicians, biomedical scientists and engineers, and it is defined by a constant flow of innovation to develop engineering solutions to address complex medical problems.
With a spectrum of capabilities which span biomedical sciences, and physical sciences and engineering, A*STAR has been engaging in collaborative cross-disciplinary research together with universities and hospitals, and have scored some successes.

Some MedTech innovations include:

2009

- **The world's first photochromic contact lens by IBN.** Recently announced during the opening of iCare on 3 Nov 2009, this contact lens will darken upon exposure to sunlight to protect the eyes against harmful ultraviolet radiation and glare.
- **Diagnostic kit to detect H1N1 virus.** This is a collaboration between IMCB and TTSH. To date, 5,000 kits were produced by IMCB that are being used in TTSH. The kits were made from May to July 2009.

- **Tool to sequence the entire genome of the H1N1 virus.** A collaboration between GIS and Roche NimbleGen was announced on 28 May 2009. The tool serves as a surveillance tool to monitor changes in the virus as it evolves in the population. This will rapidly detect any mutation of the virus that may cause resistance to anti-viral drugs.
- **MicroKit, a portable diagnostic kit.** This is a collaboration between IBN, Dyamed Biotech and NUH for fast and accurate detection of infectious diseases such as the H1N1 virus. It was announced on 15 Jan 2009.

<u>2008</u>

- **Parallelizable 3Gb Pyrosequencer with integrated DNA preparation.** This is a collaboration by IME, SIMTech and GIS to meet the $1000 per genome challenge. A JCO project that was started in 1 Aug 2008.
- **Advanced therapeutic ingestible microcapsule with a camera.** This collaborative project by IME, DSI, I2R and NTU not only allows for real-time diagnosis as it courses through the body, but which is also able to perform actions based on commands given from outside the body. This is an improvement over what is currently available on the market which offers endoscopic functions. It started on 1 Sep 2008 and the grant is for a period of 3 years.

<u>2007</u>

- **Microfluidic device and chemical kit, also known as "lab-on-a-chip".** This is a collaboration between IBN, IMCB and GIS to detect avian flu. It can be adapted for other infectious diseases eg, SARS, HIV and Hepatitis B. It was announced on 24 Sep 2007.
- **A rapid diagnosis system in a form of a toilet bowl.** This is a collaborative project started in April 2007 by IMCB, I2R, IMRE and NTU to perform qualitative analysis of certain biomarkers in urine samples for the early detection of certain illness and diseases.

<u>2004</u>

- **Novel drug-loaded contact lens developed by IBN.** Announcued in 28 Oct 2004, this invention can deliver medication more effectively than eye drops for the treatment of eye diseases such as glaucoma.

Annex B

INFORMATION SHEET
A*STAR's COLLABORATION WITH THE CENTER FOR INTEGRATION OF MEDICINE AND INNOVATIVE TECHNOLOGY (CIMIT)

Objective of the Collaboration:
A*STAR is engaging the Center for Integration of Medicine and Innovative Technology (CIMIT), in Boston (overview of CIMIT is provided in Annex A of this factsheet), in a strategic collaboration as part of its long-term goal in building a vibrant MedTech innovation ecosystem in Singapore. A sustainable clinical-engineering community is vital towards the success of a vibrant MedTech innovation ecosystem. A*STAR has achieved initial successes through its Biomedical Engineering Programme (BEP) in bringing clinicians and engineers together through a systematic approach in research collaborations.

Through the collaboration with CIMIT, A*STAR hopes to bring to Singapore, CIMIT's best practices in building such a sustainable community by implementing a rigorous and high selectivity process for finding, funding and facilitating projects with high potential for improving patient care in the near term.

Building a Strategic Alliance and Long-term Relationship:
A*STAR and CIMIT have signed a Memorandum of Understanding (MOU) in early November this year to formalise the intent and commitment of both organisations to embark on collaborations. This is the start of a long-term relationship and linkages A*STAR and CIMIT hope to build for the clinical, engineering and entrepreneurial communities in Singapore and Boston.

This strategic alliance will open doors to opportunities for collaboration between Singapore clinicians and engineers and their Boston counterparts, with research transcending geographical borders to benefit patients.

Details of Collaboration:
Under the MOU, A*STAR and CIMIT will work together to realise the following collaborative activities:

a. Adopt and adapt CIMIT's best practices through an active engagement of CIMIT Leaders to *strengthen A*STAR's Biomedical Engineering Programme* (BEP), and aimed at creating a CIMIT-like consortium among research engineers at A*STAR and clinicians in local hospitals. This will support multidisciplinary translational research in medical device and clinical technology system application.
b. Collaborate on *shorter-term projects* from a pipeline of clinically vetted ideas from CIMIT with a shorter timeline towards clinical applications.
c. Launch Joint Grant Calls to initiate *upstream and longer-term collaborative projects* between Boston clinicians and Singapore engineers and/or clinicians to build capabilities, know-how and IP in MedTech innovations.

Commencement of Collaboration:
A*STAR and CIMIT will roll out these activities in early 2010 and they will span a few years. This relationship will create a win-win situation for both A*STAR and CIMIT as they work together to build sustainable MedTech solutions with strong clinical and market relevance in Singapore with the world as the global market.

OVERVIEW OF CIMIT

1. CIMIT is a non-profit clinically-based consortium of Boston-area hospitals and engineering schools founded in 1998. It supports multidisciplinary translational research in medical device and clinical technology system applications.

2. As a network of 11[2] hospitals, research laboratories and engineering universities, CIMIT exists as an infrastructure to enable inter-institutional collaboration. On joining this mission-driven network, each consortium institution enters into a standard agreement which provides clarity for many research administration issues that would otherwise hamper multi-institutional collaboration.

3. CIMIT attracts world-class clinicians, scientists and engineers working together with industry and government to accelerate the clinical impact of innovative technology. Clinicians, scientists and engineers from Harvard teaching hospitals, MIT, Charles Stark Draper Laboratory[3], Boston University and the VA Boston Healthcare System collaborate with one another, with the goal of solving medical problems through innovative technology.

4. CIMIT has a unique way of fostering multidisciplinary collaborations between clinicians and engineers through the following 3 approaches:
   a. ***Finding*** innovative concepts in need of support – Through institutional Site Mining, web-based convening and networking strategies and weekly 2-hour forums with presentations on clinical problems in need of technological innovation and technologies with potential yet undefined clinical application.
   b. ***Funding*** mechanisms for accelerating innovation – Through CIMIT's robust selection process that span from pre-review to review and seed funding injected at key points of need to accelerate innovation.
   c. ***Facilitating*** the success of projects – Through providing assistance ranging from seeking follow-on funding, business planning, reimbursement analysis, sourcing of complementary skill sets etc.

<u>CIMIT's Research</u>

5. CIMIT provides critical seed funding for investigators whose research may be considered too embryonic or high-risk by traditional funding sources. Consistent with CIMIT's mission, grants are awarded to investigators conducting translational research projects focused on novel, technology-driven solutions to urgent healthcare problems.

6. CIMIT is extremely successful in driving translational research. It gives out grants which enable individual investigators or multi-disciplinary teams to explore emerging technologies, develop systems to improve healthcare facilities or processes, or create novel approaches to managing a specific disease.

7. CIMIT encourages grant proposals by teams that reach across member institutions and whose novel ideas may lead to technologies that can benefit several medical disciplines. In particular, CIMIT seeks innovative approaches that can benefit soldiers, civilians and populations in austere settings. Proposals must be collaborative, multidisciplinary and specific about how the work will lead to improved patient care. In 2009, CIMIT awarded

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[2] The 11 member institutions are Massachusetts General Hospital, Brigham & Women's Hospital, Beth Israel Deaconess Medical Center, Children's Hospital Boston, Boston Medical Center, Newton-Wellesley Hospital, Harvard Medical School, VA Boston Healthcare System, Massachusetts Institute of Technology, Boston University and Draper Laboratory.

[3] Headquartered in Cambridge, Massachusetts, the Draper Laboratory is a R&D laboratory, employing more than 750 engineers, scientists, and technicians on a broad array of programmes for government and commercial sponsors. It has expertise in Implantable Therapeutics and Diagnostics, Point-of-Care (POC) Diagnostics and Medical Informatics.

over US$5 million in grants. Out of more than 200 proposals, CIMIT funded 34 projects and fellowships.

8. Through providing funding support, CIMIT enables researchers from 2 or more institutions in different disciplines to work together more easily. Research teams draw on the expertise of professional staff skilled in all phases of the research process – from innovation, through demonstration, into commercialisation and ultimately, into patient care.

9. CIMIT currently funds projects in the following programmes:
   - Image Guided Therapy
   - Biomaterials and Tissue Engineering
   - Neurotechnology
   - Minimally Invasive Surgery
   - Biodetection and Sepsis Control
   - Trauma and Casualty Care
   - Simulation
   - Optical Diagnostics
   - Inhalation Technology
   - Post Traumatic Stress Disorder
   - Traumatic Brain Injury
   - Cardiovascular Disease
   - Global Health Initiative
   - Clinical Systems Innovation

10. CIMIT is particularly interested in new approaches for managing combat trauma, including hemorrhage control, extending the "Golden Hour," and traumatic brain injury. CIMIT does not support drug development, information technology-centric projects, basic research, or clinical trials.

11. CIMIT has an in-house team of experts who facilitate the complex process of introducing technological innovations into healthcare. This highly experienced, multi-disciplinary team provides support and specialised expertise to investigators in IP protection, patents and licensing, technology implementation, small business grant process, regulatory issues and much more.

12. Specifically, there are two unique features at CIMIT – Site Miners and facilitators. Site Miners are usually clinicians who spend 20–50% of their time matching clinical problems at the hospitals with potential solution providers in the universities, research institutes or industry. Due to their clinical training, these Site Miners are able to understand the needs of clinicians and facilitate collaborations with engineers in a "bench-to-bed" manner. Facilitators, on the other hand, work with grantees towards securing larger funding, such as from NIH, government agencies and foundations, beyond the seed grants provided by CIMIT, as well as helping establish industry collaborations and advising on the ensuing commercialisation plans, for example.

Annex C

INFORMATION SHEET
BIOMEDICAL ENGINEERING PROGRAMME

A*STAR's Science and Engineering Research Council (SERC) initiated the Biomedical Engineering Programme (BEP) in December 2008. Through a needs-driven approach, the BEP seeks to foster collaborations between SERC researchers and Singapore's medical professionals by harnessing engineering capabilities of the SERC Research Institutes (RIs) and the universities to address unmet needs identified by the medical community.

Changing demographics and lifestyle is a worldwide trend that has an impact on the health of the population, bringing the challenges of rising healthcare costs and stretched medical resources to an ageing population in Singapore and other countries. Medical technology can play an enabling role in optimising the use of resources, improving quality of care, as well as containing costs to meet today's healthcare challenges. With the BEP, SERC aims to spearhead development of medical technology and innovations in Singapore by establishing partnerships with hospitals and healthcare providers at a national level to jointly develop and testbed medical technologies to address unmet clinical needs. The programme seeks to provide clinically impactful and cost-effective solutions for healthcare systems, and to shape the medical technology industry of Singapore through innovations. These projects aim to develop and provide cost-effective, innovative and clinically impactful solutions for the healthcare system.

A total of 8 research projects were awarded for a period of 2 to 3 years to tackle healthcare concerns like stroke rehabilitation, epilepsy, traumatic brain injury, glaucoma, cardiac disease, complications in vascular surgery, and surgical training. They were selected by a panel of experts from A*STAR and the medical community that took into account research novelty, clinical relevance and commercial potential.

The grant recipients include SERC RIs comprising of:
- Institute of Infocomm Research (I^2R)
- Institute of High Performance Computing (IHPC)
- Institute of Microelectronics (IME)

They are partnered by doctors and researchers from:
- National University Hospital (NUH)
- National Neuroscience Institute (NNI)
- Singapore Eye Research Institute (SERI)
- Tan Tock Seng Hospital (TTSH)
- National Heart Centre (NHC)
- Singapore General Hospital (SGH)
- KK Women's and Children's Hospital (KKH)
- National University of Singapore (NUS)

Brief Descriptions of BEP Projects

1. **Project AGLAIA (more details behind)**: A rapid and accurate way to screen and diagnose large populations for glaucoma through advanced medical imaging and informatics technologies. Research institutes: I^2R, SERI.

2. **Project ArtsBCI (more details behind)**: A way to perform personalised stroke rehabilitation outside the rehab centre with minimal assistance; and provide early seizure detection and prediction to enable patients to resume normal daily routines, both through the use of Brain Computer Interface (BCI) platforms. Research Institutes: I^2R, TTSH, SGH, NUS, NNI.

3. **Biosensor Prosthetic Vascular Graft**: Vascular graft sensors that provide early detection of vascular graft stenosis in order to extend graft-life and to reduce number of routine graft scans in hospital. Research Institutes: IME, NUHS.

4. **Pressure Sensor Endovascular Catheter**: A more reliable and faster method to obtain vascular access to increase success and safety of vascular surgeries through the use of intelligent endovascular guidewires. Research Institutes: IME, NUHS.

5. **Project ISyNCC**: Advanced monitoring and alert system to enable intensive care unit (ICU) doctors to rapidly make patient-specific treatment decisions in order to improve patient outcomes relating to traumatic brain injuries. Research Institutes: I^2R, NNI.

6. **Project SEIZE**: A less labor-intensive and more skill-dependent monitoring system to automatically and reliably diagnose seizures in epileptics. Research Institutes: I^2R, KKH.

7. **Project IRAS**: An image-guided, robot-assisted training system for simulation of complex surgical procedures such as liver resectioning. Research Institutes: I^2R, NUHS.

8. **Left Ventricular Remodeling**: An accurate and quantitative way to assess and monitor post heart attack patients for left ventricular remodeling in order to prevent disease from deteriorating into heart failure. Research Institutes: IHPC, NHC.

Details on Project AGLAIA

I. Glaucoma, the world's 2nd leading cause of blindness

What is Glaucoma?

Glaucoma is a chronic and irreversible neurodegenerative disease in which the nerve that connects the eye to the brain (optic nerve) is progressively damaged and patients suffer from vision loss and blindness. Patients with early glaucoma do not usually have any signs or symptoms. Progression of the disease results in loss of peripheral vision, so and patients may complain of "tunnel vision" (being only able to see centrally). Advanced glaucoma is associated with total blindness.

How common is Glaucoma?

Two large surveys have been studied on this condition in Singapore. The Tanjong Pagar Study and the Singapore Malay Eye Study showed that the prevalence of glaucoma is 3% in Singaporean adults 40 years and above, with more than 90% of the patients unaware that they have this condition.

Worldwide, it is the second leading cause of blindness, affecting 60 million people by 2010 (Quigley & Broman, 2006) and responsible for approximately 5.2 million cases of blindness or 15% of the total burden of world blindness (*Thylefors & Negrel, 1994*). The problem is even more significant in Asia, as Asians account for approximately half of the world's glaucoma cases. Finally, because it is a condition of ageing, it will affect more people in Singapore and Asia with population ageing.

Why is early detection important?

Treatment (e.g., lowering the intraocular or eye pressure) can prevent progression of the disease in early cases, so early detection is critical to prevent blindness.

While routine screening for glaucoma in the whole population may not be cost effective and is limited by poor sensitivity of current tests, screening may be useful for high risk individuals, such as older people (e.g., 60 years and older), certain racial/ethnic group (e.g., Chinese patients who have a higher risk of glaucoma) and those with a family history of glaucoma (e.g., first degree relatives of a glaucoma patient).

II. Current Treatment Gaps

Glaucoma in Singapore

Currently, there is no systematic way to detect and manage early glaucoma in Singapore. Glaucoma patients are often unaware they have the condition, and present late to the ophthalmologist (eye doctors), usually only when severe visual loss is already present. Treatment at this stage is limited to surgery, is expensive, requires skill personnel, and does not restore vision.

Why are current glaucoma screening strategies not effective?

There are three current clinical examinations to detect and diagnose glaucoma:

1. Intraocular pressure (IOP) measurement
2. Visual field test
3. Optic nerve assessment

None of these tests, either by themselves or in combination, has been shown to be sensitive, specific and effective. IOP measurement is neither specific nor sensitive enough to be an effective screening tool and visual field testing requires special equipments only present in tertiary hospitals (Singapore National Eye Centre, National University Hospitals etc).

Assessment of structural changes in the optic nerve indicative of damage appears to be the most promising approach, and may more sensitive than IOP or visual field testing (Sim & Goh, 1999). Optic nerve assessment is currently performed by a trained specialist (ophthalmologist, usually glaucoma specialist), or using specialized expensive equipment such as the Heidelberg Retinal Tomography (HRT) system. However, optic disc assessment by an ophthalmologist is subjective and the availability of HRT is very limited because of the cost involved. Thus, there remains a lack of cost effective, sensitive and precise method to screen for glaucoma

III. Potential Impact of ALGAIA Technology

Potential Impact on healthcare costs

The healthcare cost of managing glaucoma is significant. A study conducted in United States and Europe reported that the significant potential savings and reductions in annual healthcare burden are possible if patients are diagnosed and treated at earlier stages of glaucoma.[1]

A particular form of glaucoma present in Asia, angle closure glaucoma, imposes an even more substantial financial burden on both the society and individuals. It was reported that annually, acute primary angle closure glaucoma cases in Singapore results in an additional S$500,000. [2] The costs for treating chronic open and closed angle glaucoma, the most prevalent forms of glaucoma in Singapore, are likely to be far higher.

Significance of Project

This will be the first of its kind developing such automatic glaucoma diagnosis system with a unique population-based and cross-country data validation in the world. This will also be the first of its kind doing such a large scale Glaucoma GWAS based on novel Medical Image Informatics Technologies.

The AGLAIA system will compliment and improve current clinical practices and advance the latest intelligent medical image processing based glaucoma diagnosis algorithm using 2D retinal fundus images which can be obtained through the use of existing, commercially available, low-cost equipment.

Details on Project ArtsBCI

I. Stroke - the leading cause of severe disabilities

Stroke is the third leading cause of death and the leading cause of severe disabilities in the developed world (Beers & Berkow, 2000). In Singapore, stroke has an estimated prevalence rate of 4% (Venketasubramanian et al., 2005). About 25% of people who suffered stroke will survive for at least a year, but around 50% of stroke survivors will have moderate to severe disabilities relating to movement, cognition, speech and activities of daily living. Stroke affects the quality of life of the survivors in their daily functioning in the workplace, home, and community. However, with effective rehabilitation, stroke patients could partially regain their motor control and continue with their activities of daily living. This project addresses the rehabilitation needs of stroke patients with the objectives of reducing the financial burden associated with stroke-related disability and the cost in health care from shorter inpatient rehabilitation.

Stroke causes neurological damage to certain portions of the brain, but surviving portions of the brain are capable of altering functional activity in a vicarious manner to provide a substrate for recovery. Current research is directed at understanding how this neuroplasticity phenomenon may be modulated to develop more effective therapeutic rehabilitation for stroke (Nudo, 2006). Presently, physical therapy approaches are the most widely used treatment for stroke (Pollock, Baer, Langhorne, & Pomeroy, 2008), which involves human therapists to assist the stroke patients in recovering their stroke-affected side of the body.

Robotic rehabilitation augments the physical rehabilitation by human therapists and enables novel exercises that are not currently available (Lum, Burgar, Shor, Majmundar, & Van der Loos, 2002). Current studies have shown that robotic rehabilitation helps to improve impairment of hemiparetic upper extremity after chronic stroke (Volpe et al., 2008). Recently, Brain-Computer Interface (BCI)-based robotic rehabilitation is introduced (Ang, Guan et al., 2008a). BCI is a communication system that directly translates brain signals into commands for controlling an external device, which bypasses the normal motor output neural pathways and involves motor or mental imagery practice for stroke patients. (Blankertz, Benjamin, Dornhege, Krauledat, Muller, & Curio, 2007). Motor imagery provides a promising means for stroke patients to recover limb movement with the aid from BCI.

II. Current Treatment Gaps

Physical therapy approaches are the de facto rehabilitation for stroke (Pollock et al., 2008), which involve human therapists to assist stroke patients in recovering their motor ability. Modern rehabilitation technologies include robotics, functional electrical stimulation, transcranial magnetic stimulation and virtual reality (O'Dell, Lin, & Harrison, 2009).

Robotic rehabilitation alleviates the labor-intensive aspects of physical rehabilitation by human therapists (Lum et al., 2002) and could potentially improve the productivity of stroke rehabilitation. However, it is fundamentally based on movement repetition with visual feedback that helps stroke patients improve motor ability in their weak stroke-affected arms and legs. However, the robot is still able to move the weak part of the patient even if the patient is not attentive towards the training and thus the robotic training becomes a passive activity. In contrast, BCI-based robotic training works by ensuring active engagement by the hemiparetic patients in making a volitional movement. In addition, hemiplegic or locked-in stroke patients who do not have any motor power on the affected limbs are then able to engage and perform a volitional movement on these affected limbs.

BCI-based robotic rehabilitation fills this gap by detecting the motor intent of hemiplegic patients from the Electroencephalogram (EEG) signals to drive the robotic rehabilitation.

III. Potential Impact of ArtsBCI Technology

The potential impacts of this new technology are:

1. A more responsive and effective multi-modal BCI system will enable more repetitions of the motor rehabilitation to be performed in a given amount of time. This could translate to a better outcome in motor recovery through the use of a more responsive BCI-based robotic rehabilitation.
2. The preliminary result from the clinical trials of the current system shows that stroke patients are as capable of operating BCI as healthy subjects (Ang, Guan et al., 2008a). However, each patient suffered different degrees of neurological insults and experienced varying degrees of motor recovery rate. Therefore, the proposed solution of individualized rehabilitation that is customized to the condition of each stroke patient could match the *de facto* outcome from customized therapy administered by human therapists.
3. Studies have shown that the prevalence of post-stroke depression is around 30-35% (Lenzi, Altieri, & Maestrini, 2008). Depressed stroke patients suffered higher mortality rates and showed minor rehabilitation improvements compared to non depressed stroke patients. Recent studies have revealed the feasibility of measuring happiness and sadness from EEG (Baumgartner, Esslen, & Jäncke, 2006). The use of advanced multi-modal BCI to detect the mental state of the patient is proposed in order to individualize a more effective rehabilitation therapy for each stroke patient. This could lead to an improvement in the outcome of the stoke patient when such psychological aspect is considered in addition to the physiological rehabilitation.
4. Restoring the hand function facilitates fine hand manipulation such as writing, opening of doors, operating household equipment such as washing machines and driving (Lambercy et al., 2007). This could improve the quality of life of the stroke patient.
5. Swallowing dysfunction is common after acute stroke (Mann, Hankey, & Cameron, 1999). Restoring the swallowing function could help to alleviate dehydration, malnutrition and aspiration pneumonia of stroke patients and thus enhance their quality of life.
6. Studies have shown that there is no place like home for stroke rehabilitation (Mayo et al., 2000). Hence, a portable BCI rehabilitation device could reduce the burden of stroke patients on healthcare professionals in the hospital. Complementing in-hospital rehabilitation with home rehabilitation therapy could also reduce the cost of healthcare and improve the outcome for the stroke patient.

Annex D

INFORMATION SHEET
BACKGROUND & UPDATES ON THE BIOMEDICAL SCIENCES INITIATIVE

1 BACKGROUND

1.1 In June 2000, Singapore launched the Biomedical Sciences (BMS) Initiative - a major drive to establish BMS as one of the key pillars of the Singapore economy, alongside Electronics, Engineering and Chemicals. The driving force was to diversify the economy in the wake of the Asian financial crisis. Beyond BMS manufacturing, Singapore had to move up the value chain to establish a strong base in R&D, to attract corporate R&D activities and anchor manufacturing activities in Singapore.

1.2 Phase 1 of the BMS Initiative (2000 – 2005) focused on building a strong foundation in basic biomedical research. A*STAR's Biomedical Research Council (BMRC), EDB's Biomedical Sciences Group and investment arm Bio*One Capital played a critical role in laying the necessary groundwork, including establishing a critical mass of excellent basic science research talent, a strong pipeline of local talent in training, and state-of-the-art research infrastructure, which attracted a growing base of industry R&D laboratories and activities, as well as anchored and grew the BMS manufacturing sector.

1.3 Phase 2 of the BMS Initiative (2006 – 2010) focused on building up Singapore's Translational and Clinical Research (TCR) capabilities, while continuing to strengthen our foundation in basic sciences. Such capabilities were essential to realising the full potential of our investments in BMS, as industry requires a strong TCR framework to validate potential new drugs and devices as well as meet regulatory requirements. To drive this new phase of development and its specific focus on TCR, the Biomedical Sciences Executive Committee (BMS EXCO) was re-constituted in 2006 to be co-chaired by A*STAR Chairman and the Permanent Secretary for Health.

2 ACHIEVEMENTS FROM 2000 - 2009

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2.1 Since 2000, Singapore has made significant progress in the BMS Initiative in developing human, industrial and intellectual capital. It has gained international recognition as a dynamic and vibrant centre for biomedical research that is highly competitive in terms of research output quality and impact.

Human Capital

2.2 Attracting World Class Scientific Talent: Singapore has seen considerable success in attracting world-class international scientific talent to play leading roles in driving our BMS Initiative. These internationally-renowned scientists have built up our research institutes, nurtured the younger generation of scientists and students, and tapped on their vast experience to help Singapore to identify and develop new capabilities.

2.3 Developing a Strong Pipeline of Local Research Talent: Since 2001, A*STAR has awarded scholarships and fellowships in BMS to 524 young individuals, comprising 312 National Science Scholarships, 28 MBBS-PhD scholarships, 143 A*STAR Graduate Scholarships and 41 International Fellowships. To date, more than 100 of these BMS scholars have completed their PhDs and returned to work at various A*STAR research institutes and units.

2.4 Developing Clinician Scientists and Investigators: A key objective of BMS Phase 2 was to build up a critical mass of these personnel, supernumerary to clinical service needs. To recruit and support outstanding clinician-scientists and clinician-investigators, the BMS EXCO established several initiatives to develop the human capital necessary for TCR. Following the peer-review process, a total of 44 national-level talent development awards have been funded (as of October 2009). There are more than 80 clinician-scientists in total, some holding national-level awards and others being supported by the healthcare clusters and academic medical centres (see para 2.10).

Human Capital Development-related Funding Initiative	**Number of Awards funded as at Oct 2009**
STaR Investigator Awards	7
Clinician Scientist Awards (CSAs)	15
Masters of Clinical Investigation (MCI) Programme	15
NRF-MOH Healthcare Research Scholarship	7

2.5 Scientific Talent for Industry and Academia: The public research institutes and universities have played a critical role in training scientific talent for industry and academia. Since 2001, the pool of BMS researchers in Singapore and the number of those with PhDs have more than doubled. This ready access to trained scientific talent helps to support corporate R&D activities in Singapore. A*STAR's research institutes also help to address specific gaps in skilled manpower through specialised training programmes such as the Bioprocess Internship Programme run by BTI.

Industrial Capital

2.6 Sustained growth of the BMS Sector: Since the start of the BMS Initiative in 2000, the BMS manufacturing output, value added (VA) and employment has increased significantly. Manufacturing output has increased around 3 times from S$6.3 billion in 2000 to S$19 billion in 2008 (CAGR: 13.2%). VA has shown a similar increase, from S$3.8billion in 2000 to S$10.6billion in 2008. Employment has more than doubled from 5,880 jobs in 2000 to 12,450 jobs in 2008. 4,169 were employed under the Pharmaceutical sector and 8,281 were employed under the Medical Technology sector.

2.7 Attracting BMS Manufacturing Activities to Singapore: Today, leading pharmaceutical, biotechnology and medical technology companies have invested in more than 50 commercial-scale manufacturing facilities in Singapore. The BMS industry accounted for 4.1% of Singapore's GDP in 2008 and provides some of the highest-paying jobs in the manufacturing sector. Companies manufacturing in Singapore for the global market include half of the top 20 international pharmaceutical companies, e.g. Abbott, Genentech, GlaxoSmithKline (GSK), Merck, Novartis, Pfizer, Sanofi-Aventis, Schering-Plough, Wyeth and more than 25 medical technology companies including leaders such as Siemens and Becton-Dickinson.

2.8 Catalysing Growth of New Biologics Sector: Biologics is the fastest-growing segment of the pharmaceutical/biotech industry, and involves complex manufacturing processes dealing with living biological systems and requiring specialised talent. A*STAR's Bioprocessing Technology Institute (BTI) played a key role by establishing the necessary capabilities and expertise, which helped Singapore to attract biologics investments. In 2003, BTI's Biopharmaceutical Manufacturing Technology Centre, was spun off into a company called A-Bio, a contract biologics manufacturer. Over the next few years, A-Bio successfully secured major contracts from GSK and Novo Nordisk, thus building up a strong track record for itself and for Singapore. As a result, Singapore has secured six major biologics investments over the last 3 years, totalling more than S$2 billion, from Genentech, Lonza, GSK, Novartis and Baxter. These facilities will manufacture biologics for the global market and create a total of about 1,300 new jobs.

2.9 Attracting BMS Corporate R&D to Singapore: Singapore has successfully grown the base of corporate R&D activities, and now has more than 50 companies carrying out R&D in drug discovery, TCR and medical technology innovation here. Private sector expenditure on BMS R&D increased more than 4-fold, from $88 million in 2001 to S$427 million in 2007.

2.10 State-of-the-art Research Infrastructure: Biopolis, a purpose-built biomedical research hub with state-of-the-art research infrastructure, was opened in October 2003. This dynamic and cosmopolitan BMS research campus co-locates both public and private sector BMS R&D laboratories including more than 20 companies, e.g. Abbott, GSK, Lilly, Novartis, Schering-Plough, Takeda, as well as international S&T entities e.g. RIKEN Liaison Office and Swissnex. Private sector labs enjoy access to the shared scientific services and core facilities of A*STAR and opportunities to collaborate with A*STAR scientists on joint research projects. With the establishment of Fusionopolis in 2008, Singapore is also well poised to engage in interdisciplinary research, integrating biomedical sciences and the physical and engineering sciences.

2.11 Development of academic medicine: Kent Ridge & Outram campus: Singapore is in the process of establishing Academic Medical Centres (AMCs), namely the National University Health System at Kent Ridge and the SingHealth/Duke-NUS Graduate Medical School at the Outram Campus. The AMCs, where basic scientists and clinician-scientists work together to strengthen TCR capabilities while embedded in clinical service, drive greater integration between clinical care, research and education. The AMCs provide the platform to translate discoveries from the laboratory, into new treatments and applications that benefit patients.

2.12 Enhancing Clinical Research Infrastructure: The BMS EXCO also made significant headway in enhancing the infrastructure for clinical research and clinical trials. The Investigational Medicine Units (IMUs) and the Singapore Clinical Research Institute (SCRI) play a critical role in building up our capabilities and support for clinical trials – early stage (Phase 1 to 2a) in the case of IMUs, and late stage (Phase 2b to 3) in the case of SCRI. The National Breeding Centre (NBC) and Clinical Imaging Research Centre (CIRC) were established as national resources to support both industry R&D activities, as well as the basic, translational and pre-clinical research carried out by public sector institutions.

2.13 Attracting First-in-Man and Phase 1 clinical trials to Singapore: Singapore has also attracted pharmaceutical MNCs such as Abbott and AstraZeneca to conduct innovative early phase clinical trials here. MNC clinical trials units such as Pfizer and Lilly which perform First-In-Man trials to test new drug candidates for safety. Companies such as GSK, Bristol-Myers, Takeda and Eisai also partner with local and regional hospitals to run and coordinate trials from and in Singapore.

2.14 Spin-offs: BMRC research institutes have spun off several companies over the years. Some examples include Merlion Pharmaceuticals (from IMCB's Centre for Natural Product Research), which went on to be named one of Fierce Biotech's companies to watch in 2007 and Curiox (from A*STAR's Institute of Bioengineering and Nanotechnology). Curiox produces a miniaturised bioassay, called DropArray that can be used to measure pharmacological activity of biological substances and performing other related tests.

Nanostart AG, the German-based world's leading nanotechnology investment company, is the lead investor.

Intellectual Capital

2.15 Sustained growth of R&D activity: In 2007, the BMS sector's gross expenditure on R&D (GERD) reached S$1.1billion, 37% coming from the private sector and 63% coming from the public sector.

2.16 Translational and Clinical Research Programmes: During BMS Phase 2, five TCR flagship programmes were established to encourage the translation of basic science discoveries to clinical applications. The Flagship programmes pulled together scientists from Biopolis, the universities and hospitals to work in five areas of strategic interest, viz. Cancer (gastric cancer), Eye Disease (ocular surgery), Infectious Disease (dengue fever), Metabolic Disease (developmental pathways) and Neuroscience (schizophrenia). These were chosen based on their relevance to Singapore's healthcare challenges, as well as on our existing strengths in clinical research and the presence of complementary expertise in the hospitals, specialty centres, universities and research institutes.

2.17 Early indications of economic and health impact from TCR: Although the TCR Flagship programmes are less than three years old, the Gastric Cancer TCR Flagship Programme's first systemic study of prospective screening for gastric cancer detected early gastric cancer in 10 patients out of 1629 individuals screened. This study has contributed significant new knowledge that potentially impacts how early detection and treatment for this cancer which is prevalent in this part of the world. The Eye TCR Flagship Programme has also filed two patents.

2.18 Developing indigenous IP: Singapore has seen some promising signs of early success in developing IP indigenously. Homegrown biotech companies have recently entered their first "discovered-in-Singapore" drugs into clinical trials: S*Bio, Singapore's first drug discovery company, currently has 2 candidates to treat cancer and myeloproliferative disorders in clinical trials and is entitled to receive more than US$600 million in payment under two licensing agreements with 2 US-based biotech companies, Onyx and Tragara, to develop oncology drugs.

2.19 The establishment of A*STAR's Experimental Therapeutics Centre (ETC) has helped to build up Singapore's expertise in drug discovery and development so as to translate basic science discoveries into proof of concept projects that will be more attractive for out-licensing to industry or for the formation of new enterprises. The BMS industry can also tap on the capabilities established and talent trained in drug discovery and development by ETC to enhance their own drug discovery activities.

2.20 Commercialised Research Output: A*STAR's Institute of Molecular and Cell Biology (IMCB) and the Genome Institute of Singapore (GIS) have conducted research that led to the development of the SARS and H5N1 diagnostic kits, licensed by Roche and Veredus Laboratories respectively. IMCB biologists also isolated 15,000 unique genetic markers from the zebrafish, called Expressed Sequenced Tags (ESTs) and arrayed these ESTs onto two gene chips, which allow researchers to conduct high-throughput screening for unknown gene or genes of particular interest in various biological conditions. Exploit Technologies licensed the EST library to Open Biosystems Inc., a US-based company, which specialises in supplying high quality clones.