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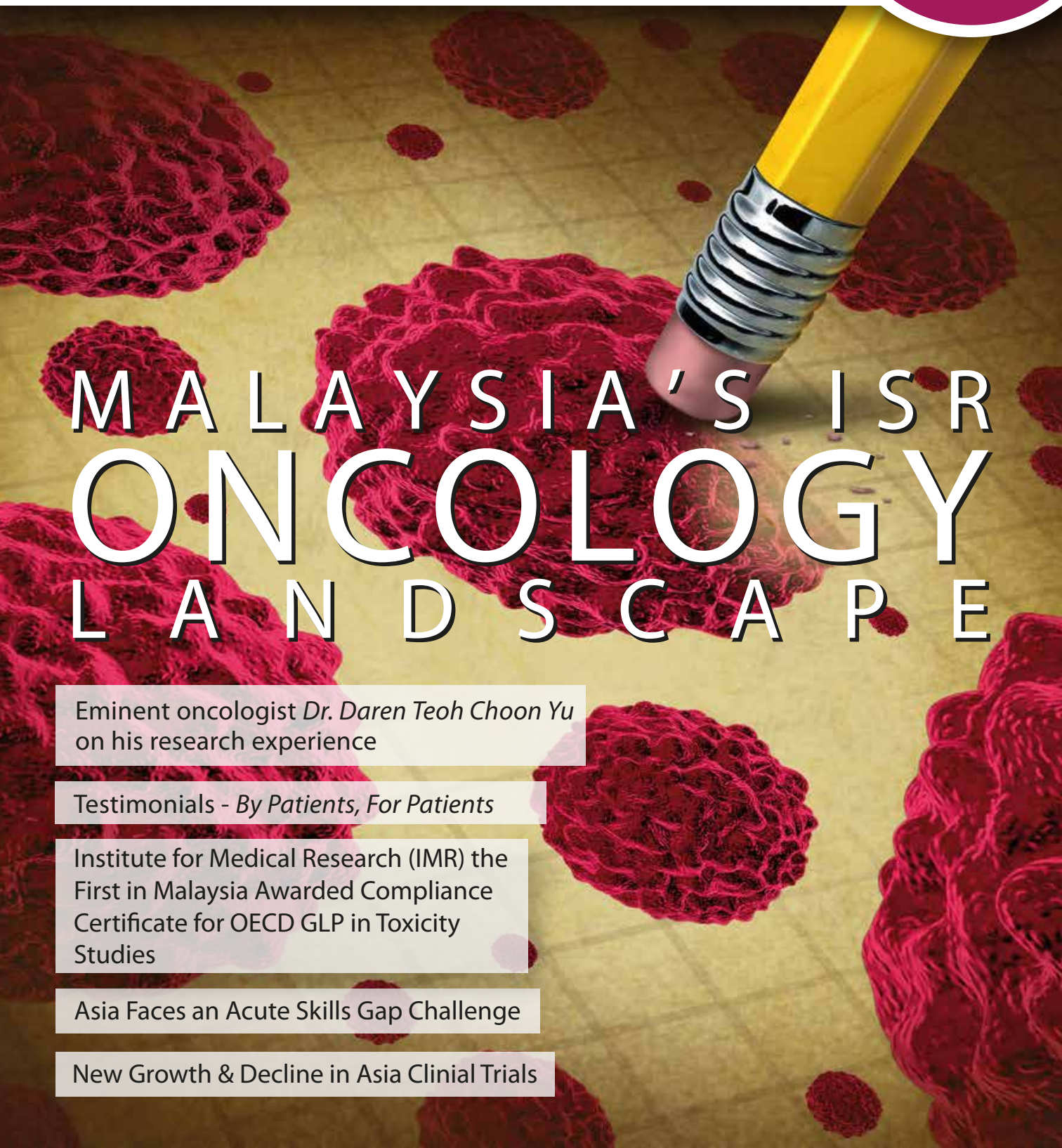

MALAYSIA'S ISR ONCOLOGY LANDSCAPE

Eminent oncologist *Dr. Daren Teoh Choon Yu* on his research experience

Testimonials - *By Patients, For Patients*

Institute for Medical Research (IMR) the First in Malaysia Awarded Compliance Certificate for OECD GLP in Toxicity Studies

Asia Faces an Acute Skills Gap Challenge

New Growth & Decline in Asia Clinial Trials

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CLINICAL RESEARCH MALAYSIA

Clinical Research Malaysia (CRM) is a non-profit organization wholly owned by the Government of Malaysia. It was established in June 2012 to promote Malaysia as a preferred global destination for industry sponsored clinical research (ISR). CRM provides a range of services to enable and facilitate sponsors (primarily from the pharmaceutical and medical device industries) and contract research organizations (CROs) to initiate a wide spectrum of clinical trials in Malaysia.

CRM's key functions encompasses three core components, the first of which is securing clinical trials. This is done through advertising and promotional activities, participation in key conferences, involvement in clinical trial distribution and strategic collaborations with major stakeholders. The second component involves closing the deals through a comprehensive feasibility study, convincing site review operation and implementation of an efficient financial, administration and approval process. The third component is conducting the trials. This is achieved through our high quality Study Coordinators and Principal Investigators, effective standard operating procedures, quality assurance of study sites and support services.

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MINISTRY OF HEALTH MALAYSIA

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From the **CEO's** *desk*

CRM
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Your Global Solutions in One Nation

I would like to congratulate and extend my deepest appreciation to the Communications and Relations team headed by Mr Rajeshpal Singh, on their perseverance in successfully publishing two CRM bulletins and the inaugural NCCR bulletin for the year 2014. These bulletins have far exceeded what we at CRM had initially envisioned. The bulletins have served as a key reference point for many in the industry and to some extent as a guiding light for those embarking on clinical research in Malaysia.

The bulletins were planned to be thematic, each centered around a particular therapeutic area. This bulletin, the third one, focusses on cancer. This is a very relevant subject to be highlighted in Malaysia. Cancer is the fourth most common cause of death in Ministry of Health (MOH) hospitals, based on 2011 figures. The incidence of cancer in Malaysia increased from 32,000 new cases in 2008 to 37,400 in 2012. This number is expected to rise to 56,932 by 2025 if no action is taken. Data from the National Cancer Registry Report 2007 showed that the most common cancer is breast cancer followed by cancer of the colon, lung, nasopharynx and cervix.

We took cognizant of these dire incidences of cancer and have, since 2012, developed and implemented specific key strategies. The strategies can be broadly categorized into patient/public centric, oncologist/specialists centric and industry centric.

On the first category, CRM is actively engaging with patient support groups, associations and NGOs which focus on cancer. This culminated in CRM participating in a cancer survival workshop organized by the Malaysian Oncology Association in June 2013. CRM took a step further in 2014 by jointly organizing the World Cancer Day Conference and Expo with National Cancer Society Malaysia (NCSM) and InfoMed Magazine. We are currently stepping up efforts in expanding these activities and building initiatives for patient recruitment.

For the category of oncologists and specialists, we have implemented multi-pronged strategies. The end objective is to increase the number of investigators for clinical research. We work with oncology-related associations, Head of Oncology services at MOH and private centers, establishing both informal and formal relationships, with the latter taking the form of Memorandums of Understanding (MOUs). The MOH is also studying a proposal to allow private oncologists to tap patients in public hospitals for clinical trials. We have also initiated Mentor-Mentee programs at various regions, by encouraging experienced oncologists to take up a mentorship role in guiding junior specialists into the field of clinical research.

The statistics on Industry Sponsored Research on page 2 of this bulletin clearly shows that oncology trials are among the top five trials conducted in the country. This sets up the path for our industry engagement. CRM has met up with numerous pharmaceutical and clinical research companies, as well as conducted an Industry Dialogue in Singapore, to attract more oncology clinical research.
We have showcased two amazing individuals in this bulletin, who in their own right, have done spectacularly well in their contributions towards the development of clinical research in Malaysia.

I wish all of you an enjoyable read as much as we enjoyed in developing these bulletins.

Dr. Mohamed Ali Abu Bakar
CEO, Clinical Research Malaysia

ISR STATISTICS

MALAYSIA

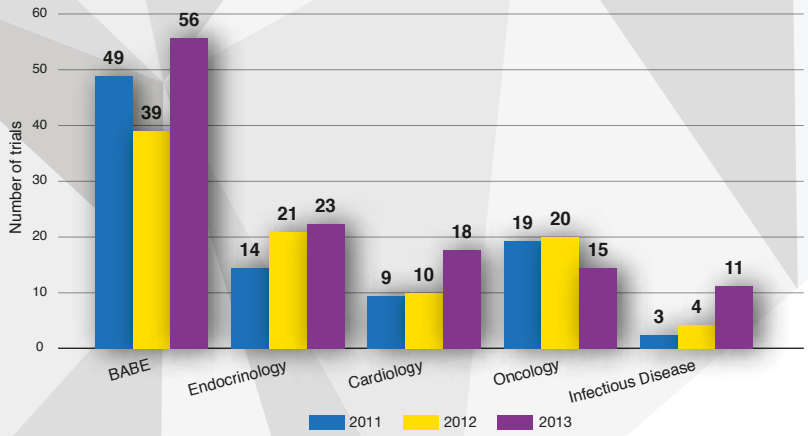


Figure 1. Shift in therapeutic focus from 2011 to 2013

Shift InTherapeutic Focus From 2011 to 2013

Majority of the trials conducted between 2011 and 2013 were BABE-related. An increase in endocrinology, cardiology and infectious diseases trials were observed between 2011 and 2013, while oncology-related trials showed a slight decrease.

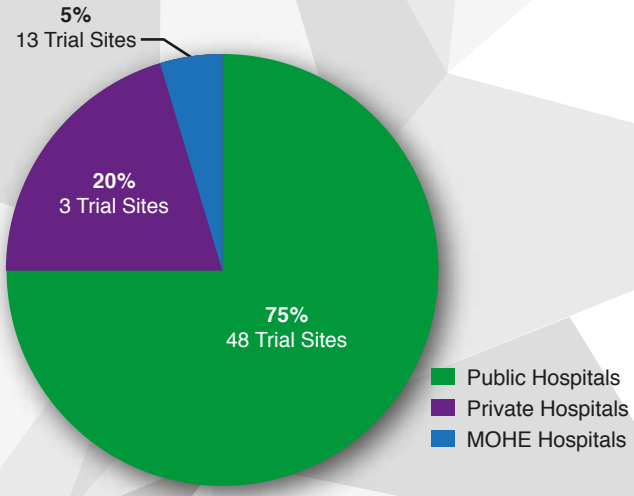


Figure 2. Breakdown of trial sites in Malaysia

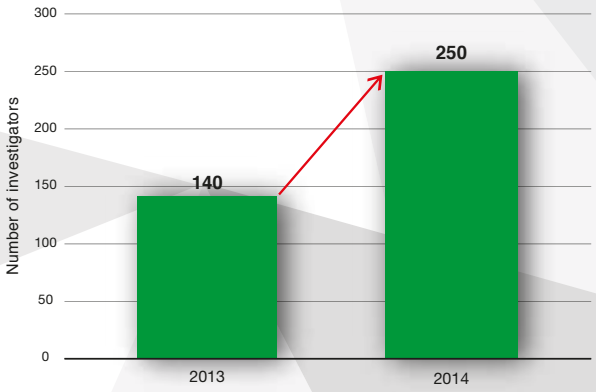


Figure 3. Projection of active investigators

In 2013, there are about 140 active investigators conducting CTs and in 2014 this number is projected to increase to 250 active investigators.

Table 1. Trial Sites in Malaysia

Public Hospitals		
Hospital Sultanah Aminah	Klinik Pergigian Gunung Rapat	Hospital Raja Permaisuri Bainun
Hospital Permai	Hospital Tuanku Fauziah	KK Greentown
Hospital Sultan Ismail	Hospital Pulau Pinang	Hospital Bahagia
Hospital Sultanah Bahiyah	Hospital Seberang Jaya	Hospital Seri Manjung
Hospital Sultan Abdul Halim	Klinik Kesihatan Bandar Baru Air Itam	KK Buntong
KK Simpang Kuala	Hospital Queen Elizabeth I	KK Lenggong
Hospital Raja Perempuan Zainab II	Hospital Mesra	Hospital Putraja
Hospital Melaka	Hospital Wanita dan Kanak Kanak Likas	KK Putrajaya
KK Tampin	Hospital Queen Elizabeth II	Klinik Pergigian Putrajaya
Hospital Tuanku Jaafar	Hospital Likas	Hospital Tunku Ampuan Rahimah
KK Seremban 2	Hospital Umum Sarawak	KK Shah Alam Seksyen 7
Hospital Tuanku Ampuan Najihah	Hospital Sentosa	Hospital Sultanah Nur Zahirah
KK Ampangan	Hospital Miri	Hospital Kuala Lumpur
Hospital Tengku Ampuan Afzan	Hospital Sibu	Pusat Darah Negara
Hospital Taiping	Hospital Serdang	Institut Perubatan Respiratori
Hospital Ampang	Hospital Selayang	KK Cahaya Suria

MOHE Hospitals
University Malaya Medical Centre
Hospital University Kebangsaan Malaysia
Hospital University Sains Malaysia

Private Hospitals
Sime Darby Medical Centre
Prince Court
National Heart Centre
Loh Guan Lye
Gleneagles
Mount Miriam Hospital
Penang Adventist Hospital
Lam Wah Ee
Nilai Medical Centre
Pantai Hospital Penang
Mahkota Medical Centre
Pantai Hospital Ayer Keroh

KK = Klinik Kesihatan

Table 2. Phase I/BABE sites, Pre-clinical and GLP-certified laboratories in Malaysia

Phase I /BABE Sites
Hospital Ampang
Hospital Kuala Lumpur
Pusat Darah Negara
National Cancer Institute
Hospital Pulau Pinang
CRC Veeda, Ampang
Hospital Raja Permaisuri Bainun
Hospital Sungai Buloh
Hospital Umum Sarawak
Hospital Sibu
Hospital Tuanku Jaafar
Hospital Putrajaya
Hospital Seberang Jaya
Hospital University Sains Malaysia

Pre-clinical Labs
Cerca Insights Sdn Bhd
IPharm Animal Research Facility (IPARF)
Environmental Technology Research Centre (ETRC), Sirim Berhad
Melaka Biotechnology Corporation
Info Kinetics Sdn Bhd
Institute Medical Research

GLP Certified Labs
Environmental Technology Research Centre
Melaka Biotechnology Corporation
Info Kinetics Sdn Bhd
Non-clinical Research, Laboratory Animal Resource Unit, Medical Research Centre, Institute for Medical Research

ASIA PACIFIC

ISR & IIR clinical trials conducted in Asia Pacific countries (2005 – June 2014)

Japan recorded the highest number of trials in the Asia Pacific region, followed by China and South Korea. Within ASEAN, Thailand and Singapore ranked ahead of Malaysia.

Of the total number of trials (47,078) registered between 2005 and June 2014, 14,041 (30 %) were industry-sponsored research (ISR) and the rest were investigator initiated research (IIR). About 734 new trials were initiated from January 2014 and a growth of 4.37 % was observed between the first and second quarter of this year.

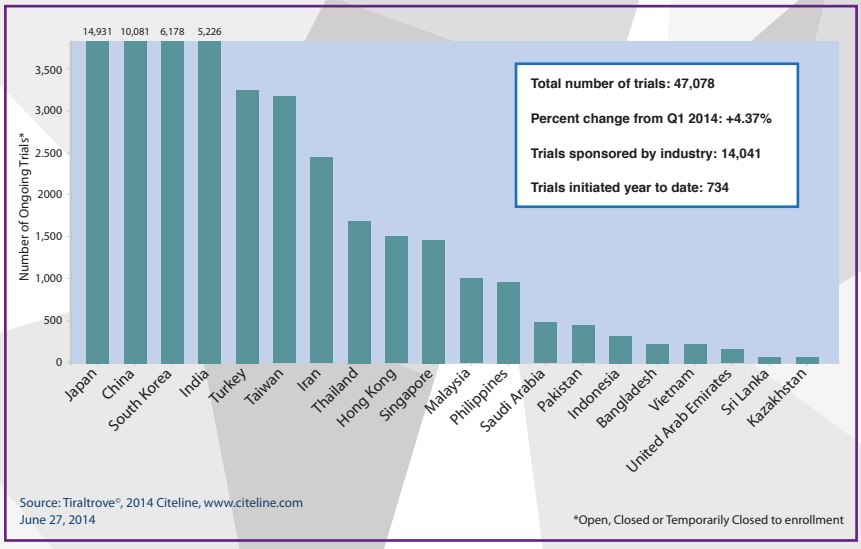


Figure 4. ISR & IIR clinical trials conducted in Asia Pacific countries (2005 – June 2014)

Ongoing clinical trials in Asia Pacific according to Phase (2005 – June 2014)

Phase III trials were the most common in a number of Asia Pacific countries, including in all ASEAN countries.

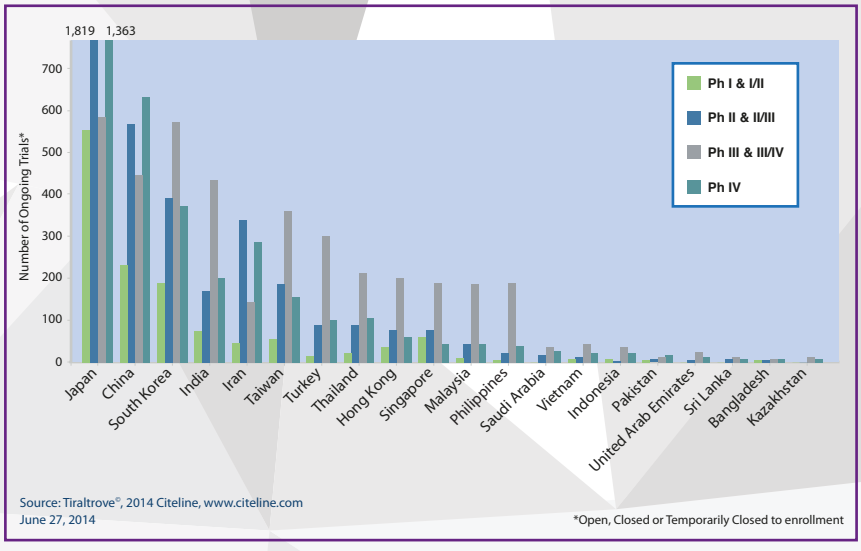


Figure 5. Ongoing clinical trials in Asia Pacific according to Phase (2005 – June 2014)

CANCER INCIDENCE IN MALAYSIA

A total of 18,219 new cancer diagnosis were made in 2007 (the most recent year for which reliable statistics are available), of which 44.6% were men and 55.4% were women. Penang (18.8%), Johor (18.4%) and Selangor (11.3%) recorded the highest number of new cancer cases among the various states in Malaysia. The ten leading cancers among Malaysians in 2007 were breast, colorectal, lung, nasopharynx, cervix, lymphoma, leukemia, ovary, stomach and liver. For men, cancer of the trachea, bronchus and lung were the most common (Figure 6), while breast cancer was the most common among women (Figure 7).

Figure 6. Ten most common cancers in Malaysian men

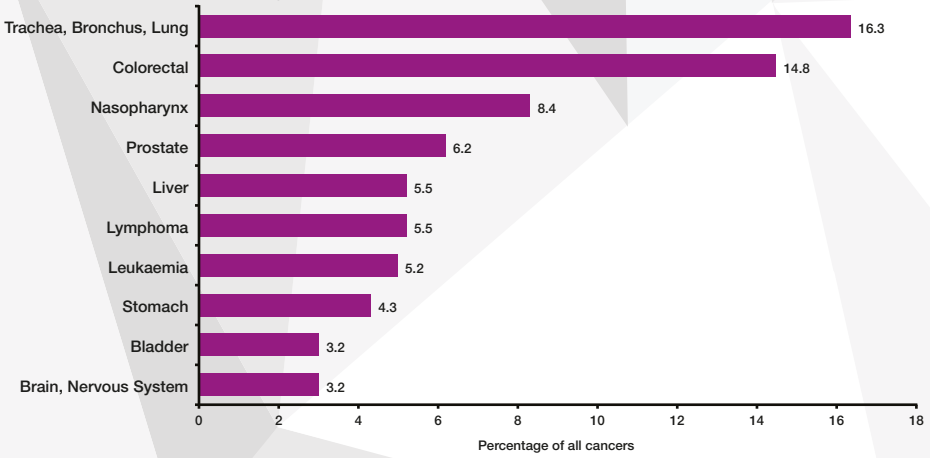
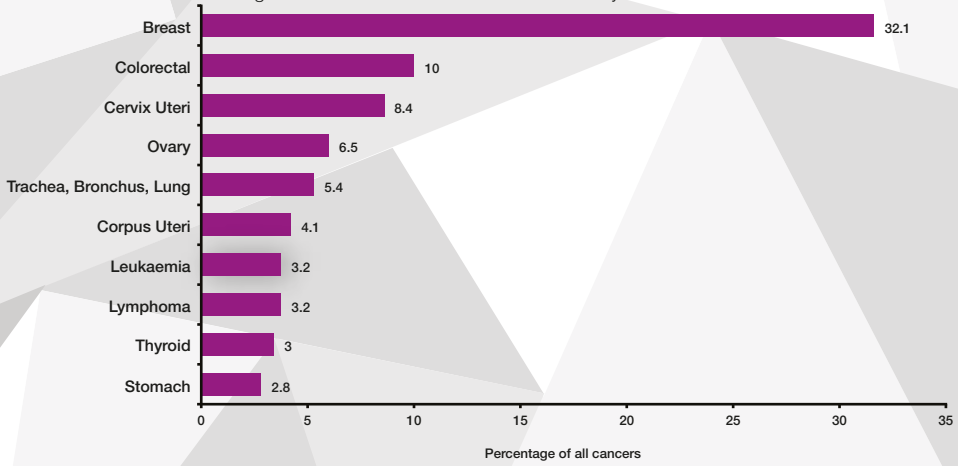


Figure 7. Ten most common cancers in Malaysian women



Staging was reported for 8,869 (48.7%) from the 18,219 new cases reported and registered at the National Cancer Registry. Of these, 17% were reported as stage I, 25.3% as stage II, 25.0% as stage III and 32.7% as stage IV. This translates into about 57.6% of people with advanced stage cancers at the time of their diagnosis.

Cancer Sites	Stage III (%)	Stage IV (%)
Breast	24.2	17.7
Colorectal	31.8	31.7
Cervix	25.6	18.7
Mouth	19.4	55.9
Nasopharynx	33.3	32.3

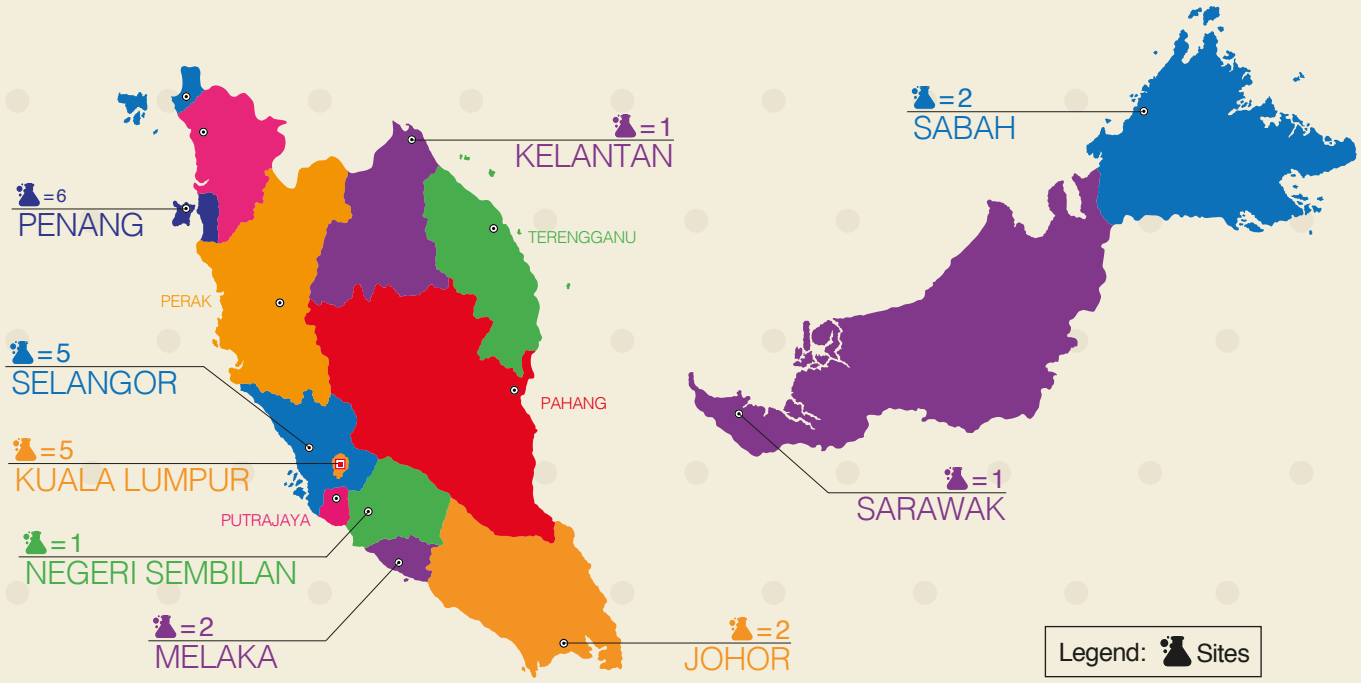
Source: National Cancer Registry Report, Malaysia Cancer Statistics 2007

ONCOLOGY

Research Capability in Malaysia

Since 2011, oncology has been among the top five therapeutic areas in relation to clinical trials conducted in Malaysia. There are over 25 potential trial sites nationwide, comprising of private and government-owned hospitals, as well as university hospitals. Between 2011 and 2013, more than 50 oncology trials have been conducted. With CRM striving to bring in more ISR trials to Malaysia, the number of oncology related PIs and trial sites will increase steadily over the coming years.

With more than 20,000 new cancer cases being diagnosed annually, and supported by the expanding network of capable PIs and trial sites, Malaysia will continue to be of interest to pharmaceutical companies and contract research organizations (CROs) as a destination for the conduct of oncology-related trials.



Kelantan
University Sains Malaysia Hospital

Kuala Lumpur
Kuala Lumpur Hospital
Ampang Hospital
Pantai Medical Centre
Prince Court Medical Centre
University Malaya Medical Centre

Melaka
Hospital Pantai Ayer Keroh
Mahkota Medical Centre

Johor
Hospital Sultan Ismail
KPJ Johor Specialist Hospital

Negeri Sembilan
Nilai Medical Centre

Selangor
Beacon Hospital
Damansara Specialist Centre
Sime Darby Medical Centre
Sunway Medical Centre
University Kebangsaan Malaysia Medical Centre

Penang
Gleneagles Medical Centre
Hospital Pulau Pinang
Lam Wah Ee Hospital
Loh Guan Lye Specialist Centre
Mount Miriam Cancer Hospital
Penang Adventist Hospital

Sabah
Sabah Women and Children's Hospital (Likas)
Sabah Medical Centre

Sarawak
Sarawak General Hospital

Research Personality

Dr. Daren Teoh Choon Yu

Consultant Clinical Oncologist,
Head of Radiotherapy and Oncology
Sabah Women and Children's
Hospital (Hospital Likas), Kota Kinabalu

Dr. Daren Teoh, popularly known as Dr. Daren, obtained a Bachelor of Medicine, Bachelor of Surgery and a Bachelor of Medical Science (1st class honours) from the University of Nottingham, United Kingdom in 1999. He went on to pursue MRCP (UK) and FRCR (UK) before completing his specialist training in clinical oncology at various notable institutions including the University Hospital Birmingham, University Hospital Coventry and Warwickshire, New Cross Hospital, North Staffordshire Hospital and Royal Shrewsbury Hospital.

Dr. Daren's expertise are in non-surgical local and systemic management of all solid organ cancers, 2D, 3D, conformal and image-fusion external beam radiotherapy techniques, as well as in gynecological and prostate brachytherapy techniques. As principal investigator with more than 10 ongoing trials currently, he has successfully published his findings in top tier international journals. Currently, Dr. Daren is a Consultant Clinical Oncologist, Head of Radiotherapy and Oncology Department and Deputy Head of the Clinical Research Centre at the Sabah Women and Children's Hospital. He is also Honorary Lecturer at the School of Medicine, University Malaysia, Sabah.

CRM recently interviewed Dr. Daren for insights on his professional journey in clinical research:

Can you describe how you got involved in clinical trials and when did it all begin?

I've been conducting clinical trials since my early training days as a sub-investigator under the guidance of Professor Robert Grieve at University Hospital Coventry and Warwickshire. Prof. Grieve strongly believed that we should have a clinical trial for each problem that we did not have an answer to. He was instrumental, inspiring and showed me the ropes in conducting clinical trials; eventually I caught the bug. This happened between 2003 and 2009.

Is there a difference in the conduct or environment of the clinical trial industry during your early training years compared to now?

Yes, there's a huge disparity in terms of infrastructure. The West had more advanced infrastructure compared to Malaysia and we were nowhere close to those countries 20 years ago. However, Malaysia has been developing the infrastructure needed to conduct clinical trials and CRM has been a step forward in building that infrastructure and research culture. Research cannot be conducted without good infrastructure and resources, and the initiative by the Malaysian Government to form a dedicated organisation within the Ministry of Health to support this ecosystem should be applauded.

How big is your clinical research team?

In 2010, my team comprised of one sub-investigator and one study coordinator. We were a small team then, but right now my team is growing with an additional Principal Investigator, three Study Coordinators, one Study Nurse and three Sub-Investigators.

Can you briefly describe your normal working day?

I get tied up with work from sunrise to sunset. Rarely do I get the luxury of indulging in a wholesome meal for lunch, most often only managing to settle with biscuits and tea to get me through the day. Unlike my daily clinical practice, clinical trials are not as rigid and can sometimes be flexible. However, when an adverse event happens, extra work needs to be done and completed before I call it a day. To sum it all, conducting clinical trials and my own clinical practice requires good time management.

How many hours a day do you spent conducting clinical trials and how often do you deal with adverse events?

It really depends on the type of trial. What's important is to be contactable at all times. In this department, we have dedicated one day a week whereby each Principal Investigator concentrates on monitoring and looking after the patients who are in clinical trials. Very rarely does a serious adverse event happen. I believe that with good management, the incidence of adverse events can be minimized.

What would be the phases of trials that you mainly conduct?

Phase II and phase III trials. We are not ready for phase I trials in this department. I believe this is how every department should start, by concentrating first on Phase II and III trials to build experience.

Can you highlight a few of the trials which you have conducted and which you particularly remember?

One will be the SAVE-ONCO phase III clinical trial. It is a multinational, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of AVE5026 in the prevention of venous thromboembolism (VTE) in cancer patients at high risk for VTE and who are undergoing chemotherapy. The other will be the SAFE-HER study which is a phase III prospective, non-randomized, multinational, open label study to assess the safety of assisted and self-administered subcutaneous trastuzumab as therapy in patients with operable Her 2 positive early breast cancer.

In your opinion, what is the most important criteria to be a successful investigator?

The most important criteria to be a successful principal investigator is the ability to pick oneself up each time after a fall. In other words, perseverance is the key ingredient. When I returned to Malaysia in 2010, I did not manage to recruit any patient for the first clinical trial which I undertook. I was not selective enough and unaware of the cultural differences of the people here. Having flopped my first clinical trial in my motherland was not a good start but in subsequent trials I went on to recruit more patients. I am proud to claim that my team and I have recruited the most number of patients in this region for some trials and had the first patient in for others. We are mostly bound to fail in new endeavours but the willingness to bounce back and learn from mistakes are essential.

What would be your biggest challenge in conducting clinical trials?

Skilled human resource. As the clinical trial industry is still very new in this country, the challenge lies in developing and improving the level of clinical research skills among clinicians and supporting staff. And to develop this we need the support from the government, CRM and non-governmental organizations.

"We are mostly bound to fail in new endeavours but the willingness to bounce back and learn from mistakes are essential"

- Dr. Daren

And the top three most rewarding part of it?

Firstly, to be able to treat patients with drugs that would either be too expensive for the patient to afford or drugs that are not yet available in the country. By doing so, patients may gain extra years of life. In certain cases, even if a patient has the money they can't get access to these drugs as it is yet to be registered. Secondly, it saves the government and hospital money. For example, when a new clinical trial drug (provided by the sponsor) is used to substitute an already available but expensive drug in the market, taxpayers money can be saved. Thirdly, the level of knowledge and skills of the investigators and supporting staff will be greatly improved because they are carrying out tasks that are beyond the regular day to day routine. It is rather exciting to know that we are trying to do ground-breaking discoveries that investigators in the West are doing.

So, how does clinical trials change your practice and management of patient care?

In a way, it had got me thinking about what I could have done if I had the medical technology or a new drug/target that could make a difference to a patient's life such as keeping the cancer from returning or giving them additional years of life.

There are many benefits a patient can get from participating in a clinical trial. Can you briefly give examples in your personal experience on how your patients have benefited from it?

I can vividly remember the case of a female patient who required a very expensive antibody drug to treat her cancer and in order to afford this drug, she would have to sell her house. When I told her that this antibody drug is available in a clinical trial and even so in a better form where it can be given in an outpatient basis over a shorter period of time with equivalent benefits to the current drug, she was thrilled. She underwent the whole treatment programme for a year. She was grateful for the fact that she did not had to sell her house or get a loan to pay for the drug, but received a better drug

Oncology clinic at Sabah Women and Children's Hospital

formulation. Her cancer went into remission and she decided to donate her travel reimbursements from the clinical trial to another person from a more distant rural area and also went around encouraging people to participate in clinical trials.

I can also tell you of another patient whose cancer cells had spread all over his body and there was no available treatment at that time. With a clinical trial that was run in partnership with an international pharmaceutical company, he had the access to a new oncology drug which was not yet approved in Malaysia and he received if for free. The drug managed to control his disease by 1.5 to 2 years.

Were there any patients whose condition did not improve and why should patients not be afraid to participate in clinical trials?

There are. In any clinical trial, the investigators will always weigh the potential benefits and side effects of a new drug/treatment before administering it and will disclose even the slightest side effect that could possibly happen. Compared to patients in standard care, those that are in a clinical trial are monitored more closely and thus should there be a serious adverse event, it will be detected immediately and treatment is quickly administered to ameliorate its side effects. In clinical trials, patients are very well informed. Even elderly patients with lower education levels are able to take a calculated risk before consenting to participate in a clinical trial.

Do you think that it is easier to obtain consent from patients in the developing countries than in developed ones?

I would like to think otherwise. In developing countries like Malaysia especially in Sabah, people are less exposed to the idea of clinical trials and thus it is more difficult to convince them to participate in one. Just like the fear of chemotherapy among Asians which are higher compared to our western counterparts because of the lack of exposure to this treatment, so it is with clinical trials. Therefore, I think that we have a bigger challenge in convincing and recruiting patients. At the same time, it is important to ensure that good clinical practice is adhered to in all trials.

What would be your advice to potential doctors who are interested in taking up clinical trials?

As Nike says, just do it! If you fail, pick yourself up and do it again.

Chemotherapy treatment centre at Sabah Women and Children's Hospital

Asia Faces an Acute Skills Gap Challenge

By Amrita Tejasvi

Article reprinted with permission from BioSpectrum Asia

BioSpectrum Asia Top 20 Survey: The lack of skilled personnel and the increasing gap between the supply and demand of well-qualified human resource is acting as a major hurdle for Asia to emerge as a center of research and innovation. Let's look at the challenges faced by Asian countries while recruiting the right human talent.

Shortage of skills and qualification among life science professionals to pursue risk laden activities is proving to be a hurdle for Asia to emerge as a center of research and innovation. Countries like China and India, which are already riding high in API production and generics business, are striving to lead innovative drug and molecules development. However, lack of skilled labor in R&D is slowing the process.

Recent growing investments by international companies to build their R&D operations in Asia have opened opportunities for domestic talent pool to work with big players of the industry and enhance knowledge sharing. In 2012, Chugai Pharmabody Research, a Japan-headquartered antibody engineering company, committed $150 million plus in antibody research over the next five years and is to hire 60 researchers in Singapore. Also, Merck Sharp and Dohme (MSD) is expanding its presence in Singapore by investing in local research activities and training collaborations between Singapore and its global sites.

Insufficient numbers of domestic skilled manpower compels foreign players to hire talent from west. International life science recruitment firm Hays Recruiting Worldwide highlights that Asia is paralyzed by mismatch between demand and supply forces, and countries like India, China, Korea, and Malaysia are facing obstacles in finding appropriately skilled manpower to carry out research complying to international standards, work at par with globally-acclaimed scientists, and execute research-oriented projects. Also in some countries like Singapore, the gap between those who work for professional growth, and who are profit-oriented is emerging as a serious HR issue, according to Ms Samantha Su, director, services and biomedical, Spring, Singapore, and Mr Simranjit Singh, chairman, BioSingapore. "We see a lack of government or educational initiatives to bridge this gap," says Mr Matt Kerr, senior manager, Hays Recruiting Worldwide.

The gap stats

Asia's pharmaceutical industry employed about 150,000 manpower in R&D division in 2012, of which Indian industry had around 70,000 researchers on its rolls and China engaged over 40,000 personnel, according to BioSpectrum estimates. The interest expressed by the international as well as domestic companies to conduct research and innovation in Asian countries including India, China, Korea, and Australia, is indicative of rising global demand for research-related skill-sets in the region. There is high requirement for employees with skills in regulatory affairs, clinical strategy and project management, and skilled and qualified researchers.

However, over the next five years, the entire region is anticipated to face a skills gap in these areas.

BioSpectrum takes a snapshot of the challenges faced by Asian countries while recruiting right human talent and implementing strategies to fill the gap.

India takes steps towards narrowing skills gap

In order to fill the talent gap, the Indian government has designed strategies to increase the influx of qualified professionals into molecular biology, biochemistry, biotechnology and assay development.

Department of Biotechnology (DBT), India, has adopted programs, such as Star College program, to strengthen undergraduate education in life science. Under the program, the DBT is establishing biotechnology education institutes over a period of 12 years. It has also introduced fellowship schemes for re-entry of scientists, who were stationed abroad, into India, and around 200 scientists have been brought back since 2009. The DBT has also proposed to initiate a short-term training program for skill improvement in areas of recombinant human monoclonal antibodies and production, drug discovery, stem cell technologies, transgenic plant related technologies, transgenic animal development and IPR, and regulation.

Mr Anurag Bagaria, chairman and managing director, Kemwell Biopharma, India, says that the fact that global players are setting up operations in Asia, including India, shows that the country is becoming a service providing destination. However, manpower retention is posing a big challenge.

One of the strategies adopted by pharmaceutical companies to enrich the human skills is through providing global exposure to its staff. Ranbaxy has established its workforce in over 50 countries with a total manpower strength of approximately 14,600 employees. As a strategy to groom international talent, Ranbaxy gives mobility to its employees across geographies to enrich work experience. "Employees greatly benefit by sharing the best practices from across the emerging markets and avoid reinventing

the wheel in many existing practices," says Mr Sourav Prakash Mohapatra, associate director, HR, Global Generics, Ranbaxy, India.

China's 12th Five Year Plan boosts human capital

IMS Health predicts that the value of the Chinese pharmaceutical industry could grow up to $165 billion by 2016. China's 12th Five Year Plan (2011-15) emphasizes on modern healthcare services and is striving to gain credibility in high end research for affordable drug pricing. The new growth model is propelling innovation and technological superiority in the country, boosting demand for high quality domestic products and trained researchers to perform cutting-edge activities.

Pharmaceutical companies in China, aspiring to develop new drugs and molecules, are concerned about the impact of skills shortage on their research pipelines. Driven by the strategy to boost China's life science industry, the country has opened doors for large international firms to invest in China.

Suggesting a solution to gain access to skilled researchers and scientists, Mr Matt Kerr, Hays Recruiting Worldwide, says, "Over the past few years we have seen a steady migration of companies, that either moved their entire regional headquarters or specific departments to China, in an attempt to capitalize on this booming market and to leverage gains to be made from the relatively low operating costs in China. One of the major areas where we have seen position growth is in R&D with companies such as Roche and GlaxoSmithKline (GSK) investing heavily in drug discovery and setting up dedicated R&D centers."

Companies such as Pfizer and GSK are diversifying their operations. They are laying off employees in the West and are increasing their representatives in China. Partnership of MNCs with local institutes and companies is helping domestic organizations to train the manpower and gain access to international knowledge.

Malaysia creates 13,600 new job opportunities

In a bid to boost the biotechnology sector, in 2012, Malaysia identified 10 entry point projects in the areas of bio inputs, bio-based chemicals, biomaterials, bio-based farm inputs, high value bio-ingredients, high value food varieties, biosimilars, drug discovery, molecular screening and diagnostics, and stem cells and regenerative medicine. These entry points are designed to create additional 20 trigger projects, creating 13,600 new job opportunities and are expected to add US$1.1 billion (RM3.6 billion) to gross national revenue. Malaysia had harnessed investments of around US$4.1 billion (RM12.7 billion) in 2012, exceeding the US$2.9 billion target set for 2015, and the sector has created 64,753 jobs.

Hays Pharma mentions that contract research organizations are experiencing a period of unparalleled growth in Malaysia. The shift by pharmaceutical companies to outsource most of their clinical functions and even some regulatory affairs work has seen a high increase in demand for clinical research associates, and clinical leaders in Malaysia. This has created an environment of fierce competition for talent and is steeply driving up salaries.

Singapore tackles HR challenges

The 2012 Yearbook of Statistics by Singapore Department of Statistics reveals that during the period from 2009 to 2011, the country witnessed a five percent lower average growth rate compared to 27 percent between 2006 and 2008, in new enrollments for life science courses at polytechnics and universities.

"Opportunities in the biomedical industry have especially attracted candidates from countries like Australia, Europe and the US, where there are more talents with the needed experience, academic qualifications and international exposure compared to Singapore," shares Ms Karen Tok, managing director of ScienTec Consulting, an executive search and professional recruitment firm. "It is a skilled market with very intensive standards," says Ms Tok. "Hiring outlook remains positive, but roles in biomedical and scientific areas for the R&D facilities require, among others, clinical exposure plus commercial experience and, at least, a PhD. Right now, there are not enough local candidates to meet end-to-end requirements."

To create aspiration among Singapore nationals to pursue higher studies in bioscience, Singapore has implemented various programs capable of attracting industrial, intellectual and human capital investment in bio-medical sciences. Brighter prospects in areas like R&D productivity, innovative medical solutions, integrated research network in basic and translational research, are being highlighted through international collaborations and exchange programs such as Singapore-Stanford Biodesign program to train the next generation of medical technology innovators in Asia.

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PhAMA is pleased to announce that this year we will kick off our inaugural PhAMA Awards 2014 as an important initiative to encourage and recognize the innovation and research, and community impact that students, researchers, members of the academia, health care professionals as well as members of the public has contributed to the society. The contest is divided into two categories i.e. the Minister of Health Innovation & Research Award and the PhAMA President's Community Impact & Awareness Award.

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TWO CATEGORIES

MINISTER OF HEALTH
INNOVATION & RESEARCH AWARD

The objective of this award is to celebrate the innovation and research of individuals or team efforts with significant contribution to healthcare and / or standards of care in Malaysia.

PRIZE
- **GRAND PRIZE WINNER WILL RECEIVE RM12,000**
- **FIRST RUNNER-UP WILL RECEIVE RM6,000**

PHAMA PRESIDENT'S
COMMUNITY IMPACT & AWARENESS AWARD

The objective of this award is to celebrate the impactful efforts or initiatives contributing towards improving an aspect of community health, wellbeing, awareness or standards of care within Malaysia.

PRIZE
- **GRAND PRIZE WINNER WILL RECEIVE RM8,000**
- **FIRST RUNNER-UP WILL RECEIVE RM4,000**

All submission shall be made online through www.phama.org.my on or before 15 October 2014.

Testimonials
By patients, for patients

In this section, two patients share their experiences in participating in a rheumatoid arthritis clinical trial in one of Malaysia's public hospitals. By sharing experiences with others, people can make a positive change in the lives of others living with chronic diseases.

Devi (age, 65)

Being diagnosed with rheumatoid arthritis came as a shock to Devi (not her real name). As the current treatment neither prevents nor cures rheumatoid arthritis, the main management aim is to reduce the impact of the disease on patients' lives by controlling inflammation and minimizing joint damage.

"I had to slow down on my daily activities and learn to cope with the disease". She had not had an adequate response to the current and available treatment and the turning point came when her doctor informed her of the option of having access to a new drug by participating in a clinical trial. "It was not an easy decision. It took me a month to finally decide to go for it". She felt jittery on her first treatment, unsure of the side effects of the new drug.

> "Patients should participate in clinical trials with more confidence…"

That began Devi's journey of participation in what now amounts to 5 years of continuous treatment. Subsequent treatments resulted in pain reduction and she was able to go about her daily routine, feeling very much emotionally relieved. As Devi's doctor continue to manage her disease, an amazing well of positive energy keeps her going. "I am now able to live a better life as my symptoms and pain have since reduced."

Be it an improved standard therapy or a clinical trial offering potentially better treatment, there are many options available to patients today. Devi was one of the lucky patients that has been accepted into a clinical trial. She asserts, "Patients should participate in clinical trials with more confidence and they should talk to their doctor before proceeding so they can be comfortable with their decisions."

Myth: I will just be a guinea pig in a clinical trial.

Fact: Patients in clinical trials receive a high standard of care and new treatment that researchers believe will be at least as good as the standard treatment. Patient safety is always the highest priority.

"Indeed, clinical trials give hope to people with rheumatoid arthritis"

Hussein (age, 57)

Hussein (not his real name) had never imagined he would find himself enrolling in a clinical trial. His children was still young when he was diagnosed with rheumatoid arthritis. "I was overwhelmed with sadness when the doctor told me that there was currently no cure for this disease."

Rheumatoid arthritis is an autoimmune disease that can cause chronic inflammation of the joints and other areas of the body. The disease can affect people of all ages and is progressive in nature.

Eventually, Hussein accepted his fate and with the help of family and friends, he found the strength he needed to carry on with life. He heard about a clinical trial possibility from his doctor and was told of a new drug that could help improve his condition. Prior to this, he had never heard about clinical trials but once he learned more about it, the choice was simple.

"It took me just about a week to decide to participate in this trial." While others cheered him on, it was his wife that has been his strongest supporter throughout the process. "I believe that for every disease, there is a cure and I am confident of the modern medications that have been developed. Indeed, clinical trials give hope to people with rheumatoid arthritis."

Today, Hussein is a grateful man and thankful for the helpful medical staff, knowledgeable rheumatologist, steadfast faith and supportive family – the team that helped him to improve his quality of life and manage his disease.

Myth: Clinical studies are not safe and can be dangerous, I'd be gambling with my health if I signed up.

Fact: Clinical trials are experiments and as a result there is always a small level of risk involved. New treatments are tested on human subjects only after there is valid scientific evidence that the treatments are effective and safe.

Each clinical trial has a screening criteria which patients must satisfy first before they can be accepted into the trial. The following trials are currently recruiting patients:

Endocrinology trials
Klinik Kesihatan Tampin • Hospital Taiping • Hospital Pulau Pinang • Hospital Tengku Ampuan Rahimah • Hospital Tengku Ampuan Afzan • Hospital Selayang • Hospital Tuanku Jaafar • Hospital Putrajaya • Hospital Serdang

Nephrology trial
Hospital Serdang

Medical device trial (for end stage renal failure)
Hospital Kuala Lumpur • Hospital Raja Perempuan Zainab II • Hospital Sultanah Nur Zahirah • Hospital Tuanku Jaafar • Hospital Pulau Pinang

Psychiatry trials
Hospital Ulu Kinta • Hospital Permai Johor • Hospital Sentosa Sarawak • Hospital Mesra Bukit Padang Sabah • Hospital Taiping

You can ask your doctor (or contact CRM) about the ongoing clinical trials. More information can also be obtained from the following websites:

National Medical Research Register
https://www.nmrr.gov.my/fwbLoginPage.jsp

International Clinical Trials Registry Platform (ICTRP)
http://www.who.int/ictrp/en/

ClinicalTrials.gov
https://clinicaltrials.gov/

Institute for Medical Research (IMR) the First in Malaysia to be Awarded Compliance Certificate for OECD GLP in Toxicity Studies

The Institute for Medical Research (IMR) is the first laboratory in the country to be awarded the OECD GLP Compliance Certificate for Toxicity Studies by the National Pharmaceutical Control Bureau (NPCB), which is accredited as a national Compliance Monitoring Authority for non-clinical safety testing of pharmaceutical products, cosmetics products, veterinary drugs and food additives.

With this achievement by IMR, Malaysia now has four laboratories listed by the NPCB as being GLP compliant.

The compliance certification awarded to IMR means that any safety data produced by the IMR laboratory in the area of toxicity will be accepted by more than 40 countries worldwide, which consist of the 34 OECD (Organisation for Economic Cooperation and Development) member countries and OECD MAD (Mutual Acceptance Data) countries comprising of Argentina, Brazil, India, Malaysia, Singapore and South Africa.

Malaysia's OECD-MAD membership and IMR's certification is an important milestone and timely in supporting the Government's efforts to grow the herbal and traditional & complementary medicine sectors, as well as the domestic pharma, biotech and cosmetic industries. The benefits accruing to Malaysia from these developments are summarized below:

- International acceptance of non-clinical data developed in Malaysia.
- Exemption of non-clinical research being repeated in OECD countries.
- Cost reduction in product development.
- Overcoming existing technical barriers.
- Facilitating trade by reducing marketing time for locally manufactured products which are marketed internationally.
- Increasing local and foreign investment in research and development of pharmaceutical products.

IMR's experimental room equipped with individually ventilated caging (IVC) system

Another view of the experimental room equipped with individually ventilated caging (IVC) system

Malaysia is the second country in Asia, after Singapore, to achieve OECD-MAD membership. Malaysia had to undergo stringent examinations by the OECD to ensure that its test facilities are on par with OECD standards, including having a robust system of management in place for GLP-compliant facilities. The membership grants Malaysia a competitive edge, as its lab test results are recognised and accepted by all OECD markets, including the United States, European Union and Japan, all of which are major biomedical markets.

Malaysia was awarded a provisional adherent status under the OECD Mutual Acceptance Data (MAD) mechanism in October 2008 and subsequently in March 2013, became a full adherent to the OECD Council Acts related to the MAD in the Assessment of Chemicals. The OECD Council Decision on MAD states that test data generated in any member country in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP) shall be accepted in other member countries for assessment purposes and other uses relating to the protection of human health and the environment.

Entrance to the IMR GLP Facility

Corridor inside the GLP facility leading to the experimental, quarantine and procedure rooms

MENTOR-MENTEE PROGRAMME

Growing the Pool of World-Class Clinical Researchers

by Communications & Relations Department, Clinical Research Malaysia (CRM)

One of the key success factors in the effort to attract the interest of major industry players and to position Malaysia as a compelling destination for industry sponsored research (ISR) is to put into place a mechanism to grow the pool of potential investigators across a wide range of therapeutic areas. By doing so, sponsors and contract research organizations (CROs) will gain a greater sense of assurance that Malaysia possesses the necessary human capital which can accept and conduct their varied clinical trials to their required high standards.

Recognizing the needs of the global industry, Clinical Research Malaysia since its establishment two years ago has implemented a series of initiatives on a nationwide basis towards this end.

These initiatives include conducting an ongoing series of heavily subsidized Good Clinical Practice (GCP) workshops and refresher courses for doctors and support staff, intensive and regular training to equip Site Research Associates (formerly known as Study Coordinators) to upgrade their skills and capabilities so that they can better support investigators and trial sites, promotion activities to grow awareness and support for ISR amongst the medical fraternity, and last but not least, a Mentor-Mentee programme to encourage younger ISR-inexperienced specialists to venture into ISR by linking them to experienced investigators.

Originally launched in 2013, the Mentor-Mentee programme sought to equip younger specialists who are interested in clinical research but with no experience in it as yet, with the motivation, skills and knowledge to take-up ISR trials by linking them to

Dato' Lawrence at his best

Mr. Goh Tse Seng (Quintiles) briefing the participants

experienced principal investigators who function as mentors. Besides providing guidance and advice to their mentees, the mentors were also encouraged to utilize their mentees as co-investigators (if their specialties match) in new clinical trials.

CRM, meanwhile, played a supportive role by sponsoring regular meetings between the participants, sponsoring their participation in relevant events and conferences, and by channeling more new ISR feasibility studies to them.

Being a new and untested initiative in Malaysia, however, the programme had mixed results in 2013. Accordingly, CRM adjusted and fine-tuned the programme in early 2014 to improve its effectiveness and intended outcome.

One of the Mentor-Mentee teams

Motivational session by Mr. Anas Zubedy

Participants pledging their commitment to the programme

Thus far in 2014, CRM has successfully conducted the Mentor-Mentee programme in the Central, Northern and Eastern Regions of Peninsula Malaysia. In total, the programme this year saw the participation of 69 mentees and 18 mentors. Each mentor was assigned a maximum of four to five mentees, and as far as possible the "matching" was done to ensure that mentors and mentees specialized in the same therapeutic area and were located conveniently to one another.

The Mentor-Mentee events held regionally were full-day affairs conducted in comfortable surroundings, with participation limited to a maximum of 25 mentees in each region. Each event featured an informative presentation by Dr. Mohamed Ali Abu Bakar, CEO of CRM, who gave an overview of the clinical research industry in Malaysia and on the roles and services provided by CRM. This was followed by a more technical presentation by CRM's Clinical Operations team on how the participants should respond to feasibility studies.

Next up was a briefing from a representative of a major CRO on the criteria that sponsors/CROs look for when deciding on an investigator. This was to equip the participants with an understanding of the essential characteristics required of an investigator and their responsibilities throughout the clinical trial process. For these sessions, CRM extends its appreciation to Quintiles and PAREXEL International for sharing their valuable insights.

The floor was then taken over by trainers, Dato' Lawrence Chan (in the Central and Northern Regions) and Mr. Anas Zubedy (in the Eastern Region). The exuberant trainers spoke about the role and responsibilities of mentors and mentees, the benefits of being in such a relationship, the key success factors in nurturing such relationships, and common pitfalls to look out for. By using case studies and giving examples of real life stories of successful mentors and mentees, the trainers were able to keep the

participants on their toes and ensure a productive session. At the end of the day, each participant was presented with a certificate as a token of appreciation for their time and commitment to engage in ISR.

Following-up on the regional events, CRM has been channeling suitable new feasibility studies to the mentees based on their individual therapeutic area, as well as sponsoring team meetings and sponsoring the participation of some mentees to relevant medical conferences within Malaysia. However, initial plans by CRM to expand the Mentor-Mentee programme to the Southern region, Sabah and Sarawak have been temporary put on hold until next year, as CRM has decided to focus on supporting the existing teams and getting as many existing mentees started on ISR first, before rolling-out the programme to these other three regions.

While a 100% success rate may be impractical due to each mentee's individual circumstances – such as the possibility of getting transferred, resignation from government service, inability to commit for the long-term, lack of new trials suited to their individual therapeutic area, etc, - CRM is optimistic that a good number of mentees will embark on ISR trials within a year.

Moving forward, this expansion in the pool of capable investigators will contribute immensely to attracting more international sponsors and CROs to conduct their clinical trials in Malaysia.

Dato' Dr. Aljafri bin Tan Sri Dr. Haji Abdul Majid with his mentees

Dr. Mohamed Ali, CEO of Clinical Research Malaysia

Composition of Participants at CRM's Mentor-Mentee Programme

NORTHERN REGION		EASTERN REGION		CENTRAL REGION	
Anaesthesiologist	1	Anaesthesiologist	2	Cardiologist	1
Cardiologist	1	Cardiologist	3	Endocrinologist	1
Colorectal Surgeon	1	Family Medicine Specialist	5	Family Medicine Specialist	1
Dermatologist	1	General Physician	5	General Physician	7
Endocrinologist	1	O&G	2	Neurologist	1
Family Medicine Specialist	1	Ophthamologist	1	Neuropsychologist	2
Gastroenterologist	1	Orthopaedic	1	Oncologist	1
General Physician	9	Paeditrician	2	Ophthamologist	3
Medical Officer	2	Psychiatrist	5	Orthopaedic	2
Neurologist	1	Respiratologist	2	Paediatrician	2
Neuropsychologist	1	**Total**	**28**	Pathologist	1
Orthopaedic	1			Psychiatrist	3
Paediatrician	3			Radiologist	1
Psychiatrist	3			Respiratologist	2
Respiratologist	1			Surgeon	3
Total	**28**			**Total**	**31**

Full house at the Northern Region Mentor-Mentee Programme

Convergence of the Government, Science and Industry

Malaysia is developing Clinical Research as an Economic Growth Engine

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Email: contact@clinicalresearch.my

www.clinicalresearch.my

Pharma Personality

Mohamad Syukri Shamsudin

Clinical Operations Manager, International Operations
Novo Nordisk, Zurich

Mohamad Syukri Shamsudin is Clinical Operations Manager for International Operations at Novo Nordisk, Zürich, Switzerland. He has over 14 years of experience in the pharmaceutical and CRO industries. Mohamad Syukri started his career as a pharmacist at the National Pharmaceutical Control Bureau (NPCB) in Malaysia, before moving to Novo Nordisk, Malaysia, where he gained experience as a Clinical Research Associate. He has also worked in Lundbeck and PAREXEL before finally stepping into his current role as Clinical Operations Manager at Novo Nordisk, Zürich.

What does a Clinical Operations Manager do?

As Clinical Operation Manager, my job is to bring trials into International Operations (emerging) countries as well as to manage and support these countries in terms of resources, training and resolving any issues that may arise. International Operations countries are countries outside the United States, Europe, China, Japan and South Korea. Novo Nordisk's International Operations has 153 countries under its responsibility in the Zürich office. - While my portfolio does not just stop here, part of my responsibility is also to deliver and achieve the promised recruitment numbers.

Which area of the biopharmaceutical business at Novo Nordisk are you mainly involved in?

I am primarily involved within haemophilia care, namely haemophilia A and B, inhibitors, factor XIII and growth hormone therapy. Recently, inflammation has been added to my portfolio and trials have already started in Argentina, Brazil, Ukraine, Russia and Mexico because of the size of the markets in these countries and their experience with inflammation trials.

Is it difficult to recruit patients with haemophilia and what is the prevalence of this disease?

The prevalence of haemophilia varies across countries. In many countries, it is under-diagnosed due to the lack of awareness and access to diagnosis. The poor prognosis of haemophilia is further exacerbated by the fact that its treatment is both costly and complex. In Malaysia, Pusat Darah Negara (PDN) has established a strong foundation in conducting haemophilia trials and this has been the drawing factor for sponsors and CROs to conduct such trials in Malaysia.

When was your first collaboration with PDN and how did it turn out?

Our first collaboration with PDN was in 2008 when we brought in the first trial to them. I am proud to say that they did very well despite the challenges and difficulties posed by that particular trial. PDN has a strong foothold in terms of developing the competencies within haemophilia and they have proved themselves to be one of the key players in this field. Without a doubt, PDN is one of the best sites globally.

How long have you been based in Zürich and where were you posted before this?

I have been here for the past three and a half years. Before this, I was a project manager for haemophilia trials based in Novo Nordisk China for three years, and with PAREXEL in Australia for two years. I believe that Malaysians have the edge when it comes to employment by international recruiters because of the level of proficiency in the English language as well as a trained workforce in the local clinical research industry.

How do you see Malaysia in terms of developing the clinical research industry?

When I first started my career as a pharmacist, the clinical research industry in Malaysia was still in its infancy. Society as a whole had not grasped the idea of participating in clinical trials. The most common perception was that those who take part are little more than "guinea pigs"; additionally there was low uptake of

trials by medical specialists. However, over the last 10 years, the government has implemented various measures and initiatives to strengthen the clinical research ecosystem in Malaysia. Many countries in emerging market have been one step ahead in terms of changing their policies to cater to the clinical research industry, and I believe that Malaysia will soon follow to enable a thriving and productive industry.

What do you think are the challenges facing this industry in Malaysia?

The regulatory process may affect the operations of a clinical trial, so I would say a bit of both of these aspects. For example, if the operation personnel can rely on the approval timeline given by the regulatory body, then they are able to inform the patients on when the study can start and when they can receive the trial drug. There are instances whereby patients are promised that they can start on a trial, but when the dateline is delayed, they would have to wait until the study gets approved. As a result, the patient loses interest in that trial.

What do you enjoy most about your job?

Being able to be part of the team that brings haemophilia clinical trials to a country and knowing that these trials can improve the lives of patients makes me happy. I was surprised to know of a Malaysian who wanted to participate in a trial because she wanted to contribute to the global clinical trial data. It just goes to show that Malaysian society is opening up to the idea of participating in clinical trials.

And the most challenging part about your job?

Having to meet my KPIs (key performance index) of course! Also, when a study closes, there is the fear that the trial drug may be inferior compared with the existing drugs. When the results do not favour the trial drug, demotivation can set in.

Within the Malaysian clinical research industry, what type of jobs do you think will see a growth/demand in the next few years?

The clinical research industry in Malaysia is definitely growing. Apart from grooming young doctors to become principal investigators (PIs), there is also a need for experienced investigators who have participated in multi-center and multi-national clinical trials to present the trial results in international conferences and to co-author clinical research papers. This is still lacking in the local clinical research industry. Although there are many potential PIs in Malaysia, only a handful of our key opinion leaders are invited to present the results of a clinical trial at the international level.

Have you ever thought of coming back to Malaysia to work?

I would love coming back to my motherland. At the end of the day, whatever we have back home is always better than what we have elsewhere. As the Malay folk saying goes, “It may rain gold in someone else’s country, and be hailing stones back in your own country, and yet it is best to be back in your own country”.

What would be your advice to the younger generation?

Explore the opportunities that the global clinical trial industry has to offer particularly if you are serious in learning the ropes in the clinical research field. Working with global partners and dealing with people from various cultures enables one to understand the international clinical research market and to emerge as more competitive in the job market.

> PDN is one of the best sites globally for hemophilia trials.

Pusat Darah Negara (PDN)

New growth and decline in Asia clinical trials

South Korea, Japan, China see big growth in 1572s, while India posts huge drop

Article reprinted with permission from CenterWatch

By Karyn Korieth and Annick Anderson

While Asia's clinical research landscape has grown significantly over the past five years, a new CenterWatch analysis paints a radically different picture of the region than anticipated 18 months ago.

Data analysis of individual countries has found new pockets of growth, particularly in South Korea and Japan, but regulatory concerns have caused a dramatic slowdown in India, which the industry had anticipated would become a leading market for clinical research by now.

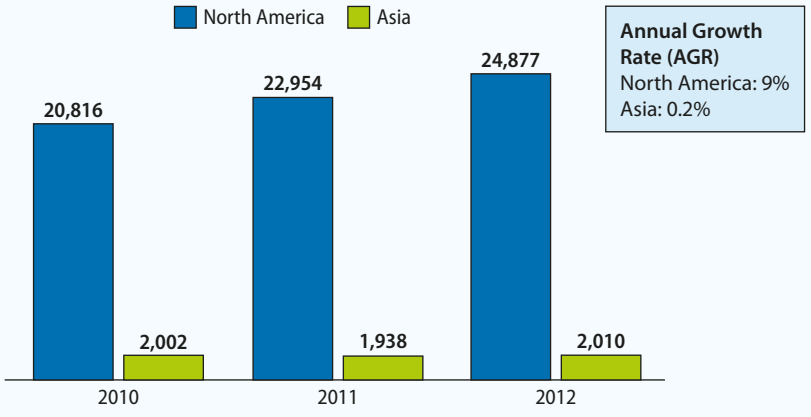
Much of the research focus has shifted from India to China where, despite substantial challenges including lengthy study start-up times and cost concerns, analysis shows the clinical trial infrastructure has begun to consolidate and mature.

The CenterWatch analysis found overall, the number of registered interventional studies conducted in Asia increased at an average annual growth rate of 8% during the past five years, the highest average growth rate among regions worldwide. In comparison, the number of similar studies conducted in North America fell by 2%, while Western Europe saw a slight increase of 1%. During the same five-year period, the number of investigators in Asia grew by an average annual rate of 14%, compared to 9% in North America.

As Asia's clinical research landscape begins to reshape itself, with new areas of opportunity emerging, the region remains an integral part of major drug developers' global programs. Pharma companies continue to make significant scientific investments in the region, including construction of R&D facilities; CROs are growing and expanding into new countries. Companies also are showing a greater willingness to invest more in training to ensure investigators meet Good Clinical Practice (GCP) and International Conference on Harmonization (ICH) standards.

Investigator growth in North America v. Asia

Total number of unique investigators filing form 1572



Source: CenterWatch analysis of FDA BMIS database

Importantly, clinical research will continue to grow in Asia, as the region offers the world's largest populations of both treatment and clinical trial naïve patients.

"It is widely recognized that Asia Pacific offers good opportunities for conducting clinical trials in view of the large patient pool, regulations that comply with ICH guidelines, a Western medical education system and medical practice that meets international standards," said Wei-Ming Goh, vice president of Asia Pacific for CRO Icon, which has more than 1,600 staff based in 13 countries across the region.

Methodology used

CenterWatch, which has monitored the clinical research landscape in Asia for the past decade, decided this year to take a closer look at variations in growth within Asian sub-regions and countries. For this analysis, the number of Principal Investigators for each country was determined using the Bioresearch Monitoring Information System (BMIS) database, operated by the FDA's Center for Drug Evaluation and Research (CDER). The BMIS database tracks the number of active investigators through a 1572 form, which sponsors must collect from each clinical investigator in each trial conducted under the FDA's Investigational New Drug (IND) regulations. The number of registered interventional studies for each country was determined through listings submitted to the Clinical-Trials.gov registry, which reflects both federally and privately funded clinical studies conducted under an IND.

Decline in India

An uncertain regulatory environment has made it nearly impossible for global sponsors and CROs to run clinical trials in India. The number of registered interventional studies in India dropped 25% between 2010 and 2012; the number of investigators fell by 9% over the same period.

During the past six months, the slowdown has intensified. Many sponsors and scientific agencies — including the National Institutes of Health — stopped conducting clinical trials in India after the government amended its rules for testing new drugs. Most troubling was a requirement for companies to compensate clinical trial participants who experienced serious adverse events or death, regardless of whether the event was caused by the study drug or the pre-existing disease. Volunteers who received placebo instead of the active study drug also were eligible for reimbursement.

"India has seen a slowdown in growth due to ongoing concerns with regulatory issues. As such, we have seen some global sponsors take a 'wait-and-see' approach to including India in their clinical trials," said Nick Wright, vice president and general

manager, clinical development services, Asia Pacific, for CRO Covance, which has operated in the region for 25 years.

The significant drop in activity was unexpected, since just a few years ago the industry projected 15% of global clinical trials would be conducted in India by 2011. Sponsors and CROs were attracted by millions of treatment-naïve patients, low operating costs and a rising incidence of Western diseases. Clinical activities surged — reaching nearly 350 newly registered interventional studies in 2010 — after the government strengthened its regulations to harmonize with those of the U.S. and the ICH. The government also had promised a fast-track approval system. Yet, according to ClinicalTrials.gov, only 1.5% of currently registered studies are being conducted in India.

"There is a complete sense of uncertainty around India as a place for trials," said Kent Thoelke, executive vice president, scientific and medical affairs at CRO PRA, which operates throughout Asia Pacific using both localized operational staff and CRO partners.

Even prior to the changes to the regulatory requirements, sponsors and CROs during the last three or four years have experienced significant uncertainty and frustration with the country's regulatory approval process. Concerns have included highly unpredictable approval times and changing requirements that created a difficult environment in which to conduct clinical research.

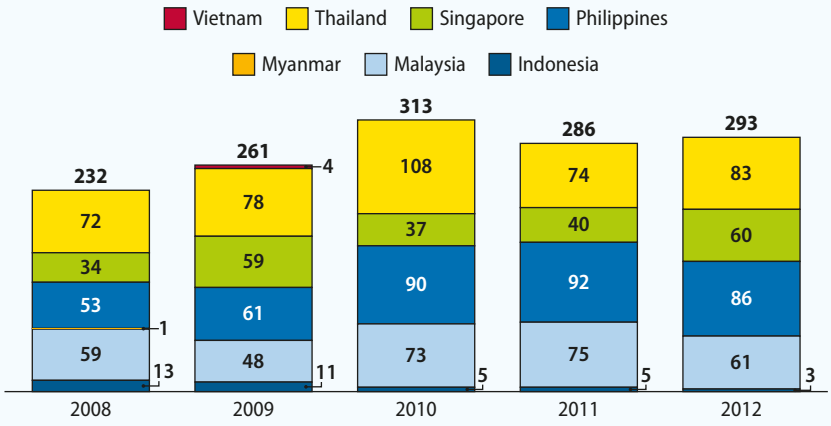
"That has given people a lack of confidence in the system," said Garth Tierney, executive vice president of CRO INC Research's Asia Pacific division, which has 20 offices across the region. "There's been a dramatic drop-off in clinical trials. Our own organization has consolidated its operation in India in response to the current demand. Our strategic position is to wait and watch India at this stage — further growth initiatives will be dependent upon the changes that will be made and the clarity and stability in the regulatory process."

Companies also are re-thinking their strategies in India after Novartis lost a Supreme Court patent case for its anti-cancer drug Glivec earlier this year. While intellectual property protection has been a longstanding concern in India, since patents granted elsewhere may not be honored in the country, increasing conflicts over this issue have led some companies to consider diverting investments to other markets.

"Unclear patent policies and regulatory guidelines remain key concerns for sponsors in India," said Icon's Goh.

Unique Principal Investigators in Southeast Asia

Submitting at least one Form 1572



Note: Region also includes Laos, Cambodia and Brunei

Source: CenterWatch analysis of FDA BMIS database

Consolidation in China

During the past 18 months, sponsors and CROs have shifted their clinical trial activity to other Asian markets, including China, South Korea and Thailand. The industry also is beginning to see the market open in Japan.

Specifically, the number of registered interventional studies in China, which is rapidly becoming a leading region for clinical research, has increased almost 90% from five years ago. The size of the economy and the population has driven considerable interest in China; the potential for growth is significant since China is expected to become the world's second leading pharmaceutical consumer, behind only the U.S., by 2020.

PRA's Thoelke said conducting clinical trials in China used to be a luxury for global sponsors, but today drug development strategies routinely include China. "For the large pharma companies, it becomes a market you just can't really ignore just from a sheer profitability standpoint," he said.

Global drug companies in recent years have made large investments in China. Merck, for example, announced plans to spend $1.5 billion to strengthen R&D in China, including building Asian R&D headquarters in Beijing. Several multi-nationals have completed deals with domestic companies to help integrate their companies into the market. For example, GlaxoSmithKline purchased Nanjing MeiRui Pharma, while Pfizer formed a joint venture with Zhejiang Hisun Pharmaceuticals. Global CROs also are expanding in China and have invested significant resources. Most recently, PRA formed a joint venture with Chinese CRO WuXi PharmaTech to conduct clinical trials in China.

"We are seeing major pharma investing heavily in China, and we're seeing a lot more global decision-makers based in China," said INC Research's Tierney. "I think for every one — pharmas, CROs, the whole industry — the focus is very much on China as the future growth region for Asia."

Improvements in China's regulatory environment have played an important role in the growth of global clinical trials, yet many challenges remain. Costs can be higher to include China in a global clinical trial since companies often must spend extra money for training, translation and shipping the comparator and active drug for a trial. In addition, the

clinical trial approval proces in China are among the longest in the world; on average it takes at least a year, sometimes 18 months, for an approval. But in recent months, regulators have adopted a fast-track process that allows approvals in seven to 12 months for studies involving novel agents, unmet medical needs and molecules.

For large trials, these higher costs can be offset by faster patient accrual, since China has a centralized public healthcare system and large volumes of patients, which can mean shorter trial timelines.

"You see accrual rates that can be two times, five times, 10 times what you would see in other parts of the world," said PRA's Thoelke. "So you are decreasing your overall timelines for a clinical trial, you are decreasing your overall spend, and you are getting your drug to market faster. For some of these drugs, you are talking about hundreds of millions of dollars in difference if you can get a trial done six months earlier and to market sooner." In addition, the analysis suggests China's clinical trial landscape has begun to consolidate and mature, as the number of investigators has dropped 40% during the past two years. Sponsors and CROs report paying closer attention to the quality of sites they use in China, returning to sites that have performed well and have invested in their infrastructure by hiring study coordinators and other staff.

Many novice investigators have left clinical research; in 2013 the Tufts Center for the Study of Drug Development reported a 50% turnover rate for investigators in Asia Pacific. At the same time, China has seen a wave of Chinese students, who studied medicine in the U.S. or Europe and speak fluent English, return to China and change the dynamic of conducting clinical trials.

"We are creating more centers of excellence and consolidating the industry," said INC's Tierney. "It's not dissimilar to what we have seen elsewhere. When you have an emerging market, there is a scattered approach with many sites and investigators being utilized. But as the region develops, we see development of centers of excellence and professional clinical research units," he said. "It's becoming less fragmented and developing into a better-organized clinical research structure."

The number of active investigators in China also relies on the China Food and Drug Administration (CFDA), the government agency that must register and approve sites to participate in trials. Approvals must be renewed every couple of years. The CFDA's ability to register and approve sites in a timely manner can affect the number of sites available for trials.

"Regulatory pathways for clinical trial conduct are clear and, with support of partners who understand how to navigate the regulatory environment, the trial activation process can be efficient in meeting the trial's timelines."

— Michael Clay, Vice President, Clinical Development for Asia Pacific, PPD

The government's site registration system also will impact the growth of clinical research in the country going forward. Icon's Goh said as of 2010, the CFDA had certified a total of 275 clinical trial institutions, mostly located in Beijing, Shanghai, Guangzhou and other large provincial capital cities, including three hospitals in Hong Kong. He said the number and type of certified institutions can accommodate most trial requirements, and some institutions also specialize in therapeutic areas such as AIDS, vaccines, pediatrics and orphan diseases. Yet growth in the number of clinical trials conducted in China means patient recruitment will become more competitive, and a strategy to identify and train sites in second-tier cities — such as Chengdu, Tiajin and Nanjing — as well as in some third-tier cities will become critical for successful study delivery.

Growth in South Korea and Japan

South Korea has become one of the fastest growing countries for clinical trial conduct in East Asia. The numbers of investigators and registered interventional studies conducted in the country both have more than doubled during the past five years; South Korea had 750 studies registered on ClinicalTrials.gov last year; China had 771.

Interest in the country has been driven by its strong medical infrastructure, which allows for high-quality research and a clinical environment that can support study start-up in only a few short months, since the IRB and Korean Food and Drug submission review processes are conducted in parallel.

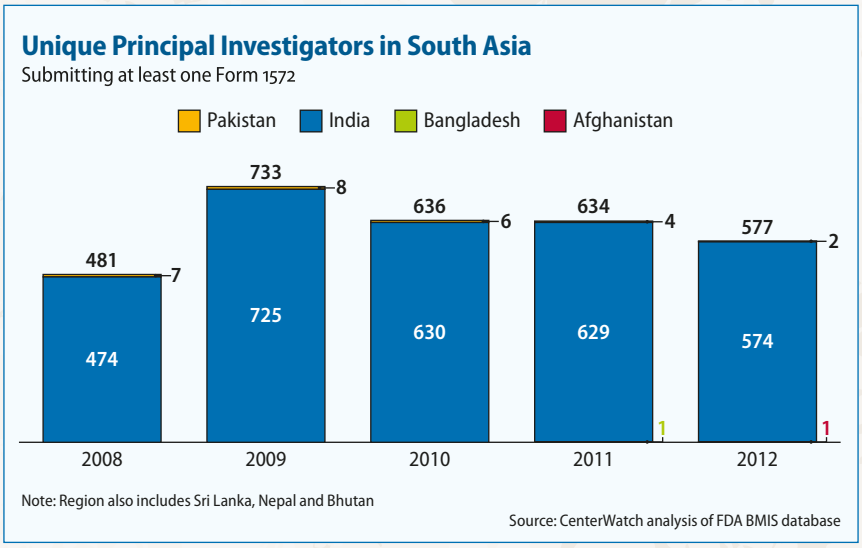
"South Korea has demonstrated strong clinical trial processes and standards and has experienced sites with highly committed and skilled investigators," said Covance's Wright. "As such, the operational aspects of the trials are more predictable and compliance with GCP requirements is high. Additionally, in South Korea access to patients is very good and the investigators are interested in clinical research."

It also has emerged as a global hub for multi-national pharma and biotech companies. Global CROs have established offices in the country and are investing in building its clinical research infrastructure. For example, both Icon and Quintiles have formed partnerships with the Korea National Enterprise for Clinical Trials (KoNECT) to support the development of high-quality clinical research professionals and a clinical infrastructure that can support increased demand from local and global sponsors.

"For South Korea, the government has been playing an important role to support its focus on healthcare and clinical development, which leads to a dramatic increase in opportunities for bio-pharmaceutical companies' drug development," said Icon's Goh.

Meanwhile, companies have seen a paradigm shift in Japan, which until recent years had been largely closed to outside research, as the government has recognized the market's potential and taken steps to attract global clinical trials to the region. The number of studies placed in Japan during the past five years increased more than 9%, while the number of FDA-regulated investigators has tripled; Japanese sponsors also are starting to run their own studies regionally and internationally.

Many companies have begun to expand operations in Japan. This summer, INC Research opened new



offices in Osaka and Tokyo to build its presence in the region. inVentiv Health established a strategic alliance with Japanese CRO Bell Medical Solutions to push further into the Japanese market. "There has been more of an initiative from both pharma and government sectors in Japan to have Japan participate in more global research. There is an increasing awareness of the changes that are required to the traditional conduct of trials in Japan to fit in with this globalization and a growing willingness to see the changes made," said INC's Tierney. "That is driving a lot more activity in Japan. We are seeing Japan participate in an increasing number of global studies."

Another benefit of the new policies is that they open the door to greater cooperation for clinical trial data sharing across the region. A number of initiatives among the Japanese, Korean and Chinese governments are addressing ways for the countries to accept data from another jurisdiction. Although these programs are in early stages, they potentially could make it easier for sponsors to conduct large trials in the region. PRA's Thoelke said a number of companies are using the initiatives now, but they have yet to go through a full approval.

New opportunities in Southeast Asia

Despite its small population and limited number of investigative sites, Singapore saw an increase in both the number of studies (15%) and investigators (76%) since 2008. During the same period, the analysis found growth in both studies (14%) and investigators (3%) in Thailand, which has highly trained investigators and low clinical trial costs. Sponsors increasingly seek to conduct studies in both countries because of their strong focus on quality and their quick study start-up without regulatory complications.

Both Singapore and Thailand have been significant areas of growth for CRO PPD. "Trial demands are high for the growing expertise within these countries, due to the increasing capabilities and experience of clinical trial industry professionals and investigators who are becoming experienced working with multinational companies, and the overall healthcare infrastructure required for the conduct of high-quality trials," said Michael Clay, Vice President of Clinical Development for Asia Pacific for PPD, which has operated in the region for more than 16 years. "Regulatory pathways for clinical trial conduct are clear and, with support of partners who understand how to navigate the regulatory environment, the trial activation process can be efficient in meeting the trial's timelines," he said.

Looking ahead

Industry experts see major growth ahead in Asian countries that have significant patient populations and maturing healthcare systems, including China, Korea and Japan. Studies also are expected to return to India once its regulatory issues are resolved. For China, in particular, infrastructure will strengthen as sponsors and CROs continue to make large investments in the country and expand operations. Although sponsors face significant challenges when conducting trials in markets such as China or Japan, including country specific regulatory, ethical and administrative requirements, they do not expect to bring large numbers of their studies back to more established markets in the U.S. or Western Europe anytime soon, since these regions lack the drug naïve populations and patients with infectious diseases needed to enroll studies.

"The biggest single driver for conducting trials in these countries is the availability of large numbers of treatment naïve patients. While regulatory start-up times can be challenging for some countries, the ability to recruit large numbers of patients once the sites are up and running is a major benefit in terms of meeting the timelines required for overall regulatory approval of the compound," said Icon's Goh.

"In essence, start-up times can be longer than in Europe or the U.S. for some countries, but this additional time is more than made up for by the ability to rapidly recruit patients," said Goh. "This is especially relevant for studies that have extended treatment periods, such as longer-term phase III studies, and enables more rapid drug development and registration."

News & Discoveries Oncology

Does cat poop parasite play a role in curing cancer?

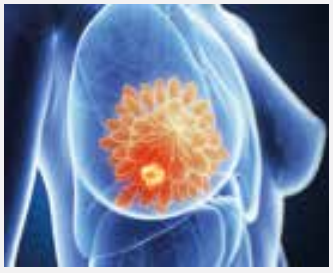
From the litter box to the laboratory, a microscopic organism native to cats shows promise in treating cancer. A mutated strain of Toxoplasma Gondii (T. Gondii) has been found to reprogram the natural power of the immune system to kill cancer cells. A healthy immune system responds vigorously to T. Gondii in a manner that parallels how the immune system attacks a tumor. In response to T. Gondii, the body produces natural killer cells and cytotoxic T cells. These cell types wage war against cancer cells. Cancer can shut down the body's defensive mechanisms, but introducing T. Gondii into a tumor environment can jump start the immune system.

Source: Norris Cotton Cancer Center Dartmouth-Hitchcock Medical Center (15 July 2014)

Cholesterol activates signaling pathway that promotes cancer

Everyone knows that cholesterol, at least the bad kind, can cause heart disease and hardening of the arteries. Now, researchers describe a new role for cholesterol in the activation of a cellular signaling pathway that has been linked to cancer. Cells employ thousands of signaling pathways to conduct their functions. Canonical Wnt signaling is a pathway that promotes cell growth and division and is most active in embryonic cells during development. Overactivity of this signaling pathway in mature cells is thought to be a major driver in the development of cancer.

Source: University of Illinois at Chicago (15 July 2014)



New method may allow breast cancer drug to be given through skin

Endoxifen, a drug that has proven effective in the prevention and treatment of breast cancer, but with serious side-effects, may be delivered effectively through the skin using a new topical drug-delivery system. Endoxifen, one of the most commonly used hormone therapy for breast cancer, has also been shown to prevent the disease. Delivering the drug directly through the breast may reduce the number of mastectomies while lessening the side-effects of oral endoxifen, says Seungpyo Hong, Assistant Professor of Pharmaceutics and Bioengineering at UIC and lead author of the paper.

Source: University of Illinois at Chicago (10 July 2014)

Drug shows promise for the first time against metastatic melanoma of the eye

For the first time, a therapy has been found that can delay progression of metastatic uveal melanoma, a rare and deadly form of melanoma of the eye. Results from a multicenter clinical trial show that a new drug called selumetinib increases progression-free survival, the length of time during and after treatment that a patient with metastases lives with the disease without it progressing.

Source: Columbia University Medical Center (19 June 2014)

Second quarter 2014 in photos

PGMES 9th Biennial Scientific Meeting, Hospital Sultanah Bahiyah, Alor Setar

APHM International Healthcare Conference & Exhibition 2014

CRM Stakeholders Dialogue: Northern Region, Hospital Pulau Pinang

Research Week, Faculty of Medicine & Health Science, UPM

Penang Research Day, Hospital Pulau Pinang

Exhibition, DIA 50th Annual Meeting 2014 San Diego

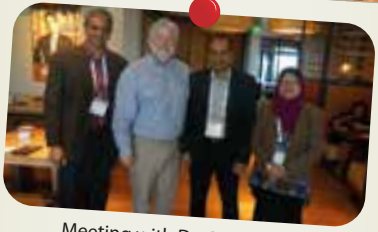
Meeting of REACTA members at the DIA 50th Annual Meeting 2014

Visit to University of California, San Diego Extension, Clinical Trials Program

Meeting with ABGI, a major CRO, at the DIA 50th Annual Meeting

Visit to Precision Research & Triwest Research, San Diego

Visit to University of California, San Diego Health Sciences & Transnational Research Institute



Meeting with Dr. Greg Koski, President & Co-Founder of ACRES

Visit to Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Centre

Dr. Mohamed Ali with Dr. Joel Neutel, Medical Director of Orange County Medical Centre

CRM-SINGAPORE INDUSTRY ENGAGEMENT, 28th - 30th April 2014

With Dr. Danny K. W. Soon, MD & PI
of Lily-NUS Centre, Singapore

With Dr. Gerard Wong, Deputy Director of
National University Health System (NUHS)

With Ms. Conie Cher, Mr. Katsutoshi Sasaki, Mr. Ranjodh Gill
& Ms. Suan Tian Koh from Parexel Asia-Pacific, Singapore

With Dr. Teoh Yee Leong, CEO of
Singapore Clinical Research Institute

With Dr. Margam Chandrasekaran, CEO
& Chief Scientist of Bio-Scaffold Pte. Ltd.

With Assoc. Prof Tan Say Beng from
Singapore National Medical Research Council (NMRC)

UPCOMING NATIONAL & INTERNATIONAL EVENTS

National
International

AUGUST

- Annual Scientific Meeting in Intensive Care (15th – 17th, Kuala Lumpur)
- Pharmacology & Physiology International Scientific Congress 2014 (22nd – 24th, Kuala Lumpur)
- Annual Scientific Meeting of Malaysian Society of Gastroenterology & hepatology (22nd – 24th, Kuala Lumpur)
- Bio Johor 2014 - Biotechnology Conference & Exhibition (25th – 27th , Johor Bahru)
- 1-World Congress in Sports & Exercise Medicine (Pre-Congress: 26th - 27th & Congress: 28th – 30th, Kuala Lumpur)

SEPTEMBER

- 10th Allied Health Scientific Conference Malaysia (9th –10th, Kuala Lumpur)
- 17th Penang Teaching Conference for General Practitioners (11th –14th, Penang)
- 39th Annual General Meeting and Dermatology Congress (15th –18th, Penang)
- 15th ASEAN Paediatric Federation Congress (17th – 20th, Penang)

OCTOBER

- Diabetes Asia 2014 Conference (16th – 19th, Petaling Jaya)
- 8th International Traditional and Complementary Medicine (INTRACOM) Conference, Exhibition and Carnival (30th Oct – 2nd Nov, Petaling Jaya)

NOVEMBER

- 2014 IASLC Asia Pacific Lung Cancer Conference (APLCC) (6th – 8th, Kuala Lumpur)
- BioMalaysia & Bioeconomy Asia Pacific Conference & Exhibition (19th – 21st, Kuala Lumpur)
- 23rd Malaysian Urological Conference (21st – 23rd, Penang)

DECEMBER

- 20th Congress of the Asian Pacific Society of Respirology 2015 (3rd – 6th, Kuala Lumpur)

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We welcome submissions of feature articles, write-ups and events related to industry sponsored clinical research for publishing in the CRM bulletin, which is issued quarterly. You can send your submission to contact@clinicalresearch.my or contact us at +60 3 7960 5153 should you have any queries. CRM has the right to edit any submission to suit the needs of the bulletin.

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