By Clinical Research Malaysia

CRM bulletin

of Clinical Research and Therapy

ISSUE 08

The frontiers in Gastro-enterology

NEWS & DISCOVERIES
in Gastro-enterology

KNOWING CLINICAL TRIALS 101
Investigator's corrective action plan fails to satisfy FDA

FEATURED HOSPITAL:
HOSPITAL Kuala Lumpur

RESEARCH PERSONALITIES:
Datuk Dr. Radzi
Dr. Tee Hoi Poh

ABOUT CLINICAL RESEARCH MALAYSIA

Clinical Research Malaysia (CRM) is a non-profit company wholly owned by the Government of Malaysia's Ministry of Health. CRM was established in June 2012 to position Malaysia as a preferred global destination for industry-sponsored research (ISR) and to function as an enabler and facilitator to the industry and medical fraternity.

By working with other stakeholders, CRM strives to improve the local ecosystem to support growth in ISR, facilitate the needs and requirements of industry players, grow the pool of capable investigators, support staff and trial sites, and improve their capabilities and capacities to conduct ISR.

With the Ministry of Health's backing and clear knowledge of the local research environment, CRM is able to provide sponsors (primarily from the pharmaceutical, biotech and medical device industries) and contract research organizations (CRO) with an extensive range of services that includes feasibility studies, investigator selection, placement and development of study coordinators, management of trial budget, review of clinical trial agreements and updates on local laws, guidelines and regulations. CRM also undertakes marketing and promotional activities to build industry awareness about the opportunities for ISR in Malaysia, and create public and patient awareness of clinical trials.

MINISTRY OF HEALTH MALAYSIA

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From the **CEO's Desk**

A year has passed since I assumed the leadership role in CRM. It has truly been an amazing and challenging journey leading this company to achieve the KPI goals it was set to. In 2015, CRM has managed to attract 201 new industry sponsored research (ISR), achieving 94% of our KPI 1.

CRM exceeded the second KPI by 7% where 128 new ISR were conducted at Ministry of Health (MOH) sites. Throughout 2015, CRM has reorganized its structure in the various departments. The Business Development Department was created to have its focus in attracting new investors. CRM reviewed its standard operations in the Legal, Clinical Operations and Finance Department to increase efficiency. This has shorten the review timeline of Clinical Trial Agreements, feasibility studies and payment to the study team.

The majority of the CRM team which consists of Study Coordinators has grown by 30% last year to provide support and manpower to the investigators. Additionally, CRM has spent RM 1.15 million in 2015 to equip the study sites with the relevant infrastructure to conduct ISR. Moving on to 2016, CRM will remain committed in providing the required resources to the investigators and sites.

Alhamdulillah, praise to Allah, our 5 key strategies have begun to deliver results. Allow me to highlight what we have already achieved in one year. CRM had supported State Research Days nationwide by sponsoring Investigator's Awards, and this initiative was met with overwhelming response from our medical professionals. In total, more than 550 research posters were presented from 7 states. The growth of feasibility studies has increase by 36% while the number of investors conducting feasibilities has grown by 300% compared to previous years.

Early this year, CRM has entered into new partnership with Drug for Neglected Disease Initiative (DNDi) for future research. CRM also works closely with the Medical Device Authority (to facilitate the ISR pertaining to medical device), Malaysian Biotechnology Corporation (BiotechCorp) and Malaysian Investment Development Authority (MIDA). The partnership with Malaysia External Trade Development Corporation (MATRADE) has brought us further to promote Malaysia as the destination for ISR.

CRM remains committed in developing human capital because we believe in developing our people's potential to be future leaders in clinical research. We have drawn the career progression of the team within CRM and externally. We practice a tight selection process and performance management to build a performance based organization. We have started to recruit medical doctors to be trained and developed into future investigators. We emphasize training programs partnering with multinational companies because we believe in creating a new value proposition for human capital.

I would like to take this opportunity to extend our appreciation to CRM's Board Members for their support in our activities. The board now has extended its membership to Professor Dr. Adeeba Kamarulzaman, Dean of the Faculty of Medicine, University of Malaya and Mr Ewe Kheng Huat, Executive Director of the Pharmaceutical Association of Malaysia (PhAMA). CRM welcomes them to the board. Their appointments reflect CRM as an organization with a national agenda to support ISR within the Ministry of Health, the universities and private centres.

Finally, I invite you to enjoy this edition which carries the theme Gastroenterology. I hope this issue will be both useful and informative in disseminating information related to clinical research in Malaysia.

Dr. Akhmal Yusof
CEO
Clinical Research Malaysia (CRM)

OUR NEW LOOK

We are very excited to announce that the CRM Bulletin has undergone a redesign.

This new look and feel of our bulletin delivers articles that have been repackaged into different sections with interesting visuals that thoughtfully complement the stories behind them.

- In the News – features events or activities that CRM was recently involved in which is newsworthy.
- News & Discoveries in Gastroenterology – find the latest news and discoveries in selected therapeutic areas for each issue of the bulletin.
- Research Personality – get to know Malaysia's very own Principal Investigators and their thoughts on being part of a clinical trial.
- CRM – Up Close and Personal – be up close and personal with CRM's key individuals and the company as a whole.
- Featured Site – each issue showcases one selected MoH site while presenting the site's capability and capacity in conducting clinical trials.
- Making Sense of the Statistics – Get up-to-date statistics on data relevant to industry sponsored research in Malaysia.
- Knowing Clinical Trials 101 – Refresh and acquire your knowledge in matters related to the conduct of clinical trials, locally and abroad.

Ministry of Health Malaysia and The Drugs for Neglected Diseases *initiative* (DND*i*)

Clinical Research Malaysia and the Drugs for Neglected Diseases initiative Sign Agreement to Launch Clinical Studies for a Public Health Approach to Hepatitis C in Malaysia

[Putrajaya, 13 January 2016] The Drugs for Neglected Diseases initiative (DNDi) and the Ministry of Health of the Government of Malaysia have agreed to work together to develop a public health approach to Hepatitis C within the framework of the future National Strategic Plan on viral hepatitis. The immediate goal is to conduct clinical studies of promising new treatment regimens for Hepatitis C, to be followed by scale-up of treatment for patients, with the overall objective of ensuring equitable access to affordable and effective treatments for patients suffering from this disease in Malaysia.

The clinical studies will be launched later this year in multiple sites, with DNDi and Clinical Research Malaysia (CRM), a non-profit company owned by the Ministry of Health, as the co-sponsors.

"If the clinical studies are successful, the data and information from these studies will provide the Ministry of Health with critical evidence of the feasibility of using recently-approved drugs and clinical-stage compounds for Hepatitis C," said Datuk Seri Dr. S. Subramaniam, the Minister of Health. "This will enable the Ministry of Health to take informed and appropriate policy and economic decisions on adopting these regimens as a public health tool in Malaysia."

Hepatitis C virus infection in Malaysia is a clinical and social burden to the Government of Malaysia. A scale-up of treatment is necessary in order to have an impact on the number of cases, which are steadily increasing. As of 2009, there were 453,700 people living with Hepatitis C infection in Malaysia, including 2.5 % of the adult population 15-64 years old. By some estimates the disease burden is as high as 3.5%.

"The Hepatitis C project in Malaysia is an integral part of DNDi's global access plan for Hepatitis C, which will include clinical studies in Thailand, to prove the feasibility of making these new combination treatment regimens available to broad patient populations at an affordable price. We are pleased to launch this landmark project with our founding partner, the Ministry of Health of Malaysia," said Dr Bernard Pécoul, Executive Director of DNDi. "If the new treatment regimens are adopted as part of the National Strategic Plan on viral hepatitis, the Ministry of Health will follow-through with the scale-up of these regimens, meaning testing and treating patients and disease advocacy with the healthcare stakeholders of Malaysia," added said Datuk Seri Dr. S. Subramaniam, the Minsiter of Health.

Drugs for Neglected Diseases initiative (DNDi)

A not-for-profit research and development organization, DNDi works to deliver new treatments for neglected diseases, in particular leishmaniasis, human African trypanosomiasis, Chagas disease, specific filarial infections, paediatric HIV, mycetoma, and hepatitis C. Since its inception in 2003, DNDi has delivered six treatments: two fixed-dose antimalarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, and a paediatric dosage form of benznidazole for Chagas disease. DNDi has established regional disease-specific platforms, which bring together partners in disease-endemic countries to strengthen existing clinical research capacity, as well as to build new capacity where necessary. www.dndi.org

Clinical Research Malaysia (CRM)

CRM is a non-profit company wholly owned by MOH, established to position Malaysia as a preferred global destination for industry-sponsored research (ISR). CRM support growth in ISR, facilitate the needs and requirements of industry players, grow the pool of capable investigators, support staff and trial sites.

Clinical Research Malaysia and **Inno Bio Ventures** Sign MoU on Treatment of Hepatitis C in Malaysia

[Putra Nilai, 5 February 2016] Inno Bio Ventures (IBV) today signed a memorandum of understanding (MoU) with Clinical Research Malaysia (CRM). The signing ceremony marked not only the collaboration between these two main players but also the Drug of Neglected Disease group. Most importantly the project also has a strong support from the Ministry of Science, Technology and Innovation (MOSTI) and Ministry of Health (MOH). The MoU covers the clinical study of three drugs for the treatment of Hepatits C.

Through the collaboration, CRM will undertake the clinical research portion whereas IBV will be leading the discussion for commercialisation initiatives. The project objective is to assess the effectiveness of these treatment regimens with the demographic population in Malaysia with different genotypes. Subsequently, the project also intends to make Hepatitis C drug available at an affordable price with the involvement of IBV.

Signing on behalf of IBV was Acting President, En Yusri bin Bulat, while CRM were represented by Dr Mohd Akhmal bin Mohd Yusof. Also present to witness the signing ceremony were En Joharizal bin Mahmud, Senior Vice President (Planning); En Mohd Saffuan bin Abd Kudus, Vice President (Sales and Marketing); Pn Emi Sharina binti Md Morad, Vice-President (Biopharmaceutical Operation) and En Yau Yit Huan, Head of Finance of CRM.

Making a Presence at the BioPharma Asia Convention 2016

23 Mar 2016, Singapore - CRM recently participated in the BioPharma Asia Convention 2016 at Suntec Singapore Convention & Exhibition Centre, Singapore from the 23-24 March. It was the perfect venue to exhibit CRM's services and network with prospects and clients from across Asia. The conference and exhibition were well attended by over 2000 biopharma industry stakeholders from research institutes to supply chain providers and contract research organizations. At the BioPharma Asia Industry Awards, Quintiles was awarded the Best CRO Award.

Drugs For Neglected Diseases Initiative And Pharco Pharmaceuticals To Test Affordable Hepatitis C Regimen With Support Of Malaysian And Thai Governments

The Drugs for Neglected Diseases initiative (DNDi) and the Egyptian drug manufacturer Pharco Pharmaceuticals have signed agreements covering the clinical testing and scale-up of a hepatitis C treatment regimen at a price of just under $300.

DNDi will be launching clinical trials to test a combination treatment of the drug candidate ravidasvir and the registered hepatitis C drug sofosbuvir in pan-genotypic patient populations in Malaysia and Thailand, as soon as the necessary approvals are received. Ravidasvir is an NS5A inhibitor, one of a new generation of direct-acting antivirals (DAAs) that are revolutionizing the treatment of hepatitis C. In a Phase III clinical trial in Egypt, conducted by Pharco, ravidasvir showed cure rates of up to 100% in patients with genotype 4 when used in combination with sofosbuvir, which also is a DAA.

DNDi has licensed rights for ravidasvir in low- and middle-income countries from Presidio Pharmaceuticals.

CRM organizes it first Industry Dialogue in 2016

16 Mar 2016, Kuala Lumpur - The Industry Dialogue organized by CRM was held at Connexion@Nexus, Bangsar South City, KL with the objective of forming a collaboration between CRM and the clinical research industry to create a conducive environment for industry sponsored research. A total of 45 representatives from the industry attended the dialogue session. Also present at the event were agencies from MIDA, MDA, MATRADE and BiotechCorp. This year's Industry Dialogue was special as CRM has initiated an Industry Recognition Award. Among the winners were Info Kinetics (highest chronicled ISR with CRM in 2015), Quintiles (highest recorded ISR conducted at MOH centres in 2015), PPD (highest extent of feasibility conducted with CRM in 2015) and Mr Jeffrey Scott Yablon for this outstanding effort in promoting Malaysia as a preferred destination for ISR. Later on, a media briefing session with CRM's CEO, Dr. Akhmal Yusof was carried out by invited media personnel.

Soft Launch of CRM Office at Hospital Pulau Pinang

24 Mar 2016, Penang - Dato' Dr. Ong Loke Meng, the Head of CRC Hospital Pulau Pinang and Dr. Akhmal Yusof, CEO of CRM launched the new CRM Office which is located behind the hospital building itself. The new office functions as a workstation for CRM's study coordinators (SCs). It comprises of a meeting room which can accommodate 10 people at a time and an office space for five SCs. The new office would also be used to store consumables for clinical trials.

Launching of Clinical Research Centre at Hospital Tengku Ampuan Afzan

23 Mar 2016, Kuantan – The new office of Clinical Research Centre at Hospital Tengku Ampuan Afzan was recently launched and officiated by Dato' Dr. Zainal Arrifin Omar, the Pahang State Health Director. The new office is equipped with a research clinic, records room, meeting room, a mini laboratory and workstations that seats 14 research personnel which will be shared between CRC and CRM staff.

Porfessor Dr. Adeeba Kamarulzaman

Professor Dr. Adeeba has been recently appointed into CRM's Board of Directors. Prof Adeeba is the Dean of the Medical Faculty at Universiti Malaya and has been a lecturer in this faculty since 1997. She received her MBBS from Monash University Australia before obtaining an FRACP and most recently earning a Doctor of Law (honoris causa) from Monash University Australia. She was the President of the Malaysian AIDS Council from 2006 to 2010 and is currently the Chairman of the Malaysian AIDS Foundation, a position she held since 2006.

Pfizer introduces first and only biosimilar monoclonal antibody therapy

NEW YORK - The United States Food and Drug Administration on Tuesday approved Celltrion's Inflectra (biosimilar infliximab) across all eligible indications of the reference product, Remicade (infliximab). Inflectra is now the first and only biosimilar monoclonal antibody (mAb) therapy, and only the second biosimilar, to be approved in the U.S.

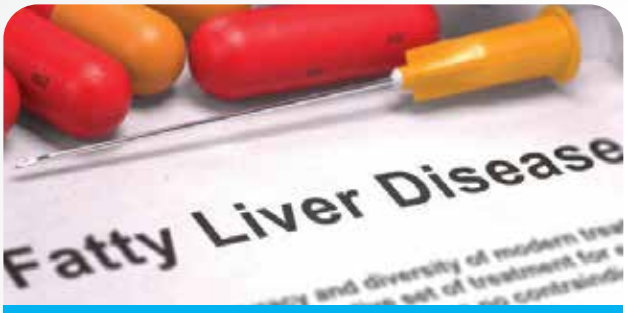
"The introduction of high-quality, effective biosimilars provides an opportunity to expand access to important medicines," stated Salomon Azoulay, SVP and chief medical officer, Pfizer Global Established Pharma Business. "As a leading global biologics company with several biosimilar products in our pipeline, we appreciate the significance of this milestone in developing a pathway for biosimilars to come to market in the U.S., and in helping advance their adoption in the healthcare system."

Source: http://www.drugstorenews.com/article/pfizer-introduces-first-and-only-biosimilar-monoclonal-antibody-therapy

Mr Ewe Kheng Huat

Mr Ewe Kheng Huat has been recently appointed into CRM's Board of Directors. Mr Ewe is currently Executive Director of the Pharmaceutical Association of Malaysia (PhAMA) and has held this position since 2013. He graduated with a Bachelor of Pharmacy (Honours) from Universiti Sains Malaysia and have an extensive experience in the pharmaceutical industry with stints in Merck Sharp Dohme (MSD) as a Country Manager and Managing Director from 1994 to 2012 before assuming his current position at PhAMA.

NEWS & DISCOVERIES *in Gastroenterology*



New target for the treatment of fatty liver disease discovered

Two proteins, p38 gamma and p38 delta, control the accumulation of fat in the liver, a process linked to the development of insulin resistance and diabetes, which are common outcomes of obesity, report scientists. These findings are presented in an article published by researchers at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC). The study, led by Dr. Guadalupe Sabio, shows that inhibition of these proteins with specific inhibitors has potential as a treatment for fatty liver disease. The results are published in the EMBO Journal.

Source: Centro Nacional de Investigaciones Cardiovasculares (February 3, 2016)

Large proportion of IBS sufferers are vitamin D deficient

A large proportion of people living with Irritable Bowel Syndrome (IBS) are vitamin D deficient, a new study has found. The British study, which is the first of its kind, found that out of 51 IBS patients tested 82 per cent exhibited insufficient vitamin D levels.

Source: University of Sheffield (December 21, 2015)

Definitive tests for irritable bowel syndrome developed

Millions of people afflicted by irritable bowel syndrome can now be diagnosed quickly and accurately with two simple blood tests developed by a gastroenterologist. The tests confirm when a patient has developed IBS because of food poisoning, a major cause of the disorder.
Toxins produced by bacteria, such as salmonella, can severely harm the digestive system by damaging nerves critical to healthy gut function. The new blood tests identify the presence and amount of specific antibodies reacting to the toxins.

Source: Cedars-Sinai Medical Center (May 14, 2015)

Age-related response to the hepatitis B vaccine linked to inflammation

Physicians have known for years that patients respond differently to vaccines as they age. There may soon be a new way to predict and enhance the effectiveness of vaccinations, in particular the hepatitis B vaccine. Researchers at Case Western Reserve University School of Medicine and Merck Research Laboratories have found that common biomarkers of inflammation can help to identify which patients might respond to vaccination and inform age-related vaccination schedules as well as interventions that might boost effectiveness, such as anti-inflammatory drugs. Their new study, "Pre-Vaccination Inflammation and B-cell Signaling Predict Age-related Hyporesponse to Hepatitis B Vaccination," was published in the current issue ofNature Communications.

Source: Case Western Reserve University (January 20, 2016)

Crohn's disease diagnosis difficult to obtain, life altering, new national study finds

A new national survey of Crohn's disease patients reveals that it was not uncommon for patients to see multiple health-care professionals, have numerous office visits, and endure multiple diagnostic tests before receiving a diagnosis. Results demonstrate an impact on such things as the ability to work or exercise, but also on overall quality of life and social activities. Respondents wished more people understood the disease and its impact.

Source: Health Union (March 1, 2016)

How relaxation response may help treat two gastrointestinal disorders

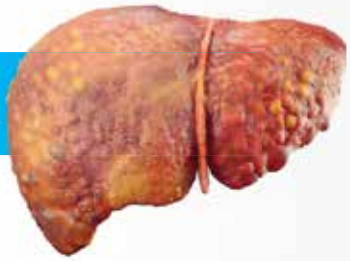
A pilot study has found that participating in a nine-week training program including elicitation of the relaxation response had a significant impact on clinical symptoms of the gastrointestinal disorders irritable bowel syndrome and inflammatory bowel disease and on the expression of genes related to inflammation and the body's response to stress. The report from investigators at the Benson-Henry Institute at Massachusetts General Hospital (MGH) and at Beth Israel Deaconess Medical Center (BIDMC), published in the open-access journal PLOS ONE, is the first to study the use of the relaxation response in these disorders and the first to investigate the genomic effects of the relaxation response in individuals with any disorder.

Source: Massachusetts General Hospital (May 5, 2015)

Hepatitis C tied to increased risk of Parkinson's

The hepatitis C virus may be associated with an increased risk of developing Parkinson's disease, according to a study. Parkinson's disease is considered the second most common degenerative brain disorder after Alzheimer's disease. Hepatitis C is a liver infection caused by a virus.

Source: American Academy of Neurology (December 23, 2015)



Scientists root out the 'bad seeds' of liver cancer

Researchers have found the "bad seeds" of liver cancer and believe they could one day reprogram them to remain responsive to cancer treatment, a new study has found.

The key to disrupting chemo-resistant stem cells that become liver tumors from multiplying is to target the stem cell marker NANOG, said Keigo Machida, senior author and associate professor of molecular microbiology and immunology at the Keck School of Medicine of USC.

NANOG is scarce in early-stage cancer but abounds in Stage III liver cancer. It promotes the cancer's spread by rewiring metabolism in the mitochondria -- a cell's energy factory.

"We identified the Achilles heel in cancer therapy," Machida said. "There are bad seeds in cancer. Even though we treat patients with chemotherapy, those bad seeds survive and force relapse. That's why we would like to target the bad seeds in cancer to eradicate recurrence problems and metastasis, which is when the cancer spreads to other parts of the body."

Source: University of Southern California (USC) (January 27, 2016)

DATUK DR. MUHAMMAD RADZI ABU HASSAN

Consultant Physician and Gastroenterologist,
Hospital Sultanah Bahiyah,
Alor Setar, Kedah.

Datuk Dr. Muhammad Radzi Abu Hassan is a consultant physician and gastroenterologist at Hospital Sultanah Bahiyah in Alor Setar. He also heads the Department of Medicine and Clinical Research Centre (CRC) at the hospital. He graduated from the Royal College of Surgeon in Dublin, completed his Masters in Medicine from HUSM and became a Member of the Royal College of Physicians (MRCP) in 1997. He then went on to obtain a Fellow of the Royal College of Physicians (FRCP Edinburgh).

Datuk Dr. Radzi is actively involved in research and has numerous articles published in reputable publications. He is currently principal investigator to five on-going clinical trials and is very active in medical education, presenting at local and international conferences. His research interest are in colorectal cancer particularly with a focus on colorectal cancer screening, fatty liver, viral hepatitis as well as clinical trials in general medicines such as diabetes. Datuk Dr. Radzi got his first taste of clinical trials in 2001, when he was undergoing fellowship training in

gastroenterology at the Royal Melbourne Hospital in Australia. At the time he was training under the supervision of Dr. Peter Gibson, a prominent researcher at Royal Melbourne Hospital.

Dr. Gibson had invited him to participate in clinical trials, relating to inflammatory bowel disease (IBD), ulcerative colitis and Crohn's disease. One of the studies that he was associated with at the time involved the use of anti-tuberculosis drugs for the treatment of Crohn's disease. He found the trial very interesting and it inspired his curiosity and passion for clinical trials.

When he returned to Malaysia, it took time before he began participating in clinical trials. After being in subspecialty training, he had focused much of his time serving his patients at clinic. The interest and passion for research at the time was there but the calling to serve his patients was a higher priority.

A few years later, he was approached by Dato' Dr. Zaki Morad, who was head of the CRC for the Ministry of Health (MOH). Dato' Dr. Zaki had approached him to be the chairman of clinical research for the state of Kedah. From then on, there was no turning back. He has been spearheading CRC Kedah, participating in clinical trials as well as auditing and monitoring of clinical trials.

When asked about how clinical trials have changed the way he practises medicine, he said clinicians, who are active in clinical trials as well as their clinical work, are best prepared to serve their patients. In clinical trials, the practice of medicine is very 'idealistic'. It is about following procedures. But as a clinician, things are rarely ideal and there are always improvisations to be made. Most importantly is finding the right balance. By getting exposure to research and clinical practice, doctors become more effective clinicians.

With his experience in clinical trials, he said with confidence that Malaysia is on par with neighbouring countries such as Singapore and Thailand. There were certain areas that he felt Malaysia was doing extremely well, especially in terms of infrastructure and logistics for clinical trials. He said the leading pioneers of clinical trials had established a good foundation for future generations of doctors. With the CRC's current leadership and the establishment of Clinical Research Malaysia (CRM), assisting with setting up industry-sponsored research, Malaysia has truly moved up the ladder.

However, there remain gaps in Malaysia's clinical research agenda. In terms of investigator-initiated research, particularly in the MOH setting, the quality and quantity of this form of research remains inadequate. This is a work in progress. He expressed hope that doctors will take the initiative to participate in investigator-initiated research.

When asked what drives his passion for clinical research, he said being a clinician is always a challenge and "you are never perfect", there is always something new to know. Doctors must keep up with the information, to find new solutions that are best for patients. There is no other way to improve the practice of medicine than getting involved in a clinical trial. Having these responsibilities will give doctors the depth to treat patients. He discussed how clinical trials benefited patients by sharing his own clinical experience. He mentioned that doctors should be well-versed in all areas of specialties and not limit themselves to their own specialties.

> *"There is no other way to improve the practice of medicine than getting involved in a clinical trial."*
>
> *Datuk Dr. Muhammad Radzi Abu Hassan*

When the gliptin drugs were undergoing clinical trials in Malaysia, his patients could get access to these very expensive treatments via clinical trials, for free. This truly benefited his patients. On the same token, he also has cancer patients and many cancer patients present at a very late stage of disease, with very limited treatment options. The newer drugs like targeted therapy are effective but also very expensive. With clinical trials he can give his patients an opportunity to use these treatments. Clinical trials also benefit clinicians by exposing them to the latest treatments.

By getting involved in clinical trials, doctors are governed by good clinical practice (GCP). GCP becomes part of the 'culture' and doctors are obligated to consider the safety of patients, quality of care, the recording and storage of data, and the patients' progress.

He expressed the sentiment that doctors with passion for clinical trials should be encouraged but there is a need for doctors, especially younger clinicians to show commitment and be passionate about research. The support and infrastructure is in place within the MOH. Opportunities are there for the taking but he observed a general lack of commitment and passion among doctors.

When asked what policy changes were needed to encourage research, he said recognition for research efforts is important to doctors. In universities, the reason why academicians are usually far ahead with publications and global recognition is because they are recognized for all their work, this encourages them to be more active in research. Recognition for research efforts remains lacking at MOH hospitals.

He also discussed protected time for research. Protected time is quite hard to define and, he believed clinicians must know how to plan their time. He cited many busy clinicians who were able to balance their time with clinic work and be active in clinical research. At the end of the day, the individual that wants to participate in research will make the time. This is why passion and commitment are important, "you will find the time".

He also dispensed advice to those interested in embarking on clinical research. The first thing to ask one's self is whether the doctor has interest and passion for research. Can the doctor sacrifice the time for research? With passion, anything is possible. Secondly, they need to find a mentor to guide them. Passion alone is insufficient, they will encounter challenges, and it will hit them hard in the beginning. They may feel demotivated and give up research altogether. Thus, a mentor is very important in keeping the doctor together and motivated.

Dr. TEE HOI-POH

Consultant Gastroenterologist
Gastroenterology Unit,
Department of Medicine Hospital
Tengku Ampuan Afzan, Kuantan, Pahang

Dr. Tee Hoi-Poh is a Consultant Gastroenterologist at Hospital Tengku Ampuan Afzan (HTAA), Kuantan. He obtained his MBBS from Bangalore University, India in 1998 and received his MRCP from the Royal Collages of Physicians, UK in 2004. He juggles his roles as consultant gastroenterologist and the Ministry of Health's Physician in-Charge for the State of Pahang. He is a board member of the National Gastroenterology Training Committee and honorary lecturer at the International Islamic University of Malaysia, Universiti Sains Malaysia and Universiti Kebangsaan Malaysia.

Dr. Tee was awarded three Excellent Service Awards by the Ministry of Health, participated in 14 clinical trials as a principal investigator (PI) and has published extensively in reputable international journals such as the Journal of Gastroenterology and Hepatology and Journal of Microbiology, Immunology and Infection.

His foray into clinical trials began in 2007 when he was a gastroenterology trainee. He was entrusted to run a trial for a proton pump inhibitor to treat peptic ulcer disease in Kota Kinabalu, Sabah. Peptic ulcer disease was quite prevalent in Kota Kinabalu at that time and he managed to recruit sufficient patients to participate very quickly. This spurred him to venture into more industry-sponsored and investigator-initiated trials. Being at the right time and place, and having the right support was crucial motivation to him.

Dr. Tee divides his time between clinical practice and trials by getting his trial patients to attend clinic on quieter days. He also credits Clinical Research Malaysia (CRM) for providing assistance through CRM's Study Coordinators, who handle the scheduling of patients' appointment days. As PI, the main challenges in performing clinical trials are meeting patient recruitment targets and maintaining the patient's health and safety. But the devil is in the details. He credits CRM and his study coordinators for helping him in dealing with budget negotiation, plan appointments for patient visits, and calling up potential trial candidates. This frees his time to concentrate on his responsibilities as a PI.

Dr. Tee said that doctors should participate in clinical trials because it gives them a new perspective of the study and practice of medicine. It also prepares them for their future when they may have to take on leadership positions. It is not just clinical issues that need to be considered when doctors participate in clinical trials, doctors must also consider the budget and amount of man power required. In addition, they must consider how best to run a trial with the resources that are currently available, to give the best to their patients. Industry-sponsored clinical trials are designed by the best brains in a particular field. At times when a PI attends the investigator meeting, one can feel the thrill of being a part of the ground-breaking research that will be cherished in future. As a PI, Dr. Tee feels that adhering to the well-designed protocols actually teaches him the best way to manage a particular clinical condition. Dr. Tee gave the example of his clinical trial for the treatment of hepatitis C. The treatment of Hepatitis C is very costly; a course of treatment can amount to RM 150,000. With a clinical trial, he is able to provide the latest treatment to his patients at no cost. Clinical trials also help doctors build good rapport with their patients, as they can offer more than just the standard treatment, when necessary. It is like having a backup plan if all standard treatments fail.

When asked about how his patients respond when asked to participate in a clinical trial, he said that the concept of a clinical trial is still new to most patients. They are not aware of what it is and some might think they are being used as a guinea pig. Most of his patients who have completed a trial, appreciate the efforts made for them. He is proud of the fact that even though his centre is in Kuantan, he can provide his patients with the latest treatment options, on par with a world-class centre.

His patients appreciate having the latest treatments available to them. He said that there will be initial hesitance from his patients, but once the information is explained to them and they are aware that clinical trials are required for all drugs to enter the market, patients become more open. Once they are assured that most drugs that reach phase 3 clinical trials are generally safe and the efficacy is backed up by sufficient evidence, patients tend to have no qualms in participating in the trial.

When asked about what drives his passion in clinical research, Dr. Tee said the satisfaction when his patients respond to the new treatments drives him on. Many of his patients have seen numerous doctors and tried many treatment options. By the time they come to HTAA, they are relying on him to offer them the option of using drugs from clinical trials, which may not be available elsewhere. Once patients participate in the trial and get better, they begin to see the benefits of being a participant in a clinical trial.

When asked about the resources and facilities at HTAA, he said that in general, HTAA does not have the luxury of having multidisciplinary teams as many centres in the Klang Valley have. Many a time, a single consultant has to shoulder on problems involving other disciplines. He gave the example of chronic viral hepatitis which is generally a gastroenterology and hepatology condition. However when complications like hepatocellular carcinoma arises, the gastroenterologist has to liaise with hepatobiliary surgeons, oncologists and interventional radiologists outside HTAA. Many of the rural residents are not keen to travel far for treatment; hence having clinical trials with options of treatment in local hospital offers an attractive option for the patients.

For the future, Dr. Tee expressed hope that there would be friendlier environment toward clinical trials. It is important for policy makers to promote clinical trials as beneficial to the people. Clinical trials, be it investigator-initiated or industry-sponsored, are performed to develop new medication or help improve existing treatment options. There should not be a perception that doctors are neglecting their regular clinical work to participate in clinical trials. In reality, these doctors are going the extra mile in taking up trials and this should be encouraged.

“There should not be a perception that doctors are neglecting their regular clinical work to participate in clinical trials. In reality, these doctors are going the extra mile in taking up trials and this should be encouraged.”

Dr. Tee Hoi Poh

A Day in the Life of the

Head of Finance & IT, Clinical Research Malaysia

What are your job functions as the Head of Finance and IT?

My main job functions are to monitor the daily operation of the department to ensure its smooth running and to work with other departments which involves Finance and IT related matters.

What are the services offered by the Finance and IT department of Clinical Research Malaysia (CRM)?

Among the services offered by CRM under this department include management of the clinical trial budget for Principal Investigators (PI), assist sponsors and contract research organizations (CROs) and PIs in budget negotiation and any ad hoc matters involving these stakeholders.

What is CRM's role in managing a clinical trial budget?

CRM acts as a trustee in managing a clinical trial budget by receiving and executing disbursement of a trial budget. Upon receiving a Payment Instruction Form from a PI, CRM releases payment to the relevant recipients (for purposes of patient reimbursement, lab tests/procedures, outsourcing services to vendors, investigators' fees, etc). CRM pays the PIs directly instead of re-routing through the CRC Trust Account in HKL. This has shortened the payment timeline to less than 2 weeks. Apart from that, CRM ensures that a monthly Statement of Account is issued to the relevant Principal Investigators.

How can CRM assist Principal Investigators with their clinical trial budget?

CRM, on behalf of the Principal Investigator (PI), can assist in negotiating a trial budget (as part of the clinical trial agreement) with a sponsor or CRO. CRM ensures that the fees paid are according to the current industry standards and fair market value, and will advise PIs if any fee needs to be revised. During the review of a trial budget, CRM ensures that all core components of a trial budget are addressed.

Can you share with us how CRM utilizes the 15% management fee that is charged to the CROs and sponsors and how does this benefit the local sites conducting clinical trials?

The 15% management fee is used for various initiative including:

- To invest in developing the capability of sites through the purchase of medical equipment related to clinical research and upgrading of the internet facilities.
- Sponsor PIs and the clinical research team to attend conferences and training for professional development and to upgrade their knowledge and skills.
- Provide human resources to the Medical Research Ethics Committee (MREC) and Medical Device Authority (MDA) to smoothen the application process of ISR studies.
- To promote Malaysia as the preferred destination for clinical research at national and international conferences.

Why is it important for CRM to manage the trial budget?

CRM is authorized by the Malaysian Government to handle clinical trial budgets that are conducted in Malaysia. It is the role of CRM to ensure that payments are made to the relevant parties involved in the conduct of clinical trials and that it is made in a fair and transparent manner. According to the General Orders, Chapter D (Article 5), an Investigator, being a government officer, shall not receive money paid directly to him/her derived from his/her clinical trial activities. In light of this, CRM legitimizes the transfer of trial funds by managing the trial budget and channeling the investigators' fees to the relevant PIs.

Is study payment subjected to GST?

No, it is not subjected to 6% GST because the study payment is not a source of revenue or income for CRM. However, if the PI chooses to use outsource services, 6% GST will be charged if the vendor is a GST-registered company with the Royal Malaysian Customs Department.

Which fees are subjected to GST?

CRM's study coordinator fees, archiving fees, imaging costs, laboratory fees and any other outsourced services used by the PI.

What do you enjoy most about your job?

The recognition by the industry that CRM is here to assist the clinical research industry as well as the opportunity to learn together with the stakeholders and key opinion leaders.

And the most challenging part of your job?

There are always new challenges. The most challenging part of it would be executing something which is beyond my control while testing my ability to overcome it.

CRM's Scope of Services

CRM currently provides the following services

FEASIBILITY STUDIES & INVESTIGATOR MATCHING

- CRM evaluates feasibility studies / request that are forwarded by sponsors / CROs and disseminates them to a large pool of potential investigators
- CRM assist investigators who are interested to take-on the trial to complete and submit the feasibility study / request to the sponsor or CRO

CONSULTATION AND MANAGEMENT OF CLINICAL TRIAL BUDGET

- CRM advices investigators and sponsors/CROs on the clinical trial budget. This service ensures that resources are sufficient in order to complete all obligations of the clinical trial.
- CRM manages the trial budget with full transparency and schedule reports to investigators and the sponsor/CRO (CRM charges a fee of 15% above the value of the trial budget which will be utilized to finance its operations and training programs to upskill investigators and support staff)

REVIEW OF CTA & NDA

- CRM assists investigators & sponsors/CROs by reviewing and advising on Clinical Trial Agreements (CTAs) & Non-Disclosure Agreements (NDAs).
- CRM's experienced legal team will provide assistance to review the CTA/NDA.

DEVELOPMENT & PLACEMENT OF STUDY COORDINATORS

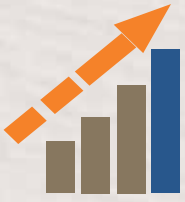
- CRM recruits suitably qualified candidates and trains them to become capable Study Coordinators (SCs) who will then be placed at trial sites in order to assist investigators.
- CRM currently has more than 80 trained SCs based in major Clinical Research Centres nationwide.

TRAINING RELATED TO CLINICAL RESEARCH

- CRM organizes various subsidized training programs for investigators and support staff in order to improve their capabilities to undertake ISR.
- Refresher courses on Good Clinical Practice (GCP) are also held for doctors and support staff.

ONE-STOP CENTRE FOR THE INDUSTRY

- CRM assists industry players in resolving issues or delays faced with government agencies and regulators (e.g. BLESS, MREC, MDA, NPCB, IRBs) that may delay the approval or initiation of trials.

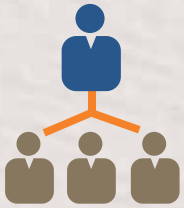


SITES CAPABILITY IMPROVEMENT & ENHANCEMENT

- CRM improves the capability of sites by assisting in both systems and infrastructure improvements.

IMPROVING PUBLIC AND PATIENT AWARENESS

- CRM engages with a variety of patient support groups and NGOs, undertakes advertising and promotional events, and seeks to generate positive media coverage to spread the word about clinical research, generate goodwill and to facilitate patient recruitment.



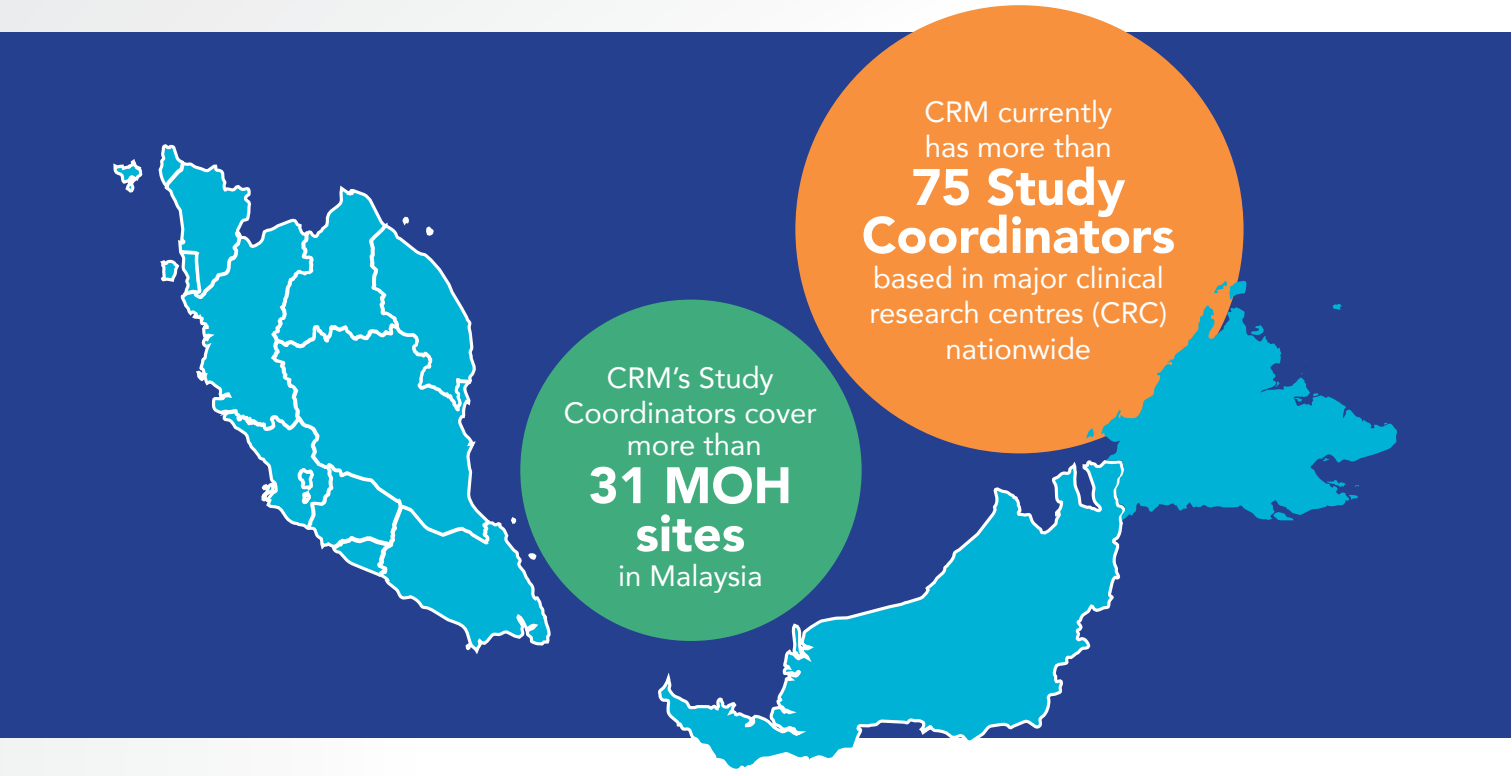
GROWING THE POOL OF INVESTIGATORS AND SITES

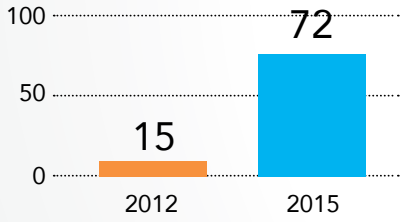
- CRM continuously attracts and develops potential new investigators and sites in both the public & private healthcare system

PROMOTING MALAYSIA AS A HUB FOR INDUSTRY SPONSORED RESEARCH (ISR)

- CRM participates in national and international events to engage sponsors and CROs as well as to promote Malaysia as a choice destination for ISR.

CRM's Study Coordinator

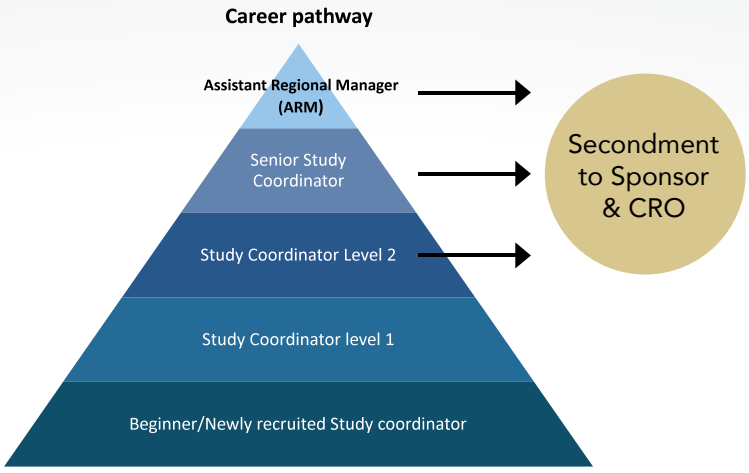




CRM's SC

CRM recruits suitably qualified Study Coordinators (SC) to support and assist investigators and study sites. CRM started off with 15 SCs in 2012 and as the clinical trial industry began growing in Malaysia, CRM have increased the number of SCs to 72 in 2015.

6 Assistant Regional Managers were appointed to supervise the SCs and ensure that the clinical trials at sites are conducted efficiently and with utmost quality. This includes managing the SCs for the trials at sites and work closely with the Investigators to ensure the success of each trial. They also identify, recommend and support the goals of the organization by working hand in hand with the Management.



ROLES AND RESPONSIBILITIES OF A STUDY COORDINATOR:

- Management of clinical trial.
- Management of study budget and SC fee.
- Management & coordination of feasibility studies received from CRM's feasibility team.
- Reporting of sites' progress and study statistics to Assistant Regional Managers.
- Coordinating with the Management at HQ on CRM's archiving services.
- Involvement in promotional activities.

- GCP Certification Course
- GCP Compliance Workshop through Effective Project Management
- Study Coordinator Workshop
- Hands-On Training
- Creating a Clinical Trial Budget Workshop
- A course on Delivering a Successful Clinical Study: A Roadmap for Study Coordinators
- Infectious Substances & Biological Specimen Awareness Course

Hospital KUALA LUMPUR

Hospital Kuala Lumpur (HKL) is the largest hospital under the Ministry of Health Malaysia and is also one of the largest in Asia. It is a government tertiary referral hospital, located on 150 acres of prime land in the heart of Kuala Lumpur. HKL strives to be an institution of excellence in health care education and research, driven by a dedicated team providing professional client-centered service. The hospital provides secondary and tertiary care to the community. It is also a training centre for house officers, paramedics, radiographers, physiotherapists, occupational therapists and other health care workers as well as postgraduate trainees and subspecialty trainees.

MISSION

Provide quality healthcare that:

- Is responsive to public, clients and employees needs;
- Is delivered by a team of skilled, innovative, committed and compassionate personnel;
- Involves partnership with individuals and the community for promotion of health;
- Will undertake education and continuous professional development for all levels of staff; and
- Conduct clinical research

OBJECTIVE

- To provide quality patient oriented service based on humanistic values emphasing customer satisfaction and encompassing promotive, preventive, curative and rehabilitative aspects;
- To provide health education service to its clientele and provide post basic and continuing medical education to its staff to promote professionalism;
- To instil excellent work culture and to create a conducive environment to deliver quality services;
- To make HKL a centre of excellence and national referral centre,
- To establish HKL as a clinical research centre.

HOSPITAL KUALA LUMPUR AS A PRIME SITE

Hospital Kuala Lumpur was selected to be included in the initial wave of Prime Sites, a collaboration between the Government of Malaysia (represented by the Ministry of Health) and Clinical Research Malaysia (CRM) with Quintiles.

Prime site is defined as a site targeted for intensified infrastructure and human resources development for improved participation of investigators in conducting clinical trials. The vision is to establish Prime Sites locally for clinical research, conducting benchmark trials with global impact.

The Prime Sites will develop long term strategic relationship with Quintiles to increase the number of industry sponsored research, improve start-up time and to meet or exceed patient recruitment targets.
There are currently 11 Prime Sites in Malaysia and this include:

- Hospital Umum Sarawak
- Hospital Sibu
- Hospital Queen Elizabeth II
- Hospital Raja Permaisuri Bainun
- Hospital Sultanah Bahiyah
- Hospital Raja Perempuan Zainab II
- Hospital Tengku Ampuan Rahimah
- Hospital Selayang
- Hospital Kuala Lumpur
- Hospital Pulau Pinang
- Hospital Seberang Jaya

history

1870

It was developed as a district hospital comprising of 3 wards i.e., the Tai Wah Ward, the Choudhry Ward and the Malay Ward.

1920

Upgraded to 25 wards

1962

Development of HKL from Phase I to Phase IV. The development of the various phases were as follows:

1973

HKL started functioning as a teaching hospital for UKM medical students.

1989 - 1992

Paediatric Institute was constructed.

1994 - 1997 (Phase II)

Upgrading of the Institute of Radiotherapy, Oncology and Nuclear Medicine.

2013

Specialist Complex & Ambulatory Care Centre (SCACC) was constructed.

2015

Multi-storey Car Park opened to the public on 15 February 2015.

2016

Current ongoing construction of Maternal & Child Hospital.

Phase I (1962 - 1968)

Maternity Hospital, North Ward Block, Radiotherapy Department and Hostels for staff were built.

Phase II (1968 - 1972)

South Ward Block, Neurology Institute, Surgical Block, Radiology Block, National Blood Transfusion Centre and more hostels were added.

Phase III (1972 - 1973)

Specialist clinics, Outpatient Department and Doctor's hostel were constructed.

Phase IV-A (1973 - 1974)

Trainee Nurses hostel and Clubhouse added.

Phase IV-B (1975):

Orthopaedic Institute, Urology Institute, Artificial Limb Centre and Radiology Block built.

LARGE POOL OF PATIENTS & STAFF (Statistics of year 2014)

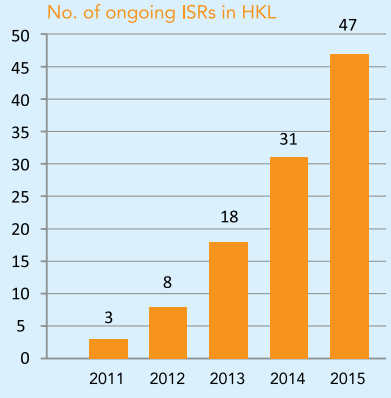
TOTAL STAFF	DOCTORS	NURSES	SURGERIES
10,184	1,809	3,768	13,588

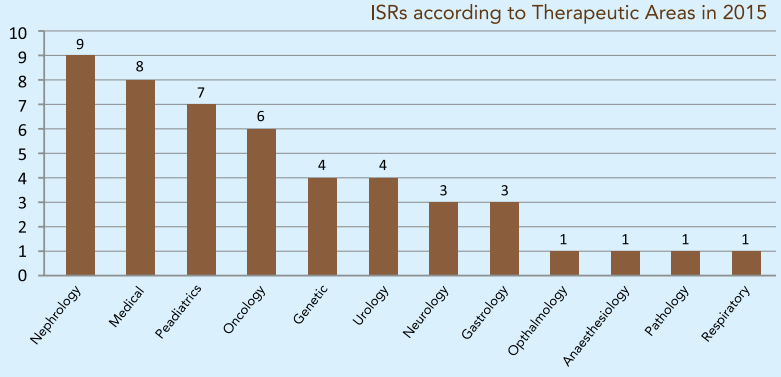
HOSPITAL BEDS	NUMBER OF INPATIENTS	NUMBER OF OUTPATIENTS
1,567	128,853	1,172,307

Doctors Breakdown

Consultants	Specialists	Medical Officers	House Officers
71	323	909	506

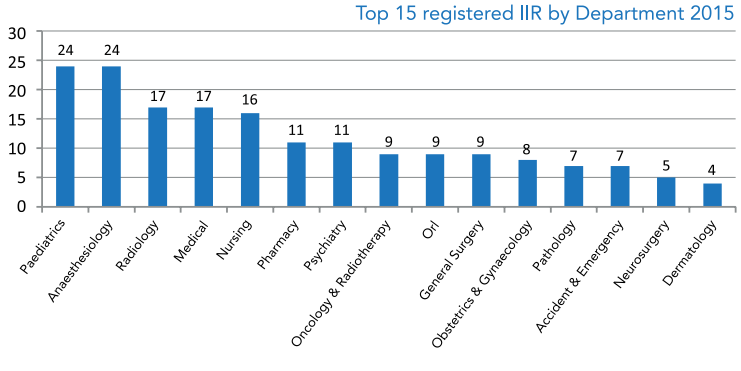
Industry Sponsored Research (ISR)





INVESTIGATOR INITIATED RESEARCH (IIR)

CRC HKL aims to capture investigator initiated research (IIR) conducted within HKL to observe the departmental performance. In 2015, a total of 217 IIRs were registered with CRC HKL. It has been encouraging to note that IIR spans across the 33 clinical departments in the hospital, with increasing activity among certain departments.



CRC HKL was established in November 2012. It is located at Level 7, Specialist Complex & Ambulatory Care (SCACC) Building, HKL where it actively assists investigators in various clinical research areas including Investigator Initiated Research (IIR) & Industry Sponsored Research (ISR). Since then, it expanded very well by leaps and bounds. The establishment of CRC HKL is essential to the growth of the research spirit among healthcare providers in HKL.

Currently, Dr. Hajjah Salina Abd Aziz spearheads the unit consisting of 8 dedicated medical officers and 5 allied health staffs. The symbiotic relationship with Clinical Research Malaysia (CRM) enables both sides to achieve our common goal. As of 2016, 11 CRM study coordinators have been placed in HKL to work hand in hand with CRC HKL and various investigators within the hospital.

CRC HKL aims to make HKL a main clinical research hub in Malaysia. Its' mission is to improve the quality of health of patients through the application of high quality research studies.

Together, the team at CRC HKL is very committed to promote positive research attitudes and also in creating awareness amongst healthcare providers. The outreach is not only to doctors, but to all health care providers. Excellent programs have been implemented and are currently running to deliver that message to everyone especially to HKL staff. We hope to place Hospital Kuala Lumpur on the world map as a renowned hub of clinical research.

CRC HKL Facilities

Dedicated room for medical equipments

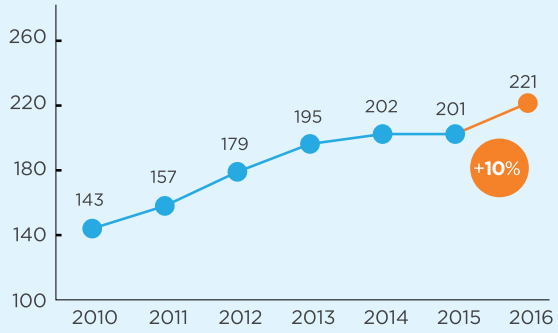
HOSPITAL RESEARCH REVIEW COMMITTEE

HRRC was established in May 2014. It began as one of the implementation of a new framework for research approval in Ministry of Health (MOH) through a pilot study that involved 3 other public hospitals. Recruitment of the HRRC members was done from various departments in HKL; consisting of Consultants, Specialists, Surgeons and Allied Health Officers. It started off with only 15 members and has since expanded to 38 members. The meeting is held every week and reviews an average of 4 proposals each week.

Malaysia's ISR Statistics in a Nutshell

ISRs approved by Ethics Committees in 2015

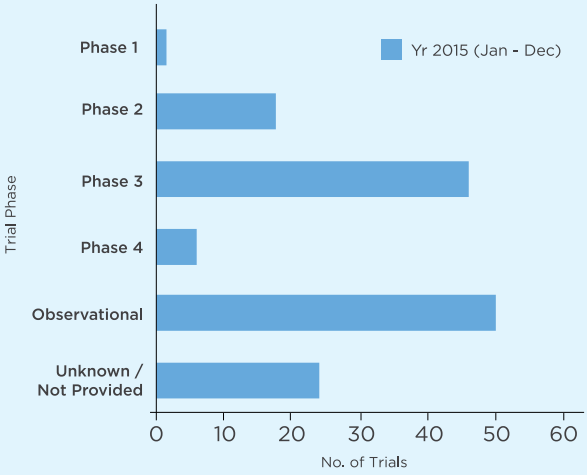
201 new ISR trials were approved in 2015 by the various ECs (94% of CRM's 2015 KPI 1).



Note:
The number reported includes ISRs approved for MOH and non-MOH sites, using the data reported monthly by the 13 ECs in Malaysia

EC = Ethics Committee; ISR = Industry Sponsored Research

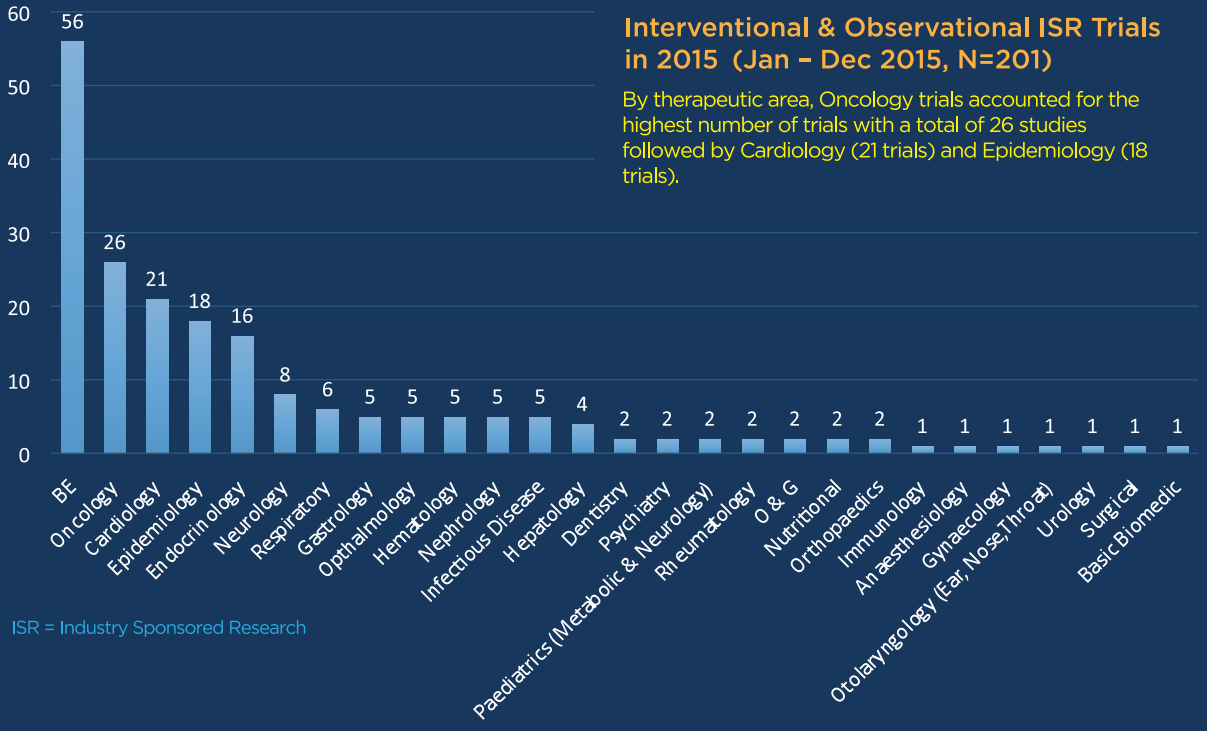
ISRs Approved by Ethics Committees in 2015 According to Phase



Note: BE studies are not included as it is not a trial phase

Interventional & Observational ISR Trials in 2015 (Jan – Dec 2015, N=201)

By therapeutic area, Oncology trials accounted for the highest number of trials with a total of 26 studies followed by Cardiology (21 trials) and Epidemiology (18 trials).

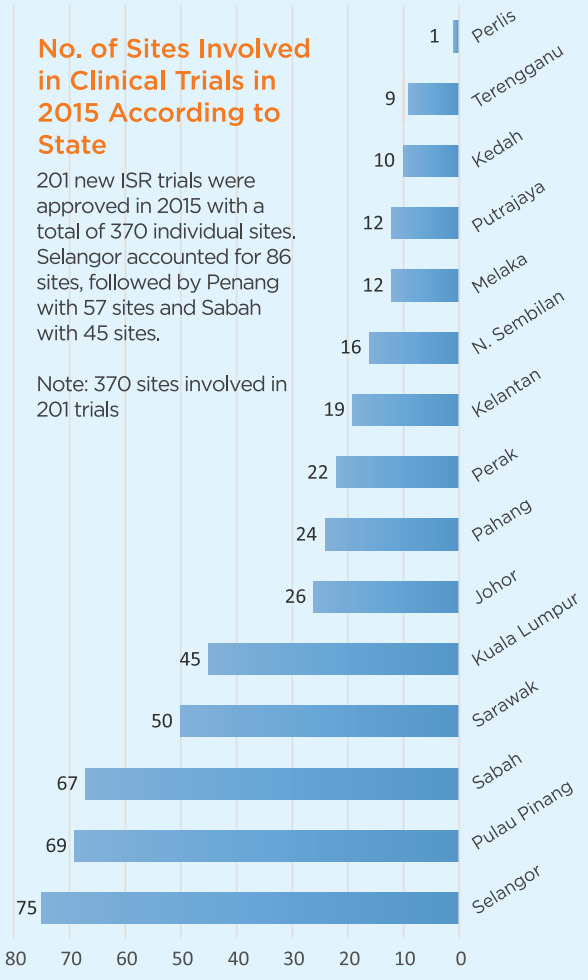


ISR = Industry Sponsored Research

No. of Sites Involved in Clinical Trials in 2015 According to State

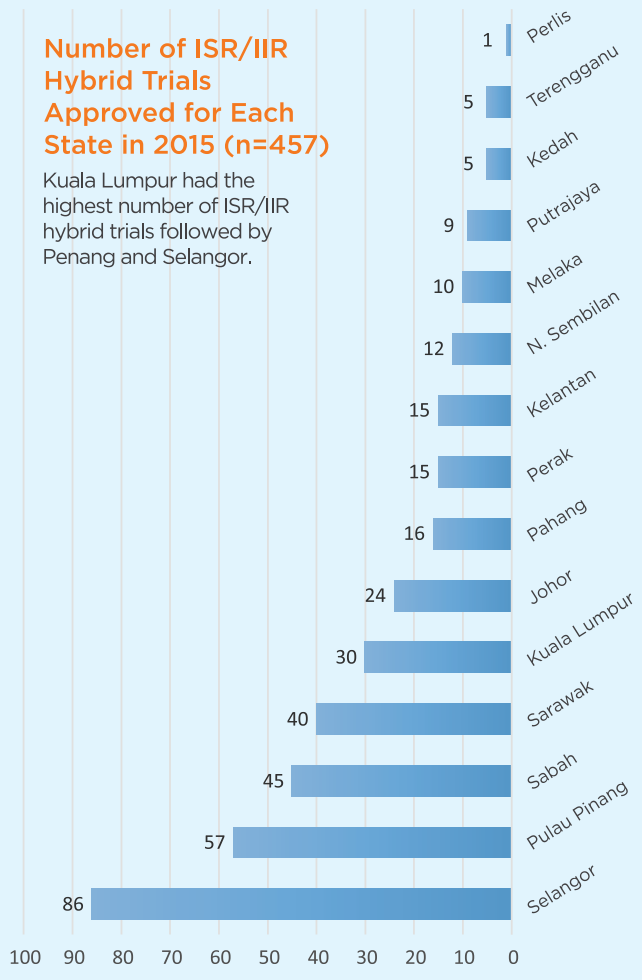
201 new ISR trials were approved in 2015 with a total of 370 individual sites. Selangor accounted for 86 sites, followed by Penang with 57 sites and Sabah with 45 sites.

Note: 370 sites involved in 201 trials



Number of ISR/IIR Hybrid Trials Approved for Each State in 2015 (n=457)

Kuala Lumpur had the highest number of ISR/IIR hybrid trials followed by Penang and Selangor.

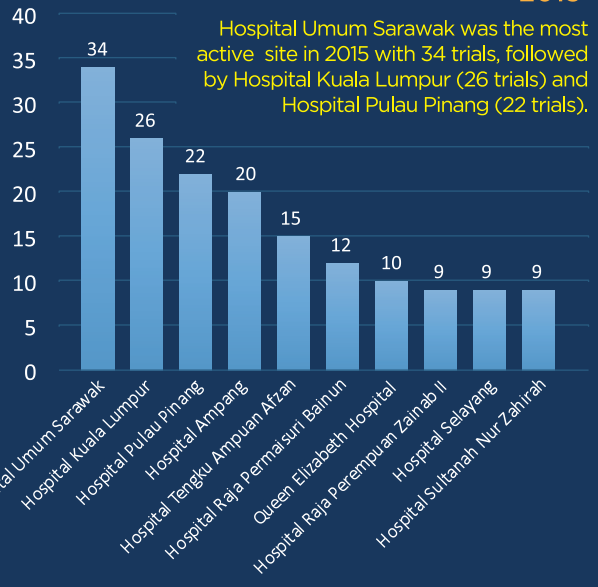


Notes:
The number reported for each state includes ISR approved for MOH and non-MOH sites, using the data reported monthly by the 13 ECs in Malaysia
The number represents individual ISR/IIR hybrid at each state; there may be duplicates of the same trial at other states with different PIs.
201 new trials were approved in 2015.

IIR = Investigator Initiated Research; ISR = Industry Sponsored Research

Top 10 Most Active Sites in 2015

Hospital Umum Sarawak was the most active site in 2015 with 34 trials, followed by Hospital Kuala Lumpur (26 trials) and Hospital Pulau Pinang (22 trials).



INVESTIGATOR'S **CORRECTIVE ACTION PLAN** FAILS TO SATISFY FDA

Following an FDA inspection, the agency lists identified deficiencies in a Form FDA 483, Inspectional Observations, and in the FDA Establishment Inspection Report. There is no regulatory requirement for the inspected party to respond to the Form FDA 483. Nevertheless, a well-reasoned, complete and timely response is generally in the inspected party's best interests, not least because it may mitigate a decision for further action and demonstrates commitment and intent to comply, which will establish credibility with the FDA. When the inspected party chooses to provide a written response, any subsequent FDA warning letter is likely to include a judgement on the appropriateness of that response. From a review of even a small number of FDA warning letters, it is evident that the agency often finds that the corrective and preventive actions (CAPAs) proposed by inspected parties are inadequate. One such case is described below.

MISSED LABORATORY EVALUATIONS

An investigator participating in two oncology trials failed to perform a large number of protocol-required laboratory tests, including coagulation profile laboratory tests for four out of five subjects on up to 15 occasions. In addition he failed to perform liver function tests for all five subjects on at least three occasions. In his written response to these violations, the investigator confirmed that the protocol-required laboratory tests were missed for subjects enrolled in the two studies. He indicated that, as a part of his corrective action plan (CAP), he had added a "clinical trials link" to the site's electronic medical record (EMR) to provide study staff with access to study information. He further stated that he will review the process of accessing study information and the importance of following the study calendar with his staff. The FDA replied that the response was inadequate because it did not include sufficient information to enable the agency to evaluate the adequacy of the CAP for use in any future clinical research. In particular, the FDA stated that it was unclear how adding a "clinical trials link" to the site's EMR would ensure that protocol requirements would be met for studies at the site. The response did not provide details of a CAP to prevent similar violations from occurring in the future, or sufficient details to implement additional measures and procedures to address the inspection findings. The FDA was therefore unable to determine whether the CAP was sufficient to prevent similar violations in the future.

LESSONS LEARNED

A corrective action can be defined as any action designed to eliminate the cause of a detected non-conformity or other undesirable situation. A preventive action is one intended to eliminate the cause of a potential non-conformity or other undesirable potential situation. Thus preventive action is taken to prevent occurrence, whereas corrective action is taken to prevent recurrence. A CAPA should describe the implementation of actions taken to detect and eliminate the cause of an area of non-compliance; it should also prevent the recurrence of non-compliance. As evidenced by the FDA's reaction to many proposed CAPAs, it is important that the CAPA is written correctly, with those responsible following a defined process, typically taking in the following:

- stating the problem, including the root cause
- breaking the solution into discrete measurable actions
- identifying the person accountable for each action
- setting achievable deadlines
- monitoring progress.
  Regulatory agencies will expect a CAPA to address each observed inspection deficiency or violation in a complete and transparent way, ie. it should
- address the specifics of the inspection findings but also consider potential system-wide or global implications
- reflect the outcome of the root cause analysis and include, where appropriate, plans to achieve immediate, short and long-term corrections within stated timeframes
- provide a way to verify and/or monitor the effectiveness of the planned corrective actions
- include copies of any referenced supporting documents.

Depending on the extent of the observed deficiencies and their potential to impact upon the study, it may also be necessary to report the inspection findings to other entities such as the affected ethics committee(s)/ institutional review board(s). Again, depending on the nature of the observations, this may require several communications (eg. an immediate report followed by updates as and when more information becomes available and corrective actions are implemented and monitored).

As highlighted above, FDA warning letters usually evaluate the CAPA proposed in response to the Form FDA 483. Common deficiencies in proposed plans include:

- insufficient detail or inadequate documentation on the specific corrective actions to be taken
- not addressing why a specific problem occurred or not describing the extent of the problem; quantifying the number of affected studies/subjects may be helpful
- not describing the preventive measures to be taken
- not describing the extent/pervasiveness of the problem (ie. how many subjects were affected in the current study and whether the problem extended to other studies)
- not providing the timeframe in which corrective actions have been or will be undertaken and/or completed.

Source: Clinical Research Advisor/Clinical Quality Assurance - November 23, 2015

MINISTRY OF HEALTH MALAYSIA

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PROCEDURES TO INITIATE A CLINICAL TRIAL IN MALAYSIA

1 PROTOCOL DEVELOPMENT

- If protocol yet to be developed, sponsors can engage a CRO which offers this service.

Responsible party: ***Sponsor/CRO***

2 FEASIBILITY

- CRM or a CRO can be approached by sponsor to conduct feasibility assessment.
- CRM does not charge sponsors for feasibility assessment. Duration: 7-5 working days.

Responsible party: ***CRM/CRO***

3 SITE SELECTION

- Sponsor to decide on the clinical trial sites based on feedback from CRM or CRO.

Responsible party: ***Sponsor***

4 STUDY START-UP

- Ethics Committee submission [1]
- CTIL submission [2] (Parallel submission for CTIL and Ethics approval)
- Contract negotiation
  - CTA review [3]
  - Budget review [3]

Responsible party: ***[1] PI; [2] Sponsor/CRO; [3] CRM***

Note: CRM charges RM 4000 per review of a CTA and a management fee of %15 of the value of the total trial allocation to manage the trial budget.

5 STUDY INITIATION & CONDUCT

- Investigator meeting, Site Initiation Visit followed by Monitoring.
- Study Coordinator (SC) allocation: CRM provides on-site fulltime SC to assist PIs.
- Budget Management: CRM offers budget management services to PIs.

Responsible party: ***CRO; CRM***

6 STUDY CLOSE-OUT

- Confirmation that all site investigators obligation have been met, study document files completed and balance IP is returned to responsible party (or prepared for destruction).

Responsible party: ***CRO***

7 ARCHIVING

- PI to outsource archiving services to archiving companies.
- CRM able to assist PI.

Responsible party: ***PI/CRM***

CRM = Clinical Research Malaysia; CRO = contract research organization; CTA = clinical trial agreement; CTIL = clinical trial import license; IRB = independent review board; MREC = Medical Research Ethics Committee; NPCB = National Pharmaceutical Control Bureau; PI = principal investigator; SC = study coordinator.

CRM in Photos

Industry Talk - Clinical Research and Life Sciene Ecosystem, Kuala Lumpur (28th November 2015)

The 5th Asia Pacific Primary Care Research Conference (APPCRC), Putrajaya (4th - 6th December 2015)

Signing Ceremony between CRM & DNDi, Putrajaya (13th January 2016)

CRM 2nd National Conference 2016 (15th - 19th January 2016)

CRM visit to Miri Hospital Sarawak (31st March 2016)

The 18th AFES Congress 2015, Kuala Lumpur (10th - 13th December 2015)

1st Acute Internal Medicine Conference, Academy of Medicine Malaysia, Kuala Lumpur (25th - 27th March 2016)

Launching of CRC HTAA Pahang New Office (23rd March 2016)

Launching of CRC Building at Hospital Sultanah Aminah (HSA) Johor (1st March 2016)

BioPharma Asia Convention 2016, Singapore (23rd - 24th March 2016)

NPCB meeting regarding the clinical research issues in Malaysia, Petaling Jaya (7th March 2016)

Introduction to Clinical Research, Hospital Umum Sarawak (31st March 2016)

CRM bulletin

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The CRM Bulletin is published three times a year with a print run of 3000 copies per issue. These are delivered complimentary to a local and foreign readership base comprising of: Doctors and investigators (public and private); Hospitals (public and private); Sponsors and CROs; Universities and academics involved in clinical research; Medical research centres; Senior government and MOH officials; Clinical Research Centre (CRC) staff and investigators; Ethics Committees, Patient support groups; and selected medical schools.

The print run is complemented by an online subscriber base of 2000 readers currently, who receive an online copy of the CRM Bulletin.

The bulletin's objectives are to spread awareness about Malaysia's capabilities in industry sponsored clinical research (ISR), inform and attract industry players to Malaysia, motivate and educate potential investigators and support staff, build public awareness about the importance of clinical research, and finally serve as a forum to share news and development relevant to all stakeholders.

OTHER PUBLICATIONS BY CRM

Guide to BA/ BE Centres in Malaysia

Malaysian Guide on the use of Human Biological Samples for Research

NCCR bulletin

Guide for Industry

Patient Brochure

NCCR 2016

10th National Conference For Clinical Research 2016

27 - 28 JULY 2016 | HOTEL ISTANA, KUALA LUMPUR

BIG DATA DRIVING CLINICAL RESEARCH FOR HEALTH

This 10th edition of the NCCR celebrates a decade in pioneering and popularising clinical research in Malaysia. For 2016, we are proud to present cutting edge innovations and developments globally and evaluate their applications and aspirations locally.

Invited speakers are renowned researchers and practitioners who are able to communicate their passion and struggles to inspire a new generation.

The two-day conference will also feature opportunities for networking and connecting people and teams.

HIGHLIGHTS

- Evolution or Revolution – Big Data and Evidence Based Medicine;
- The role of Big Data in research and health outcomes;
- The strategic effect and influence on policy and procedures – a paradigm shift?;
- Health Economics and use of Big Data.

OBJECTIVES

- Discover the usage of 'Big Data' – its impact and challenges in research and healthcare;
- Examine its potential and discover the profound benefits to patients and populations;
- Consider the enhancement to clinical outcomes and healthcare;
- Present health economics and use of Big Data.

OTHER MAJOR TOPICS

- Industry Sponsored Research;
- Clinical Research in Public Health and Management;
- Assess the evolving contribution of clinical research teams in global innovations.

> *"I know some people think data is boring. And global development still has a lot of catching up to do.... But you know what isn't boring? **Saving people's lives**. And the richer our troves of data, the more lives we can save. 2016 is the year we're going to start getting it."*

Melinda Gates *on Big Data in Wired Nov 2015*

Call for ABSTRACT | **Mark Your Calendar**

DR WU LIEN TEH RESEARCH AWARDS COMPETITION

Submit BEFORE or ON March 31, 2016 (5.00pm)

An opportunity to display your research, present research findings and obtain recognition for your work. Cash and medals await the winners:

Young Investigator Awards
(Oral Presentation)

- First prize: RM 1000 + medal
- Second prize: RM 500
- Third prize: RM 250

Best Poster Awards

- First prize: RM 250 + medal
- Second prize: RM 200
- Third prize: RM 150

All abstracts accepted/qualified will be given certificates of participation.
**Rules and deadlines will be posted on the conference website.*

SPECIAL NOTICE

Look out for ADDITIONAL prizes and awards this year!! There will be additional prizes and awards according to CATEGORIES for this 10th NCCR conference. This includes a RM5,000 prize money to attend a research conference/meeting abroad sponsored by Clinical Research Malaysia (CRM).

Showcase Your Company or Institution And Be Noticed!

Contact us if you would like to enhance your brand visibility and target the right audience either by becoming a sponsor, taking up a booth or an ad page.

For more information, please contact:
Conference Secretariat NCCR 2016 | Tel: +603 - 7726 8000 | Fax: +603 - 7733 7007 | Email: contact@crestevendz.com.my
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