By Clinical Research Malaysia

CRM bulletin
of Clinical Research and Therapy

ISSUE 06

PERSPECTIVES ON PATIENT RECRUITMENT

Contents

Published by:

MINISTRY OF HEALTH MALAYSIA

CRM CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

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From the CEO's desk

Six months have passed since I last assumed the leadership role in CRM. It has truly been an amazing journey being in CRM and leading this company to achieve the goals it was set to. Alhamdulillah, praise to Allah, our 5 key strategies have started to deliver results. Allow me to highlight what we have already achieved in this short period of time.

Our first strategy to grow the number of Principal Investigators and Sites is beginning to bear fruits. CRM has invested its resources in improving the capability of our sites to conduct ISR. We have improved the internet capability and wifi connections in Hospital Selayang and developed the CRC sites in Hospital Seberang Jaya, Hospital Tengku Ampuan Afzan and Hospital Raja Perempuan Zainab II. Additionally, CRM has provided the necessary equipment to conduct clinical trials to Hospital Seri Manjung and Hospital Queen Ellizabeth II. We have also supported State Research Day by sponsoring Investigator's Awards, and this initiative was met with overwhelming support from our medical professionals. For instance, the Kedah Research Summit managed to generate 88 poster presentations. In order to inculcate research at every level in each state, this is the result that we expect. I encourage more states to take up this opportunity provided by CRM to build their respective research capability.

We have also made considerable progress in growing industry-sponsored research (ISR), our second strategy. By improving the efficiency of our feasibility team through a dedicated Standard Practice and database, we have yield a better success from 10% in 2014 to 18%. The number of feasibility has increased by 300% compared to previous years, with a 50% growth in new Sponsors.

CRM has also entered into new partnerships with the Medical Device Authority and the Malaysian Biotechnology Corporation to facilitate the use of medical device in industry-sponsored research. By collaborating with these stakeholders, we hope to improve the number of ISRs in Malaysia. Other new partnerships are with the Malaysian Investment Development Authority (MIDA) and Malaysia External Trade Development Corporation (MATRADE) where we wish to promote Malaysia as the destination for ISR.

Turning to our fourth strategy to create awareness of CRM, we have been actively participating in larger national meetings like the National Heart Association of Malaysia (NHAM), Family Medicine Scientific Conference, National Conference for Clinical Research (NCCR), etc. to build awareness at the local level. We were also represented in international exhibitions in Singapore, Europe, USA, Korea and Australia. The result: a 200% growth in inquiries from interested parties about ISR opportunities in Malaysia.

Finally, CRM remains committed in developing human capital. In CRM, we believe that developing our people's potential to be future leaders is an investment to the company and the country. Our people have started to attend training and development programmes like Franklin Covey's 7 Habits of Highly Effective People as well as Communications and Human Relations Skills by Dale Carnegie. Training programmes for our Study Coordinators have also ran its course, with trainers hailing from the US and UK. These trainers are invited to train our SCs to meet international standards and to attain the necessary skills and knowledge.

I would like to take this opportunity to extend our appreciation to our Board Members for their support in our activities and their time for bouncing ideas off each other. We would also like to spell out our gratitude to CRC who continues to deliver most of the ISRs to Malaysia. Finally, I'd like to say my gratitude to all my team in CRM who embraced the new strategies and made the change. We believe all future collaboration would yield better results and please watch this space in six months' time.

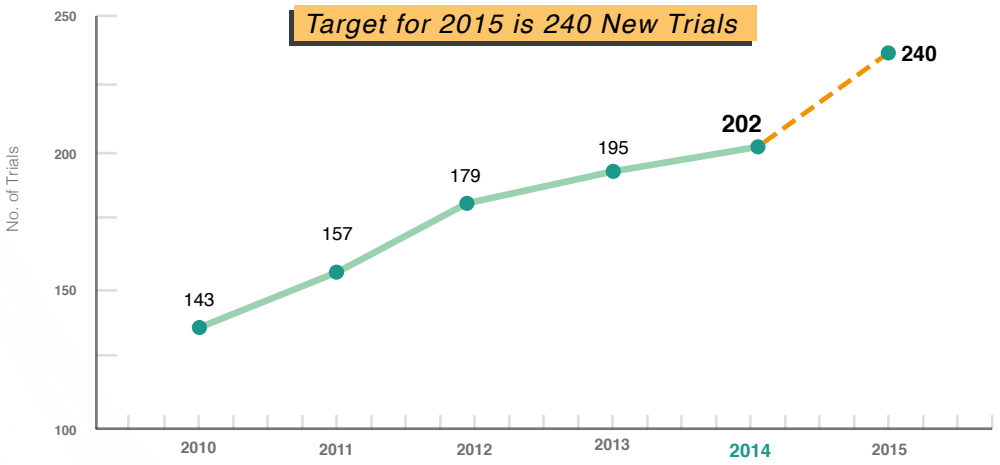
Dr. Akhmal Yusof
Chief Executive Officer
Clinical Research Malaysia
akhmal.yusof@clinicalresearch.my

2015 ISR STATISTICS

Jan – Aug 2015: New ISRs Approved by IRBs

From January to August 2015, a total of **153** new ISR trials were approved by the IRBs. The KPI target for 2015 is 240 new trials.

Note: Global industry intelligence indicate that the number of ISR has reduced this year and Malaysia is expected to be also affected by it.

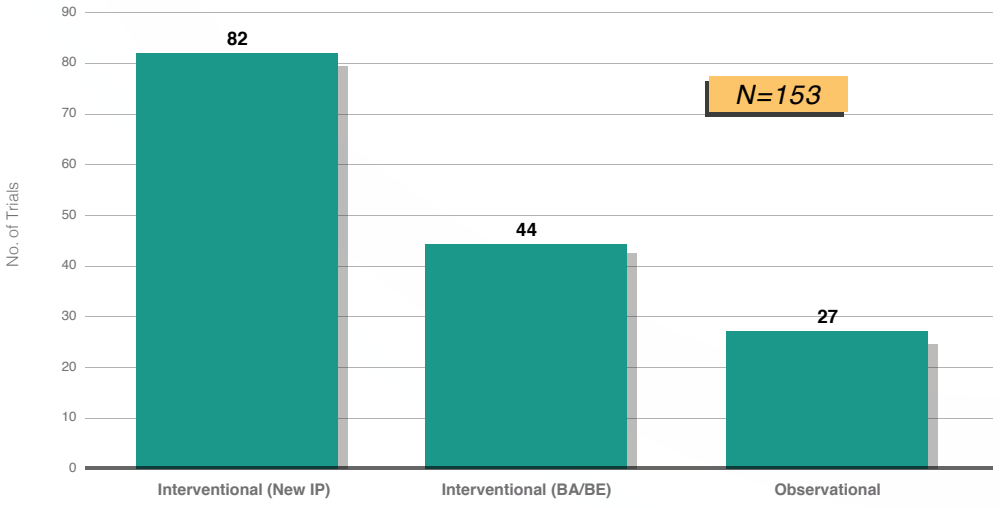


Jan – Aug 2015: Approved ISR by Classification

82 new interventional trials were approved between January and August 2015. This was followed by 44 BA/BE trials and 27 observational studies.

Note: BA/BE trials are separated in the major classification of trials as they are conducted to compare bioequivalence of IP and comparator and may be conducted in patients or in healthy volunteer subjects.

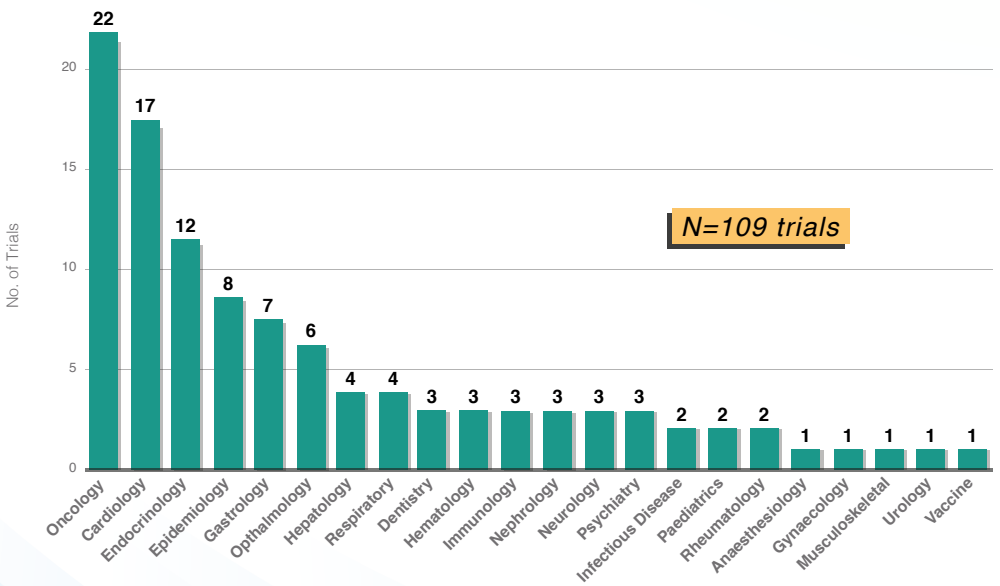
The category of trial (interventional & observational) follows the guideline as provided by FDA.



Jan – Aug 2015: New Interventional & Observational ISR Trials According to Therapeutic Area

Oncology accounted for 22 trials, followed by cardiology with 17 trials, endocrinology with 12 trials and epidemiology with 8 trials.

Note: The therapeutic clasification follows the guideline as provided by FDA.



12 INSTITUTIONAL REVIEW BOARDS + 1 CENTRALISED ETHICS COMMITTEE
Medical Research Ethics Committee (MREC)
Joint Penang Independent Ethics Committee (JPEC)
Medical Ethics Committee University Malaya Medical Centre (MECUMMC)
Independent Ethics Committee Sime Darby Healthcare (IECSDH)
Sunway Medical Centre Independent Research Ethics Committee (SREC)
International Medical University (IMU) Joint Committee of the Research and Ethics Committee (IMUJC)
National Heart Institute Ethics Committee
IIUM Research Ethics Committee (IREC)
Joint Ethics Committee School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM) – Lam Wah Ee Hospital on Clinical Studies
Ethics Research Committee Universiti Teknologi MARA (UiTM)
Ethics Research Committee Universiti Putra Malaysia
Ethics Research Committee Universiti Sains Malaysia
Ethics Research Committee Universiti Kebangsaan Malaysia

TRIAL SITES IN MALAYSIA

Public Hospitals / Health Clinics			
Hospital Ampang	Hospital Raja Permaisuri Bainun	Hospital Tengku Ampuan Afzan	KK Karak
Hospital Bahagia Ulu Kinta	Hospital Seberang Jaya	Hospital Tengku Ampuan Rahimah	KK Lenggong
Hospital Duchess of Kent	Hospital Selayang	Hospital Tuanku Ampuan Najihah	KK Lukut
Hospital Kajang	Hospital Sentosa	Hospital Tuanku Fauziah	KK Pasir Gudang
Hospital Kuala Lumpur	Hospital Serdang	Hospital Tuanku Jaafar	KK Putrajaya
Hospital Melaka	Hospital Seri Manjung	Hospital Umum Sarawak	KK Seremban 2
Hospital Mesra Bukit Padang	Hospital Sibu	Hospital Wanita dan Kanak Kanak Likas	KK Setapak
Hospital Miri	Hospital Sultan Abdul Halim	Institut Perubatan Respiratori (IPR)	KK Shah Alam Seksyen 7
Hospital Permai	Hospital Sultan Ismail	KK Ampangan	KK Simpang Kuala
Hospital Pakar Sultanah Fatimah	Hospital Sultanah Aminah	KK Bandar Baru Air Itam	KK Tampin
Hospital Pulau Pinang	Hospital Sultanah Bahiyah	KK Bandar Sungai Petani	KK Tampin
Hospital Putrajaya	Hospital Sultanah Nora Ismail	KK Cheras Baru	KK Tanglin
Hospital Queen Elizabeth	Hospital Sultanah Nur Zahirah	KK Greentown	Klinik Pergigian Gunung Rapat
Hospital Queen Elizabeth II	Hospital Sungai Buloh	KK Jaya Gading	Klinik Pergigian Putrajaya
Hospital Raja Perempuan Zainab II	Hospital Taiping	KK Jelapang	Klink Pergigian Cahaya Suria
Pusat Darah Negara (PDN)		Pusat Jantung Hospital Umum Sarawak	

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

Private Hospitals		
Beacon International Specialist Centre	Lam Wah Ee Hospital	Pantai Hospital Ayer Keroh
Chinese Maternity Hospital	Loh Guan Lye Specialist Centre	Pantai Hospital KL
Columbia Asia Medical Centre	Mahkota Medical Centre	Pantai Hospital Penang
Gleneagles Medical Centre	Metro Specialist Hospital	Penang Adventist Hospital
International Specialist Eye Centre (ISEC)	Mount Miriam Cancer Hospital	Prince Court Medical Centre
Ipoh Specialist Hospital	National Heart Centre (IJN)	Sabah Medical Centre
Island Hospital	Nilai Medical Centre	Sime Darby Medical Centre
KPJ KL	Normah Medical Specialist Hospital	Sunway Medical Centre
Tun Hussein Onn National Eye Hospital		

KK = Klinik Kesihatan

PHASE I / BABE SITES, PRE-CLINICAL AND GLP-CERTIFIED LABORATORIES IN MALAYSIA

Phase I / BABE Sites
Info Kinetics Sdn. Bhd.
Cardiology Ward, Penang General Hospital
Clinical Trial Complex (CTC), Advanced Medical & Dental Institute, Universiti Sains Malaysia
Clinical Research Centre (CRC), Penang General Hospital
Clinical Trial Unit, Clinical Research Centre, Seberang Jaya Hospital
Clinical Research Ward, Ampang Hospital
Bioequivalence Centre, Pharmacy-Hovid Research Sdn. Bhd., School of Pharmaceutical Sciences, Universiti Sains Malaysia
CRC Research Ward, Sarawak General Hospital Heart Centre
University of Malaya Bioequivalence and Testing Centre (UBAT)
Questra Bio-Clinical Research Centre

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

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

Research Personality

Dr. Shanthi Viswanathan

Consultant Neurologist
Department of Neurology, Kuala Lumpur Hospital

Dr. Shanthi Viswanathan obtained her MBBS from Kasturba Medical College, Manipal, India, before completing her MRCP from the Royal College of Physicians, Ireland. She subsequently pursued a one-year fellowship at the Queen Elizabeth Hospital, Birmingham and went on to obtain a fellowship in Neurology from the Ministry of Health, Malaysia. Dr. Shanthi currently serves as Honorary Lecturer and ad hoc examiner for undergraduates and postgraduates who are sitting for membership from the Royal College of Physicians of Ireland, and as Honorary Lecturer for University Teknologi MARA, Malaysia.

As a Consultant Neurologist at Kuala Lumpur Hospital, Dr. Shanthi has a keen interest in demyelinating diseases and movement disorders. She has been responsible for leading the establishment and development of the Demyelinating Diseases Registry, Demyelinating Diseases Clinic and Plasmapheresis Suite at the Department of Neurology, where she deals with the assessment of suitability of patients for disease modifying therapies and immunosuppressants.

Dr. Shanthi combines her professional clinical duties with the role of Chairman in the task force for the development of the Clinical Practice Guideline (CPG) on the Management of Multiple Sclerosis in Malaysia, as well as in the past has served as a Member of the development group for the CPG on Management of Dementia.

She is actively involved in various societies at the national and international level and has been part of the Malaysian team that won the “Tournament of Minds” at the World Neurology Congress in Bangkok in 2009. She has participated in a number of investigator initiated and industry sponsored drug trials, particularly in demyelinating diseases,dementia and epilepsy. Dr. Shanthi has published in various local and international peer review journals and given talks both locally and abroad on a number of neurology-related topics. She is currently involved in an ongoing research that looks at the role of Human Leukocyte Antigen (HLA) alleles in susceptibility of multiple sclerosis in Malaysia and various other investigator initiated projects on demyelinating diseases.

Dr. Shanthi recently shared her experience with Clinical Research Malaysia (CRM) on her research journey as a Principal Investigator.

Please share with us your experience in research.

My initial involvement in research focused more on Investigator Initiated Research (IIR) where most of the core work involved are non-interventional, observational and retrospective in nature. My long-standing interests are in movement disorders and demyelinating diseases, where I spend most of my time studying the latter and updating the registry which I have established in this Department in 2004. This registry has allowed me to develop various manuscripts and case reports which I have sent for publishing. As for Industry Sponsored Research (ISR), I make it a point to at least undertake one trial each year and so far have been involved in at least five trials since embarking on this research journey. Being involved in ISR has been fulfilling but not without its challenges.

Can you describe the challenges you encounter when conducting Industry Sponsored Research?

We all know that having a reliable study coordinator is crucial in any ISR studies and without one, conducting a trial can be a very time consuming for a Principal Investigator (PI). This goes without saying that a dedicated research team is required to ensure that trials are performed according to the protocol and applicable guidelines.

In addition, neurology-related trials that require intensive imaging or in particular biomarkers might be difficult to be carried out here due to the lack of specialized facilities in our centre. Also, obtaining cerebrospinal fluid may have its challenges by itself because of certain beliefs that exists with regards to lumbar puncture.

What are your major concerns when it comes to conducting a clinical trial?

I feel that it is of utmost importance to ensure that when a study is closed, the subjects continue to receive the same drug that were given to them during the study period. Generally, most pharmaceutical companies anticipate that once the patients start responding to the investigational product (IP), the government will agree to bring in that drug into the country. However, while this may happen in other countries, it is not the case here.

In Malaysia, patients are enrolled into these trials based on a very holistic and genuine need since there are currently no other treatment for certain neurological disorders. If at all we do not ensure the continuity of the IP in our subjects, they would have to return to their previous treatment, which is either ineffective or absent altogether.It is because of cases like these that I work very hard with the hospital's pharmacy and Ministry of Health (MOH) to ensure that these patients continue to receive the IP that has shown promising results in treating their disorder.

When it comes to patient recruitment, what type of approach do you practice when enrolling them into a clinical trial?

An open and honest communication with patients are necessary when explaining the objective, risks and benefits of the trial. In most cases, patients with neurological disorders such as multiple sclerosis are confined to only a few treatment options. Medications that are available are costly while those that have access to these may find them ineffective.Being in a trial provides accessibility to medications they otherwise would not have access to.

"At the end of the day, the benefits accrued to the patients should be the ultimate reason for clinicians to get involved in clinical trials."

– Dr. Shanthi Viswanathan

However, most of my patients have the fear of the unknown since an IP is a new drug that has not been tested, let alone marketed. It is my responsibility to reassure them that their safety is my utmost priority and that I will be with them at every step of the clinical trial process.

That being said, I also believe that patient enrollment is not just about achieving the target number of subjects in a trial but to address the patients' needs and how they can benefit from the IP. It is also helpful to include the patients' families and care givers into the discussion as it may help in ensuring that the patients obtain the necessary support and remain committed throughout the duration of the trial.

How has conducting clinical trials improve the way you manage your patients?

Conducting a clinical trial enhances my clinical acumen and skills over time. Making the right judgement on how best to manage patients who present with side effects from the IP can only come through experience in conducting numerous trials. It can also help one acquire and hone the skills needed to interpret and apply treatment strategies appropriately according to the circumstances that arises.

In your opinion, what are the qualities a PI should possess?

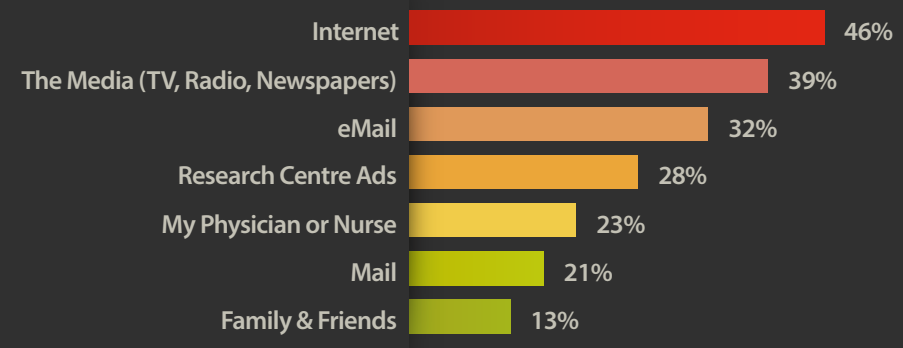
A PI should be vigilant at all time during the course of the trial to ensure that adverse events are identified and resolved early. Equally important is for PIs to have good ethical conduct to ensure that the rights and safety of their subjects are protected and upheld at all times.

What would be your take home message to potential investigators?

Be passionate and remain committed and dedicated to the roles and responsibilities of a PI. At the end of the day, the benefits accrued to the patients should be the ultimate reason for clinicians to get involved in clinical trials.

Patient Recruitment in Clinical Trials

Top Ways that People Find Out About Clinical Trials



Source: CISCRP, 2013; N=5,701 people worldwide

What are the main reasons people participate in clinical trials?

Source: CISCRP, 2013; N=5,701 people worldwide

Platforms used by companies to recruit patients

Facebook	Patient Community	YouTube	Twitter	Mobile Apps	Blog
11	7	7	5	3	1

Source: Tufts CSDD, 2014

90% of trials are extended by at least **6 weeks** due to failure of investigator to enroll patients on schedule. Only one third of the sites engaged in any multicenter study manage to enroll the requisite number.

Source:Tufts CSDD, 2011

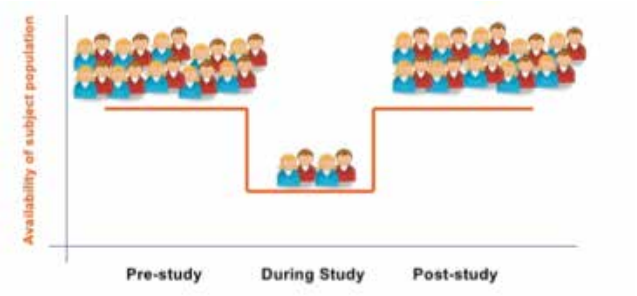
Around the world, between **40%** and **70%** of trials face delays because of a lack of volunteers.

Source: JAMA. 2014;311(10)

Patient Recruitment & Lasagna's Law

Thoma A, Farrokhyar F, McKnight L, Bhandari M. How to optimize patient recruitment. Can J Surg. 2010;53:205–210

One of the most common challenges of randomized controlled trials (RCTs), both published and unpublished, is related to problems with recruitment. Investigators' enthusiasm for ambitious recruitment in a trial often dissipates quickly with the realization that ambitious recruitment is often misguided. This common error has been dubbed "Lasagna's Law"1 and Muench's Third Law.[2] Both laws point to the same principle: investigators greatly overestimate the pool of available patients who meet the inclusion criteria.[3]



The number of patients available to join a trial drops by 90% the day a trial begins. They reappear as soon as the study is over.

Insufficient or untimely patient recruitment into RCTs has serious consequences. The length of the trial may need to be extended, leading to increased resource use and costs. Lengthy trials delay the availability of potentially beneficial treatments to the public.4 The integrity and validity of the study also rely on an adequate sample size. If the sample size is not achieved, there is an increased chance of committing a type II error (e.g., you are more likely to find no difference between treatments when one actually exists). The trial may have to be abandoned, and the results may not be publishable.

The recruitment rate is influenced by both patient and investigator factors. A recent systematic review by Abraham and colleagues5 identified reasons why eligible patients may not want to participate in real or hypothetical surgical RCTs. Surgeons were also asked why they did not want to enroll eligible patients into real or hypothetical surgical trials.

The top reasons for patient nonentry were that:

- The patient had a preference for a certain therapy
- The patient did not understand the trial (trial too complex)
- The patient did not want to be randomly assigned to a treatment
- He or she feared a negative outcome or receiving a treatment that he or she felt was inferior.

Investigators had similar reasons for not entering eligible patients and these include

- Difficulty in following the study protocol (trial too complex) and completing the follow-up requirements
- Preference for a certain therapy
- Difficulties obtaining informed consent from patients.

Thus, investigators planning to conduct clinical research need to consider the issues of patient recruitment ahead of time and plan different strategies to minimize and avoid these potential difficulties at different stages of their study. Understanding and addressing potential patient and investigator concerns are important when developing a recruitment strategy.

> ***Lasagna's Law states that medical investigators overestimate the number of patients available for a research study***

Tips to avoid or minimize recruitment issues at different stages of surgical research studies

Study protocol phase

- Achieve an adequate sample size
- Know the patient population and the likely sources of patients
- Simplify the study protocol

Study conduct phase

- Re-evaluate the inclusion and exclusion criteria if recruitment is low
- Identify sites with consistently low recruitment and address the site-specific problems. Add new investigators and sites if necessary
- Set recruitment quotas and provide incentives to maintain investigator interest
- Spend adequate time with patients and answer any questions they have about the study

Study follow-up period

- Exclude patients who are unlikely to comply with the required follow-up
- Schedule follow-up visits to coincide with routine visits to the office or clinic and facilitate patients' preferences
- Make every effort to locate lost patients

References
1. Lasagna L. Problems in publication of clinical trial methodology. Clin Pharmacol Ther. 1979;25:751–3.
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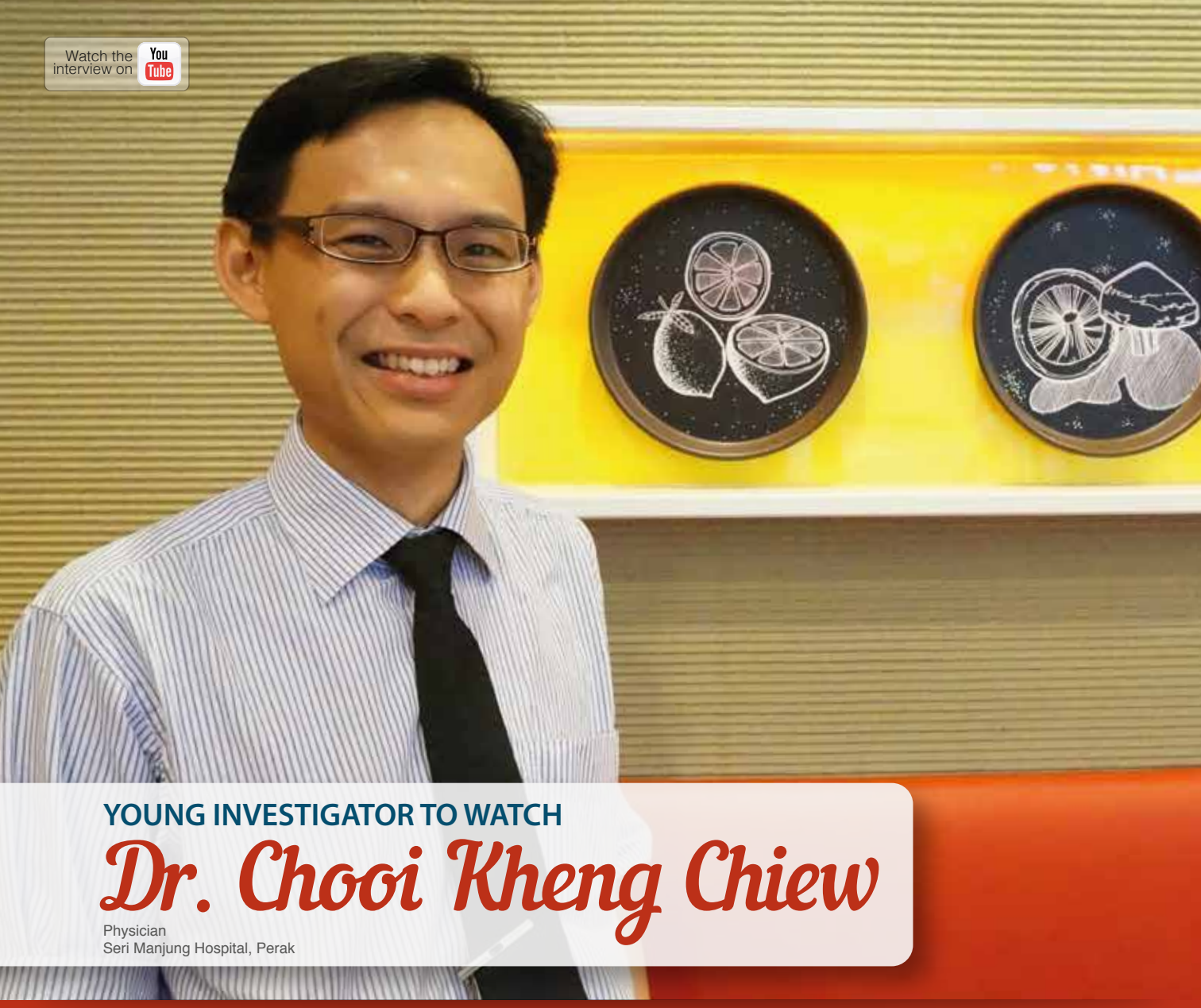
4. Watson JM, Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials. BMC Med Res Methodol. 2006;6:34.
5. Abraham NS, Young JM, Solomon MJ. A systematic review of reasons for nonentry of eligible patients into surgical randomized controlled trials. Surgery. 2006;139:469–83.



YOUNG INVESTIGATOR TO WATCH

Dr. Chooi Kheng Chiew

Physician
Seri Manjung Hospital, Perak

Dr. Chooi Kheng Chiew is a Physician at Seri Manjung Hospital, Perak. He graduated in 2008 from the University of Glasgow, UK with a MBChB before going on to obtain an MRCP (UK) in 2011. Dr. Chooi was instrumental in the setting up of the Clinical Research Centre at Seri Manjung Hospital and has initiated industry sponsored trials at this facility. With just three years in the clinical research field, he has been an investigator and sub-investigator in more than 10 multicenter prospective clinical trials. Dr. Chooi is also an Adjunct Senior Lecturer at the Quest International University Perak and has won numerous awards including the Trades House Medical Prize, Top 10 placing in the Duke Elder Undergraduate Prize in Ophthalmology, Medical Council on Alcohol Prize and the Dr. Saidi Hashim Memorial Gold Medal.

Dr. Chooi is the next generation of Principal Investigator that has his sights set on the clinical research field. Passionate and steadfastly committed to both his clinical practice as well as industry-sponsored trials, Dr. Chooi divides his time between seeing patients and actively conducting clinical trials. Clinical Research Malaysia was fortunate to be able to interview this promising Clinical Investigator who is currently based at Seri Manjung Hospital.

CRC Unit Hospital Seri Manjung

Being one of the few young Principal Investigators in Malaysia who had an early start in the clinical research field, can you briefly tell us when and how did you get involved in clinical trials?

The journey began when I was still a medical student at the University of Glasgow. At that time, the Clinical Trials Unit was looking for healthy volunteers for a drug delivery study, and I decided to participate as a patient volunteer. It was from this initial exposure that I became interested in clinical trials.

Being a district hospital in the state of Perak, how did Seri Manjung Hospital build its reputation among the sponsors and contract research organizations (CROs) as one of the potential sites in conducting clinical trials?

We were earmarked to start a Clinical Research Centre (CRC) at Seri Manjung Hospital back then and being one of the first few clinicians who was involved in the CRC, I had the opportunity to be certified in Good Clinical Practice. We worked towards developing and establishing the necessary infrastructure needed to carry out clinical trials and eventually got the first trial in. Our research team comprising of principal investigators and study coordinators worked very hard in recruiting patients and ensuring that the protocols are strictly followed. We managed to set a good track record in patient recruitment and since then we have been receiving many new trials from sponsors and CROs alike.

Can you briefly describe your experience conducting your first trial? Is there anyone who inspired you or that you look up to?

It was in 2013 that I first got involved as a Sub-Investigator for a phase III trial. It is with every new trial that I undertake that I learn how to conduct them according to the required protocol and to manage adverse events appropriately.

I am grateful to Dr. Lee Li Yuan, whom I respect as my mentor. He has always encouraged and supported me in my clinical research journey. Dr. Lee has also given me the opportunity to be Principal Investigator in various clinical trials, for without which, I would not have gained the experience I have today.

Being in a district hospital setting, do you think that it limits the type and number of trials that you are able to take up?

The unavailability of certain therapeutic area specialists necessary for certain type of studies will definitely limit the type of trials that we can conduct. However, we try to capitalize on our strength by tapping into the patient population in Seri Manjung and the surrounding areas. In fact, there are many trials that match our capability and our population demographics.

How has clinical trials changed your perspective of being a doctor?

By conducting clinical trials, I had the opportunity to do more than to treat my patients based on the current standard of care and treatments available. It opens a whole new world to clinicians and gives patients hope that an investigational product may translate the promise of a more effective medication into reality. Conducting clinical trials certainly makes my job more exciting and makes one believe in the extraordinary possibilities of modern medicine.

Can you tell us how your patients have benefited from a trial?

In one of our diabetes trials, the patients recorded very good improvement in blood sugar control while some have become more compliant to their medications and improved their lifestyle as a result of intensive monitoring. Thus, while the investigational product may not produce the expected therapeutic effect, the patients can still indirectly benefit from a clinical trial by being a participant in it.

Dr. Chooi with Sasikala and Audrey

What are usually your patients' concern when you approach them to participate in a clinical trial?

Most patients have the perception that we are treating them as guinea pigs and thus are reluctant to join. With proper explanation, some will then be open up to the idea and eventually these patients will be thankful for the opportunity to participate in a trial after experiencing the benefits derived from it, whether directly or indirectly.

What have you learnt from conducting trials?

Clinical trials require good time management skills and being very meticulous. It has also exposed me to many other areas above and beyond my normal clinical practice.

What kind of assistance do you feel would be helpful for budding investigators?

Sufficient trained Study Coordinators, assistance with budget negotiation, trainings for clinical investigators as well as sharing of experience from experienced investigators may be helpful for those of us who have just started out in clinical trials.

Do you have any words of encouragement for those keen in taking up clinical trials?

I would say just go for it. One definitely has to learn by doing it. If you ever have the opportunity to be involved in a clinical trial with an experienced investigator, by all means don't give up that opportunity.

ACKNOWLEDGEMENT OF HIGH-ENROLLING SITES

In order for clinical research to be meaningful, researchers need to be able to complete their study within an acceptable time frame. They also need to be able to meet recruitment targets – the number of patients or subjects required to make the study feasible. In this section, Clinical Research Malaysia highlights the high-enrolling sites in Malaysia in 2015 in an effort to encourage research commitment and performance excellence in the clinical research industry. CRM congratulates the investigators and their teams at these sites who have shown immense dedication and an outstanding performance in their respective industry-sponsored studies.

VISION Study

VISION Study is a prospective, multinational, multicenter observational study of patients with Type 2 Diabetes (T2D) receiving insulin injection therapy for the first time. Its objective is to assess the proportion of patients with T2D who, within 18 months of initiating insulin injection therapy, undergo a significant treatment change.

This study, coordinated by PAREXEL, included patients from Algeria, Egypt, Saudi Arabia, United Arab Emirates, Hong Kong, Malaysia, Philippines, Taiwan, and Thailand. The last day of recruitment was on 21st April 2015, and a total of 2477 patients were recruited globally; of which 1172 patients were enrolled from the Asia-Pacific region.

Malaysia successfully enrolled 248 patients to the study, and this surpassed the final recruitment target of 235 patients set by the sponsor. Hospital Seri Manjung and Hospital Sultanah Bahiyah exceeded its recruitment target, thus making up for the shortfall of the other sites that faced certain recruitment challenges. Meanwhile, Hospital Universiti Sains Malaysia achieved its target.

Hospital Seri Manjung (Site 505)

Hospital Seri Manjung has been consistent in their recruitment progress. This site was led by its Principal Investigator (PI), Dr. Lee Li Yuan, and supported by the active participation of Sub-Investigators, Dr. Chooi Kheng Chiew and Dr. Richard Chan Tze Ming, as well as Study Coordinators, Ms Christina Anak Kim Mui and Ms Nooraini bt Hussain.

While the target recruitment number for this site was 115 subjects, Hospital Seri Manjung exceeded its target by 12.2%, recruiting 129 subjects in total (Figure 1). Apart from being the highest enrolling site in Malaysia (contributing 52.2% of Malaysia's recruitment), Hospital Seri Manjung was also the second highest enrolling site in the Asia-Pacific (APAC) region. This made Malaysia the second highest recruiter in APAC after Thailand, outperforming the Philippines, Taiwan and Hong Kong (Figure 2).

Despite having a relatively new study team, the achievement of this site was fueled by the unwavering determination and superb teamwork skills of the study team as well as proper implementation of recruitment strategies prior to site initiation.

Hospital Sultanah Bahiyah (Site 509)

The team at Hospital Sultanah Bahiyah was led by Principal Investigator, Dr. Nor Shaffinaz Yusoff Azmi Merican and supported by Sub-Investigators, Dr. Madihah bt Ahmad, Dr. Noor Shahrazat bt Ahmad@Hamad, Dr. Tan Wei Leong and Dr. Mohd Azri bin Mohd Suan. Study Coordinators, Ms Siti Ertina Asli and Ms Nor Hafiza Johari, have also equally contributed to the success of this site in their attempts to boost study recruitment.

Despite a slow start in recruitment rate, the study team managed to achieve and subsequently exceeded their target.

The VISION Study team at Hospital Seri Manjung

Principal Investigators are real heroes who quietly perform work that benefits our community, our society, our civilization.

These medical heroes often perform their work in anonymity. Their labor is characterized by painstaking determination and re-validation of findings, which grow into incremental accomplishments, which in turn, lead the investigator to a new, fundamental insight or discovery.

We applaud our heroes, our Principal Investigators. Their qualities of professionalism, commitment and focus are an inspiration to all.

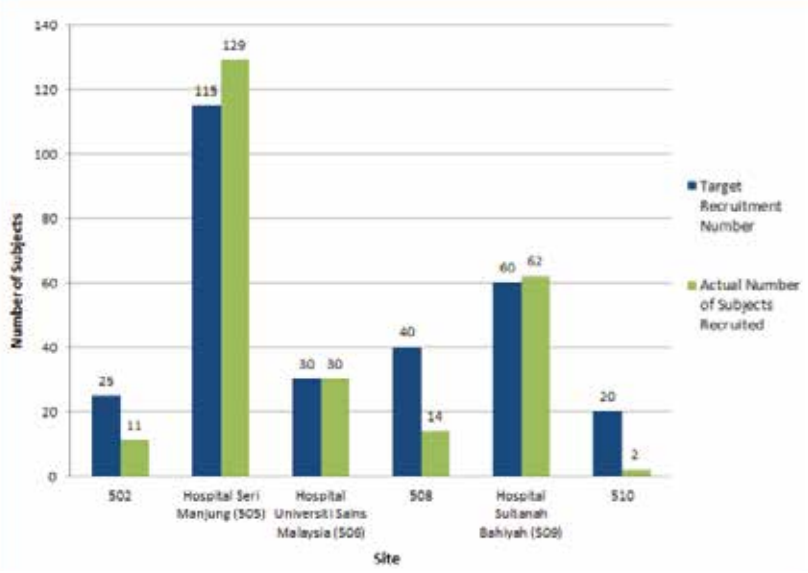


Figure 1. VISION Study: Target recruitment number and actual number of subjects recruited at various sites in Malaysia

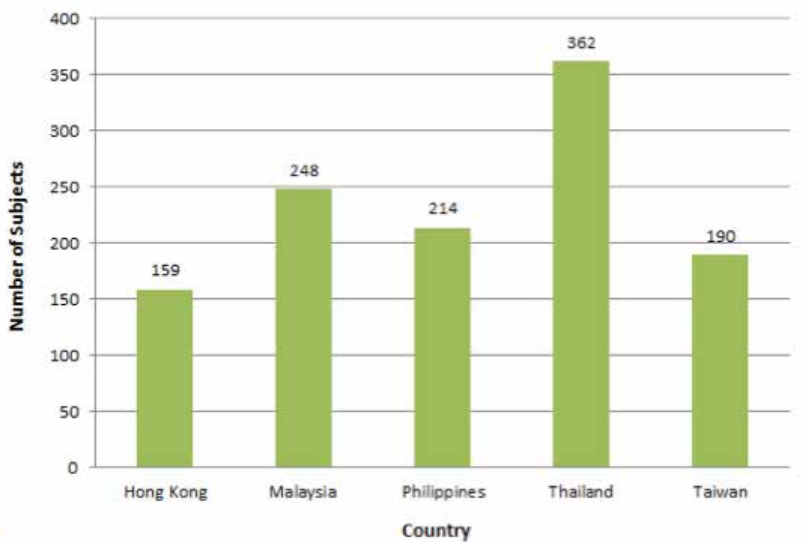


Figure 2. VISION Study: Total number of subjects in the Asia-Pacific region

"Our achievement was due to the large pool of diabetic patients at Hospital Seri Manjung and a dedicated team of diabetic nurses who played the role of study coordinators. As with every trial, we conduct them to the best of our ability, and work consistently in building a good rapport amongst our patients who went on to give their consent to participate in this study. It requires hard work when dealing with the large number of patients but we managed to press ahead. Our goal has always been to enable Malaysia to achieve the country's recruitment target. We want Malaysia to be competitive globally and to attract more clinical trials to Malaysia."

Dr. Lee Li Yuan
Highest recruiting PI in Malaysia for the VISION Study

Other Studies:

Multiple dose trial examining dose range, escalation and efficacy of oral Semaglutide in subjects with type 2 diabetes

Hospital Seri Manjung was the highest recruiter in Malaysia followed by Hospital Raja Perempuan Zainab II and Hospital Island Penang with a total of 13, 10 and 7 subjects respectively. The study team at Hospital Seri Manjung was led by Dr. Chooi Kheng Chiew (PI) and supported by Dr. Lee Li Yuan and Dr. Chang Meng Lee as Sub Investigators.

A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Assess Cardiovascular Outcomes Following Treatment with MK-3102 in Subjects with Type 2 Diabetes Mellitus

As of September 2014, Malaysia was one of the top 12 recruiters, and its recruitment numbers was contributed by the study team under Dr. Lee Li Yuan (PI) from Hospital Seri Manjung.

A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa) in the Treatment of Bone Disease in Subjects with Newly Diagnosed Multiple Myeloma

As of 15th January 2015, a total of 1118 subjects were enrolled globally. This translates into 74% of the total enrolment goal of 1520 subjects. The top enrolling sites in Asia are South Korea (28 subjects), Malaysia (10 subjects), Singapore (8 subjects), Taiwan (6 subjects) and Hong Kong (3 subjects).

Both Hospital Pulau Pinang and Hospital Umum Sarawak (HUS) which participated in this study enrolled 5 subjects each. Dr. Goh Ai Sim (PI) led the Hospital Pulau Pinang Study team and was supported by Sub Investigators Dr Teoh Ching Soon, Dr. Chiang Su Kien, Dr. Chew Teng Keat and Dr. Norasmidar Abdul Aziz. Meanwhile, Dr. Chew Lee Ping (PI) from HUS led his study team which consisted of Sub Investigator Dr. Cheong Yaw Kiet and Study Coordinators Ms Tan Hoon Yian, Mr. Tan Sia Hong and Mr. Ko Ching Tiong.

am in Asia Pacific

Alan Ong, Executive Vice President for the Asia/Pacific region at INC Research, outlines the key challenges and opportunities that CROs face in the Malaysian clinical trial segment and describes the role of INC in raising the country's profile as a destination for research.

am INC Research

Extending our success story into Malaysia

INC has grown significantly in the Asia/Pacific region in recent years, and we're looking forward to extending our success story into Malaysia. With Singapore as the Asian headquarters for the region, focusing on nearby Malaysia represents a natural extension of our development.

A country with great sites

Malaysia already has a strong clinical trials infrastructure, and our mission at INC is to promote sites like the University Malaya Medical Center, which has long been considered a great institution. It has good research centers with experienced and well-trained investigators with a good command of the English language. These factors allow clinical trials to be executed to global standards.

A supportive government

The Malaysian government is supportive of clinical trials and its objective is to reach 1,000 trials by 2020. Currently Malaysia hosts approximately 200 trials, so the goal is for a five-fold increase in the number of trials in the next five years.

> " Malaysia has one of the fastest timelines for trials"

Fast timelines

With such great institutions in Malaysia, it is an ideal location for conducting clinical trials in all phases. We aim to conduct more trials, particularly in Phase II, III and IV, using the regional infrastructure that we have developed.
The advantages of conducting clinical trials in Malaysia, besides government encouragement, are the short timelines. Malaysia has one of the fastest timelines for trials and has strong institutions across a broad spectrum of disease areas.

Leveraging strong site relationships

As well as the expertise and relationships within the institutions that can deliver trials, we also have strong site relationships. We know that when a country is selected for clinical research, it is important to consider the key opinion leaders present in the area. Building and maintaining relationships with them is critical.

> " Encouraging more CRO and clinical development activity"

An important role to play in new drug development

The correlation between CRO activities and innovation in healthcare is very strong, as CROs provide a more productive and efficient way to conduct clinical trials thereby freeing up companies to focus more on innovation. Encouraging more CRO and clinical development activity will give Malaysia the potential to become an important incubator for new drug development.

Collaborating with local institutions

Finally, we will focus on more collaboration with local institutions in Malaysia. One of the key focus areas for INC Research is to develop relationships with hospitals and clinics to get them involved in pursuing clinical trials. We already have a solid base in Malaysia and will take an active role in continuing its development. We are optimistic about seeing the country succeed in its clinical trials initiative with INC Research as a leading protagonist.

inc Research®

i am everywhere

I've always liked being around people, but it was surprising how important that was when I started managing global clinical trials. Developing strong connections with people across the world allows me to influence events for the better. And that makes it easier to pull everything together and deliver, whether the study's in Montreal or Marrakech.

i am INC Research

To see how our global Phase I-IV experience can help you feel more connected, visitincresearch.com

inc Research®

CHICKEN SOUP FOR THE BUSY COORDINATOR

By: Ms. Xu Xiao Ying, Research Nurse Manager, Johns Hopkins Singapore, Edited By: NHG-RDO
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Managing Communication With Oncology Patients and Their Family Members for Research Participation

In Oncology research, there may be occasions of conflicting interests where the doctor needs to inform the patient of his/her cancer diagnosis to enroll the patient into a research study, but the patient's family members wish to conceal the diagnosis from the patient. This commonly happens for elderly oncology patients, and here we share a research nurse's account of managing such a situation.

Scenario
Mr Tan, a mentally alert 70-year-old gentleman with no significant medical history, was diagnosed with lung cancer. His children met with the oncologist Dr Zoe to discuss treatment options while Mr Tan waited outside the meeting room. During the meeting, Dr Zoe explained Mr Tan's diagnosis and presented the viable treatment options for Mr Tan, which included participating in a clinical trial to gain access to new treatment options. While Mr Tan's children were keen for him to participate in the trial, they asked Dr Zoe if the cancer diagnosis could be kept from their father, as they were concerned that Mr Tan might not be able to accept the terrible news.

What did Dr Zoe do?
Dr Zoe assured the family members that it would be normal also for Mr. Tan to experience emotions of shock, disbelief, fear, anxiousness, guilt, sadness, grief, depression or anger upon receiving the news. She shared that there were psychological support services available for the patient and their caregivers to help cope with the disease. As a doctor, she was also ethically obliged to provide Mr Tan with accurate information on his condition. In relation to participation in the clinical trial, she would also need to explain relevant information on the research study to Mr Tan and obtain informed consent from him for participation. After some deliberation, the children agreed for Dr Zoe to break the news to Mr Tan himself.

This was done in the presence of his children, and to everyone's surprise Mr Tan took the news calmly and requested to find out from Dr Zoe on the available treatment options for his diagnosis. He subsequently agreed to participate in the clinical trial.

Best practices/ Lessons Learnt
It is important to communicate with elderly patients on their condition and involve them in managing their disease. Where they are mentally competent and can decide on research participation, informed consent should be sought from these elderly patients in person.

When taking consent from an elderly patient, be mindful of the following:

- Be patient and take time to explain the informed consent form.
- Speak in an language understandable by the subject (e.g. local language or dialect).
- Speak clearly and slowly, and use short sentences.
- Avoid using medical terms and technical jargon.
- Pause in between explanations and check the patient's understanding on what has been communicated (e.g. "Mr Tan, do you understand what does 'Blood samples will be taken from you at different time points through out the study' mean?").
- Involve a family member for physical and psychological support.
- Encourage the patient to ask questions and address each question to the patient's satisfaction.
- Give the patient sufficient time to decide on participation in the research study.

Resources:
NHG Investigator's Manual (2nd edition), Chapter 6.0 Research in Vulnerable Populations and chapter 8.3 Responsibilities of the Principal Investigator

***Disclaimer:** All characters appearing in this article are fictitious. Any resemblance to real persons is purely coincidental.*

Principal Investigator's ROLES AND RESPONSIBILITIES

1 Provide Evidence of Qualifications, Training and Experience

- Update CV regularly and provide to Sponsor and IRB/IEC
- Ensure that GCP Training is completed
- Be thoroughly familiar with the use of Investigational Product (IP) as described in the Protocol, current Investigator's Brochure (IB), in the product information and other sources provided by the Sponsor

2 Ensure all Necessary Agreements /Forms are In Place

- Sign Confidential Disclosure Agreement (CDA) forms when required
- Disclose all relevant Conflicts of Interest
- Sign Investigator's Agreement / Protocol Signature Page
- Sign Clinical Trial Agreement (CTA)

3 Determine Adequate Resources are Available to Conduct the Study

- Determine the number of patients seen by the study team who could fit the study criteria before setting a target enrolment number
- Ensure adequate number of qualified staff and adequate facilities are available to conduct study properly and safely
- Ensure that all study team members are adequately informed about the protocol, IP and their study related duties and functions
- Set aside sufficient time to conduct, supervise and complete the study

4 Manage the Medical Care of Trial Subjects

- Provide adequate medical care to trial subjects for any adverse events that occur during or following the subject's participation in the trial
- Evaluate Adverse Events and Provide Severity and Causality Assessment
- Investigator should make a reasonable effort to ascertain the reason(s) of subject withdrawing prematurely from the trial while fully respecting the subject's rights

5 Communicate with IRB/IEC

(a) Obtain Approval to Conduct Study
- Provide all trial related documents (e.g. Protocol, IB and ICF) to the IRB/IEC for review and approval
- Submit updated trial documents (e.g. updated IB and clinical trial insurance) to IRB/IEC

(b) Progress Reports
- Submit interim reports (summary of the trial status) to IRB/IEC annually or more frequently, if requested by IRB/IEC
- Provide written reports to Sponsor and IRB/IEC on any changes significantly affecting the conduct of the trial or increasing the risk to subjects
- Promptly report any deviations from or changes of the protocol to eliminate immediate hazards to the trial subjects

(c) Safety Reporting
- Report SAEs /SUSARs to the IRB/IEC
- Supply IRB/IEC with any additional information (e.g. autopsy report) for reported deaths

(d) Premature Termination /Suspension of Trial
- Promptly inform/notify IRB/IEC with a detailed written explanation of the termination or suspension of a trial

(e) Final Report
- Provide IRB/IEC a summary of the trial's outcome and submit any reports required

6 Assure Protocol Compliance throughout Study

- Check that participants meet all Inclusion / Exclusion criteria before enrolling into study
- Supervise to make sure procedures, evaluations and follow-up visits required of the protocol are closely followed by study team
- Document and explain any deviations from the approved protocol
- Any changes of the protocol should not be implemented without agreement by the Sponsor and prior review and documented approval from IRB/IEC

7 Ensure Investigational Product is properly administered and stored

- Store IP as specified by Sponsor (refer to Product Insert/IB/Protocol)
- Ensure IP is used only in accordance with the approved protocol
- Explain the correct use of IP to each subject and ensure that each subject follows the instructions
- Properly account for the receipt and dispensing of the IP (maintain records of IP receipt, inventory at site, use of IP by each trial subject and return of IP to Sponsor/alternative disposition of unused IP)

8 Direct all Relevant Site Operations

- Regularly communicate with study team members, Sponsor and trial subjects
- Ensure study team members are familiar with the protocol and IP
- Maintain a list of study team members and their responsibilities

9 Assure that the Rights and Welfare of Research Participants are Protected

- Obtain Informed Consent from participants before starting any study procedures
- Ensure that the subject receive a copy of the signed and dated Informed Consent Form (ICF) and copy of any amendments to the ICF
- Ensure participants have sufficient time to ask questions and decide whether or not to participate in the study
- Any new information about the study or IP that may affect the subject's decision to remain in the study should be communicated to the subject and this communication should be documented
- Ensure timeliness of safety reporting to Sponsor and IRB/IEC

10 Provide Proper Documentation of Study Related Procedures and Events

- Document in the medical case notes that informed consent has been obtained from the subject
- Document all adverse events, their causality, severity, treatment, outcomes, and start and end dates in the medical case notes and case report forms
- Ensure that source documents are available to support information recorded in data collection form or case report form. Any discrepancies should be explained
- Maintain the trial related documents and take measures to prevent accidental or premature destruction of these documents.
- Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the IP
- All requested trial related records should be made available for direct access for Monitor, Auditor, IRB/IEC or Regulatory Authority

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: 5-7 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.

Drug lag and approval time metrics - are they good markers to assess the global regulatory environment?



Magda Bujar • Prisha Patel • Neil McAuslane
Centre for Innovation in Regulatory Science – CIRS, London UK

Introduction

- The Emerging Markets (EMs) of Asia-Pacific, the Middle East, Africa and Latin America are increasingly being incorporated into global development plans for registration of medicines in order to make them available to patients worldwide in a timely manner.
- The time needed to bring a New Active Substance (NAS) to market can be influenced by the submission gap (between first market approval and submission at the particular authority) and the agency approval process.
- Since 2004, CIRS has been carrying out an Emerging Markets benchmarking study to identify patterns in agency and company timelines that reflect activities that influence time to market. CIRS also carries out an annual Mature Market (MM) agency benchmarking study to monitor regulatory performance in Europe, USA, Japan, Canada, Australia and Switzerland.
- The results from the Emerging Markets and the Mature Markets CIRS studies were used to evaluate how the drug lag and approval time metrics can be used to assess the global regulatory environment.

Objectives

- Evaluate time to submission and approval of new active substances (NASs) in 2009-2013 in EM and MM countries
- Identify the influences on the time taken for new medicines to be licensed across multiple jurisdictions
- Discuss the usage of drug lag and approval time metrics as markers for assessing the global regulatory environment

Methodology

- Data were analysed for submission and/or approval period 2009-2013
- 105 NAS approvals in 16 EM countries were collected from 12 pharmaceutical companies and assessed including time from first world submission to submission to EM and the timing of the CPP
- 371 NAS approvals in 6 MM countries were collected from the public domain and agencies, and analysed for approval time and submission time
- 15 NASs were identified that were approved by at least three MM and three BRICK-TM countries; these were analysed in more detail

Figure 1: Participating EM and MM agencies

Included Emerging Market countries :
Latin America: Argentina, Brazil, Colombia, Mexico
Europe, Middle East and Africa: Egypt, Saudi Arabia, South Africa, Russia, Turkey
Asia Pacific: India, China, Indonesia, Malaysia, Singapore, South Korea, Taiwan

Included Mature Market countries
Europe* (European Union and Economic Area countries), USA, Japan, Canada, Switzerland, Australia

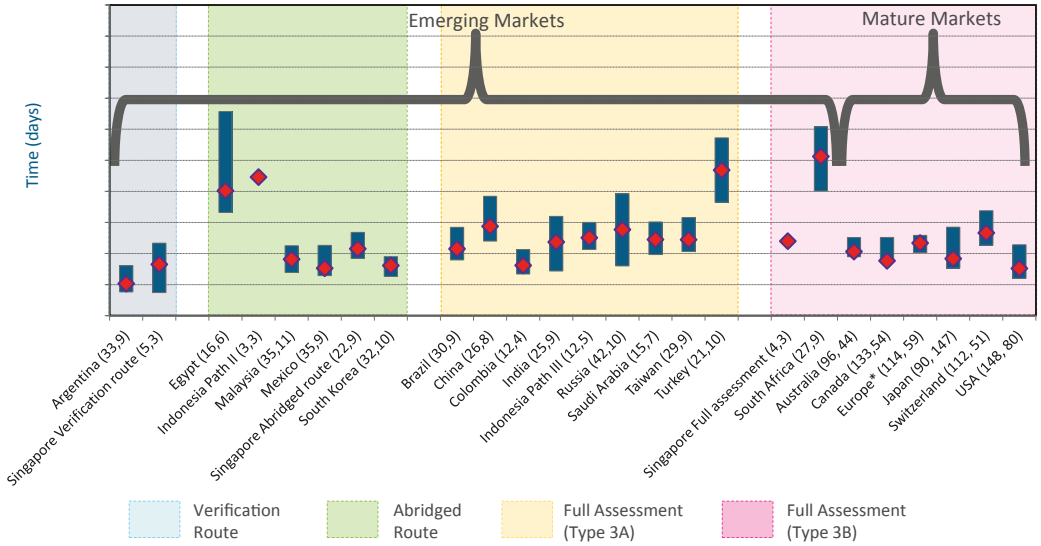
*Data for Europe refers to the EMA Centralised procedure; the approval time also includes the European Commission time

Definitions

- BRICK TM: grouping acronym that refers to Brazil, Russia, India, China, South Korea, Turkey, Mexico.
- CPP: Certificate of Pharmaceutical Product is issued in the format recommended by the World Health Organization (WHO), which establishes the status of the pharmaceutical product and of the applicant for this certificate in the exporting country
- Drug Lag (Submission Gap): Date of submission to the first regulatory agency to the date of regulatory submission to the target agency
- New active substance (NAS): A chemical, biological, biotechnology or radiopharmaceutical substance that has not been previously available for therapeutic use in humans and is destined to be made available as a 'prescription only medicine', to be used for the cure, alleviation, treatment, prevention or in vivo diagnosis of diseases in humans
- Verification Route: Recognition of an authorisation by a 'reference' or 'benchmark agency'; verification process to validate the status of the product and ensure that the product for local marketing conforms to the authorised product
- Abridged Route: Pre-requisite that the product has been registered by a 'reference' agency; abridged assessment carried out in relation to the use of the product under local conditions
- Full Assessment: Agency capable of doing a full assessment of quality, pre-clinical (safety) and clinical (efficacy) data. Information on prior registration may still be a pre-requisite to final authorisation (Model 3A) or the review is 'self standing' (Model 3B)

Figure 2: Regulatory approval times for NASs approved in Mature and Emerging Markets in 2009-2013- by *type of Scientific Assessment Model*

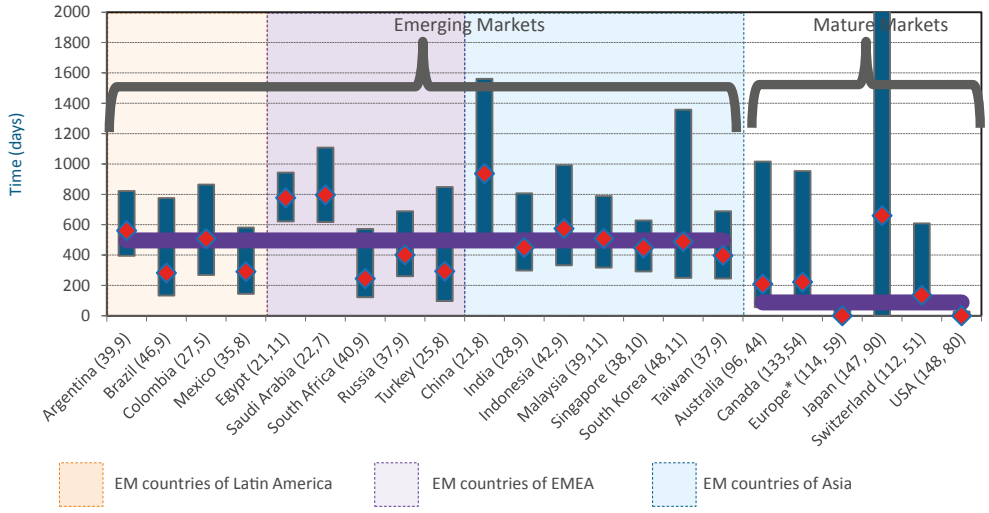
n1) = number of drug applications, (n2) = number of companies. Box: 25th and 75th percentiles. Diamond = median.
*Data for Europe refers to the EMA Centralised procedure; the approval time also includes the European Commission time



- For 2009-2013, the overall median approval time by Scientific Assessment Model was 209 days for Verification Route, 381 days for Abridged Route, 530 days for Full Assessment (Type 3A) and 413 days for Full Assessment (Type 3B) across all EM and MM countries.
- An evaluation by country showed that regulatory approval times could vary by the type of review route within and across regions, e.g. approval time for Argentina using a verification approval route was 2.1x faster than Brazil which does a full review, but both require a CPP.
- For 2009-2013, overall median approval time for all EM countries studied was 456 days (329 days for Latin America, 440 days for Asia Pacific and 740 days for Europe, Middle East and Africa (EMEA)).
- The overall median approval time for all MM countries studied was 406 days (304 for US, 353 for Canada, 367 for Japan, 412 for Australia, 468 for Europe*, 533 for Switzerland)

Figure 3: Time between the first world submission and submission to regulatory authority (submission gap) in the EM or MM for NASs in 2009-2013

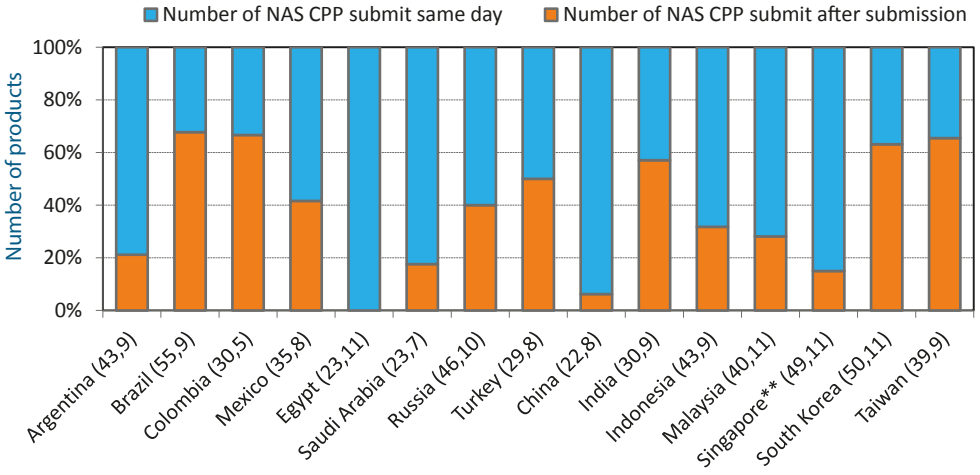
(n1) = number of drug applications, (n2) = number of companies. Box: 25th and 75th percentiles. Diamond = median. Purple line = overall medians
*Data for Europe refers to the EMA Centralised procedure



- Overall median drug lag between first country and EM country was 496 days; 462 for Latin America, 493 for Asia, 555 for EMEA.
- Overall median drug lag between first MM country and a specific MM country was 88 days; 0 for EU, 0 for US, 135 for Switzerland, 209 for Australia, 222 for Canada, 660 for Japan.

Figure 4: Number of products and timing of CPP submission for NASs approved in Emerging Markets (2009-2013)

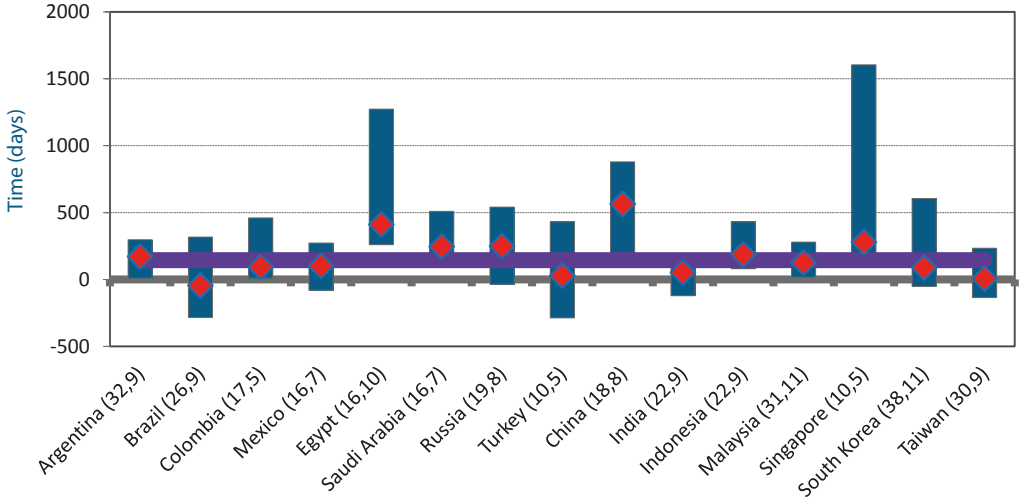
(n1) = number of drug applications, (n2) = number of companies
**Data for Verification and Abridged Routes



- A major factor in estimating the time taken to make new medicines available is the requirement for submission of the CPP
- Of the EM countries in the study, only South Africa (not shown) and Singapore can approve NAS applications without a CPP
- Some agencies now allow flexibility around CPP submission, where the NAS application is accepted without a CPP (but required before granting approval); such countries include Brazil, Colombia Mexico, Indonesia and Turkey
- Additionally, companies are also sometimes able to negotiate with the authorities more flexibility around CPP submission; countries that allow such negotiations include Saudi Arabia, India, Malaysia, South Korea and Taiwan

Figure 5: Time between the authorisation in the CPP issuing country and submission in the importing country for NASs submitted 2009-2013

(n1) = number of drug applications, (n2) = number of companies. Box: 25th and 75th percentiles. Diamond = median. Purple line = overall median



- The NAS application submission is dependant on CPP submission timing.
- Overall median time between approval in CPP issuing country and submission to the country was 144 days; Brazil had the lowest median (-45.5 days) indicating that many companies submit to Brazil prior to receiving approval in the CPP issuing country
- However, other factors may also have an impact on the NAS submission timing, such as company strategy, local requirements (e.g. clinical trials) as well as CPP source.
- Having the CPP issuing country the same as the first world approval country lead to earlier availability of NASs in 9 of the of EM countries (Argentina, Brazil, Mexico, China, India, Indonesia, Malaysia, South Korea, Taiwan)

Figure 7: Approval timing for 15 NASs approved in the MM and BRICK-TM jurisdictions in 2009-2013

(n1) = number of drug applications, (n2) = number of companies. Box: 25th and 75th percentiles. Diamond = median.

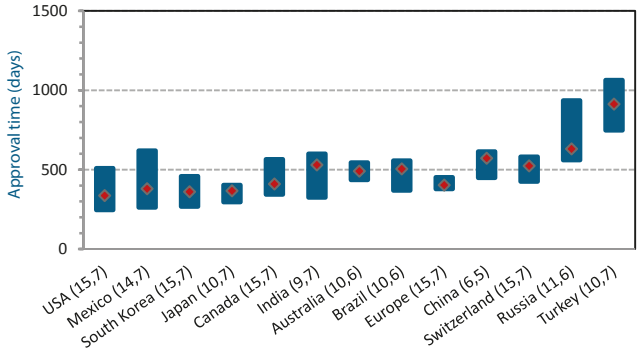
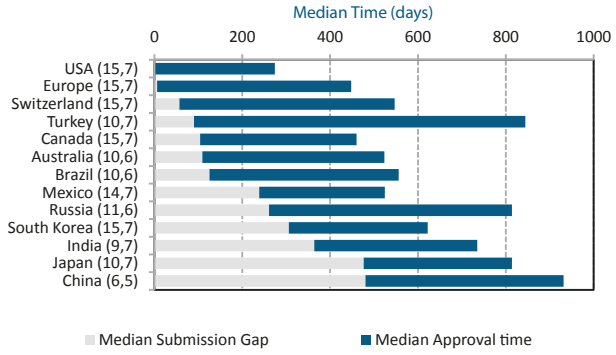


Figure 8: Drug lag and approval time for 15 NASs approved in MM and BRICK-TM jurisdictions in 2009-2013

(n1) = number of drug applications, (n2) = number of companies. Box: 25th and 75th percentiles.



- For a cohort of 15 NASs that were approved by 6 MM countries and BRICK-TM countries in 2009-2013, approval timing (Fig, 7) and submission timing (Fig. 8) differed across the jurisdictions
- For the 15 NASs, although companies submitted to USA and Europe first, some EM countries received a submission before first world approval. This indicates that local requirements within those EM agencies allow early submission and/or that companies are now including these countries in their global development strategies.

Conclusion

- Surrogate markers, such as approval time and drug lag, can be used to assess the regulatory environment across a number of countries, but a clear understanding of the markers' influencers, which often stem from the differences between country processes, is needed. Indeed, EM agencies apply different review routes based on the type of product and supporting data, which may influence approval time.
- Regulatory approval was in general faster for MM than EM, likely due to a larger agency size and availability of resources. Nevertheless, time to license is not only dependent on agency time, but it is a complex mix of other factors such as company strategy and local requirements in EM countries.
- In terms of company strategy, although companies submit first in EU and US which carry out a full review, they also submit to some EM countries before first world approval (Turkey and Brazil). This is partly due to the fact that these EM jurisdictions do not require a CPP at time of submission.
- Measuring drug lag and approval times to EM and MM countries enables company-agency and cross-agency discussions to identify possible enablers of improving the regulatory environment e.g. changing CPP timing and requirements, and utilisation of risk stratification models of review. Such changes would have an impact on company global submission strategies and therefore licensing time of medicines worldwide.

Figure 7: Time to license a new medicine is a complex mix of various factors that influence the regulatory approval time and the drug lag

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Center For Innovation in Regulatory Science

Mission
To maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and HTA policies and processes in developing and facilitating access to medicinal products

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Disclosure
Author(s) of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Magda Bujar: nothing to disclose; Prisha Patel: nothing to disclose; Neil McAuslane nothing to disclose

Presented on 14-18 June 2015 at the 2015 Annual DIA, Washington. Poster will be available for download at http://www.cirsci.org/content/posters

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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 relevant to all stakeholders.

If you are seeking a means to reach out to the clinical research "ecosystem" in Malaysia, then talk to us about advertising your message in the CRM Bulletin.

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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

Top 5 Trends in the Pharmaceutical Industry in 2015

If the surge in TV commercials for prescription drugs is an indicator of the economic health of drug companies, then the pharmaceutical industry is indeed going strong. The industry's advertising spending rose from $3.5 billion in 2012 to $4.5 billion in 2014[1].

Such growth is likely to continue judging by a report from the IMS Institute for Healthcare Informatics, which forecasted a 30 percent increase in global medicine spending by 2018. It also cited the anticipated launch of 200 new revenue-boosting drugs within the next five years[2].

Amid this unprecedented growth, what are some of the things that consumers, patients, and health-care providers can look forward to? Lane Hirning, MasterControl's product management director, discussed five trends that are likely to affect the industry in the near term.

Hirning, a pharmacologist with extensive IT experience in the pharmaceutical industry, is also a technical product manager at MasterControl. He specializes in product development for the pharmaceutical, blood, and biologics industries, especially large-tier companies[3].

Five Trends in Pharma

#1 The Outbreak of Measles and Ebola Highlights the Importance of Vaccines.

The outbreak of measles and Ebola in 2014 highlighted the importance of vaccines and the role of the pharmaceutical industry in developing them. "Geographical boundaries no longer exist. We have no time to react anymore," said Hirning. "Measles is a good example of that."

From Jan. 1 to April 3, 2015, the U.S. Center for Disease Control and Prevention (CDC) reported 159 cases of measles in 18 states and the District of Columbia, part of an outbreak that originated in Disneyland4. Canada reported 21 cases, stemming from families who visited the theme park5. The majority of people who got measles were unvaccinated, according to the CDC.

"Measles is one of those diseases that's almost gone, thanks to effective vaccine," said Hirning. "Unfortunately, there are some people who are resisting vaccination." Measles was "eliminated" in the United States in 2000, which means the disease was absent for 12 months or more in a specific geographic area, according to the CDC. When travelers to the U.S. bring the "eliminated" disease, it typically affects few people. The latest outbreak is the largest in the country since 2000[6].

Hirning said there's a need to re-educate parents about the importance of vaccination and to counter the misinformation that autism is caused by vaccines. "I don't want to question parents' decisions, but they need to get all the data. Those who are afraid of vaccines might not have the right information," he said.

Hirning was referring to a retracted 1998 study in the U.K. by Andrew Wakefield, which falsely linked autism to vaccines. The British Medical Journal (BMJ) concluded that Wakefield deliberately altered the medical histories used in the study as part of an elaborate fraud. Wakefield, who was paid by a law firm that intended to sue vaccine makers, has been stripped of his medical license7.

Unlike measles, there is no vaccine for Ebola at present—39 years after the disease was discovered in Africa. The World Health Organization said more than 25,000 people have contracted the disease and 10, 584 have died from the recent outbreak, mostly in Guinea, Sierra Leone, and Liberia8. Dr. Margaret Chan of WHO called it the most severe public health emergency in modern times. She blames the industry's "greed" for the lack of vaccine, saying "A profit-driven industry does not invest in products for markets that cannot pay."[9]

Hirning conceded there is some truth to Chan's opinion. "Developing a product is expensive. Pharmaceutical companies need to do a balancing act between addressing a public need and running a business, which is hard to do," he said.

#2 The Prices of Generics Continue to Rise.

Generics are supposed to be cheaper than brand-name drugs because they are produced after the brand drug's patent has expired. But a report by Elsevier showed that out of a sample of 4,421 drug groups, 222 of those groups increased in price by 100 percent or more between November 2013 and November 2014. Seventeen drug groups increased by 1,000 percent or more.[10]

The price hike is partly due to mergers of manufacturers, resulting in fewer players in the market. The FDA has also become stricter in regulating generic manufacturers. Both factors have contributed to drug shortages, which when combined with increased demand, led to price increases.

Hirning pointed out a third reason. "Generic prices are going up because of more complex medicines, which are more expensive. Biologics are extremely difficult to make," he said. Within this context, expect the prices of generic drugs to continue to go up.

#3 Pharmaceutical Apps are Becoming More Popular.

Today pharmaceutical mobile apps range from aggregating top cancer news to glucose monitoring and identifying high-risk heart patients. "I'm for apps that give people more information than what they would find in an insert to a medication package," said Hirning.

He thinks apps can be very helpful for consumers doing comparison shopping of prescription-drug prices and getting the latest information and research pertaining to diseases. However, he added, "The purveyors should be responsible in providing science-based information and be accountable for that information."

Given the current popularity of apps in general, their use in the pharma field is bound to grow. Some potential uses include patient information collection and doctors' management of information for the purpose of prescribing drugs.

Hirning said apps can potentially be helpful in conducting clinical trials, particularly in patient recruitment. At the same time, he cautioned about the possibility that apps could lead to a biased study. "You will probably recruit patients out in the field faster, but you might be limiting yourself only to patients who have access to the apps or the specific devices, which could create a bias," he said.

The FDA has clarified its oversight of apps for medical devices in separate guidances, but it hasn't expressed its opinion on the use of pharma apps. Expect any FDA opinion or guidance on pharma apps to also impact the growth of usage.

#4 Drug Development Costs Continue to Rise.

The costs of developing a new medicine and getting it approved continue to go up. The Tufts Center for the Study of Drug Development estimated the cost at about $2.6 billion in 2014, up by more than three times from $802 million in 2001.[11]

"Production costs are rising because companies have more hurdles to pass during the testing phase. The FDA has raised the bar in terms of safety, requiring a larger sample population," said Hirning.

He cited the anti-nausea drug Zofran (ondansetron), which can lead to an abnormal and potentially fatal heart rhythm among patients with underlying heart conditions and those who are predisposed to low levels of potassium and magnesium in the blood. As a result, the FDA put the drug under ongoing review and the manufacturer, GlaxoSmithKline, was asked to conduct a thorough
study.[12]

Hirning said to cope with the inevitable increase in drug development costs, manufacturers should try to increase efficiencies and optimize productivity on a daily basis. For example, companies can stretch their limited resources by automating labor-intensive tasks related to document, training, and supplier management.

He said an electronic, centralized quality system will provide companies with compliance tools necessary to mitigate and avoid expensive regulatory actions (Form 483s, warning letters, and recalls).[13]

#5 U.S. Initiative Gives Precision Medicine a Boost.

The movement toward development of precision medicine or personalized medicine got a boost from President Obama's The Precision Medicine Initiative introduced in January 2015. Launched with a $215 million budget, the initiative is meant to pioneer a new model for patient-driven research to provide clinicians with new tools and therapies.[14]

Precision medicine refers to the customization of treatments for individual patients based on genetic and other information. It's here already, according to Hirning, referring to advancements in genetic testing. For example, most pregnant women undergo prenatal genetic screening to see if their fetuses suffer from chromosomal abnormality that causes diseases like cystic fibrosis and Down syndrome.

Pharmacogenomic testing is also increasingly used to avoid side effects or to improve treatment of diseases such as cancer and leukemia. Pharmacogenomics refers to how certain genes affect a person's reaction to medications. For example, some breast cancer drugs work only in women with specific genetic variations.

The FDA has been working on targeted drug therapies since the 1990s. It has approved 30 such therapies, including Kalydeco (ivacaftor) for cystic fibrosis. Last year alone, eight out of the 41 novel drugs approved by the agency were targeted.[15]

Hirning thinks precision medicine will help drug companies pick the right people and the right clinicians for specific clinical trials, which should lead to more effective trials. "Genetic testing can help clinical trials achieve better outcomes," he said. However, he cautioned about companies capitalizing on people's fears to market genetic screening and testing products and services.

There are also concerns about misuse of genetic information that could lead to insurance discrimination and social stigma. Nevertheless, the march toward precision medicine is slowly but surely advancing.

Conclusion

These are but a few of current trends that reflect the big picture. All of them show the impact of technology on medicine and the health-care process. Awareness and understanding of these trends will help put your organizational and business goals firmly within the context of the industry's direction and hopefully guide your future decisions.

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[2] From a press release issued by the IMS Institute for Healthcare Informatics on Nov. 20, 2014, http://www.imshealth.com/portal/site/imshealth/menuitem.c76283e8bf81e98f53c753c71ad8c22a/?vgnextoid=8269f454d4ac9410VgnVCM10000076192ca2RCRD&vgnextchannel=5ec1e590cb4dc310VgnVCM100000a48d2ca2RCRD&vgnextfmt=default

[3] Lane Hirning began his career as a research scientist at NPS Pharmaceuticals Inc. for seven years. He then went on to serve various roles as an IT executive for 12 years. He joined MasterControl in 2006.

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[11] Tufts Press Release, Nov. 18, 2014, http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study

[12] From the FDA website, viewed on April 21, 2015, http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm272041.htm

[13] To learn more about automating quality processes go to: http://www.mastercontrol.com/solutions/all_access.html

[14] Fact sheet issued by the White House, Jan. 30, 2015, https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

[15] From the FDA's blog, FDAVoice, March 23, 2015, http://blogs.fda.gov/fdavoice/index.php/tag/precision-medicine-initiative/

About MasterControl Inc.

MasterControl produces software solutions that enable regulated companies to get their products to market faster, while reducing overall costs and increasing internal efficiency. MasterControl securely manages a company's critical information throughout the entire product lifecycle. Our software is known for being easy to implement, easy to validate, and easy to use. MasterControl solutions include quality management, document management, product lifecycle management, audit management, training management, document control, bill of materials, supplier management, submissions management, and more. Supported by a comprehensive array of services based on industry best practices, MasterControl provides our customers with a complete information management solution across the enterprise. For more information about MasterControl, visit www.mastercontrol.com or call 1.800.825.9117 (U.S.); +44 (0) 1256 325 949 (Europe); or +81 (03) 5422 6665 (Japan).

Analyzing the Relative Recruitment Performance between Highly-Utilized and Low-Utilized Sites in 5 Therapeutic Areas in 4 Asian Countries

HyunJoo Rhee; Wendy Bilham; HyunSuk Hong; NaYoung Kim

Objective

The objective of this study is to assess the site performance in 5 major Therapeutic Areas (Cardiovascular, Endocrinology, Oncology, Psychiatry, and Rheumatology) of 4 Asian countries (Korea, Malaysia, Taiwan and Thailand), with stratification of the site utilization.

From this analysis, a better site identification strategy can be built based on data of past site performance.

Methodology

The Median Enrollment Factors* were reviewed from the studies conducted in 2010-2014. The data was captured at 183 sites in 4 Asian countries where performed the trials with 5 Therapeutic Areas and they were identified in Quintiles internal database.

The identified sites have been stratified with its utilization and all the sites have been divided into 2 sectors based on their number of clinical trial experience. Those 2 categories have been named as highly-utilized and low-utilized sites.

- **Highly-utilized site**: involved in greater than average number of trials in particular Therapeutic Area in the country.
- **Low-utilized site**: involved in not greater than average number of trials in particular Therapeutic Area (less than or equal to average number of trials) in the country.

Each site has an attributed Median Enrollment Factor and this median has been stratified by highly-utilized and low-utilized sites.

- *__Median Enrollment Factor (MEF)__ = Subject Enrollment Rate (number of enrolled subject per site per month) / Country Median Enrollment Rate in a particular study.

In case that a site exceeds 1 MEF, it means that the site exceeded median country performance while below 1 MEF means that the site is not up to the country's overall performance.

Results

Figure 1. Median Enrollment Factor in 5 major Therapeutic Areas by 4 Asian Countries

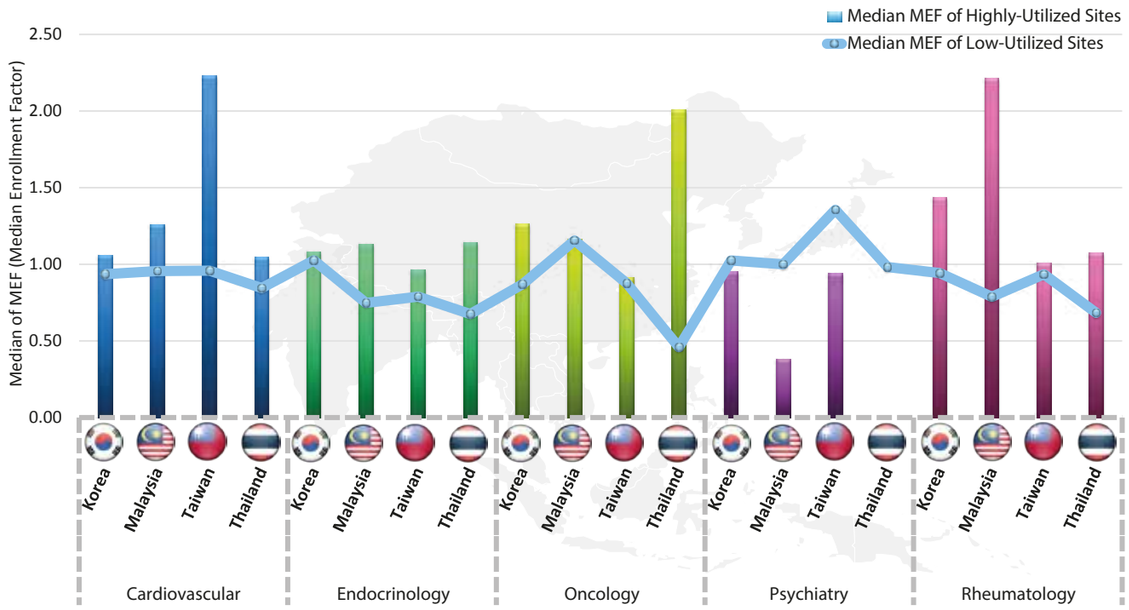
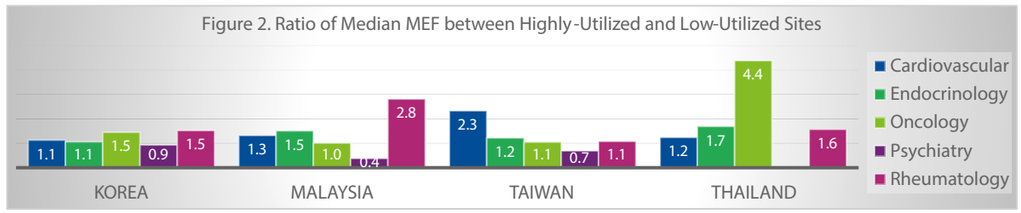


Figure 2. Ratio of Median MEF between Highly-Utilized and Low-Utilized Sites



Conclusions

- Overall, the data suggests that, in all 4 Asian countries, Psychiatry studies show good recruitment capability in Low-Utilized sites and the enrolments are independent of site clinical trial experience.
- For Cardiovascular, Endocrinology and Rheumatology studies it is recommended to have a combination of low and highly utilized sites. However, Taiwan and Malaysia are unique, as highly-utilized sites have shown doubled MEF in Cardiovascular and Rheumatology respectively.
- In Oncology, the data strongly implies that the participation of highly capable sites with extensive exposure to clinical trials are necessary for effective recruitment.
- In Korea and Taiwan, there was no significant differences in recruitment performance between highly and low-utilized sites in general (except Cardiovascular trial in Taiwan).
- Strategic Site Identification is essential to achieve faster recruitments in Clinical Trials. In this assessment, the data shows how to map the site leverage plan of 4 Asian Countries in major Therapeutic Areas. In certain Therapeutic Areas, there is a clear correlation between site utilization and subject recruitments, which gives important and tactical insights into Site Identification Strategy. This analysis offers constructive guidance for strategic site identification within Asia.

Disclosure

1. HyunJoo Rhee – Associate Director and Head of Site ID Services in Asia Pacific, Quintiles Transnational Korea Co., Ltd., South Korea
2. Wendy Bilham – Sr. Director and Head of Therapeutic Science & Strategy in Asia Pacific, Quintiles East Asia Pte. Ltd., Singapore
3. HyunSuk Hong – Director and Head of Regional Feasibility in Asia Pacific, Quintiles East Asia Pte. Ltd., Singapore
4. NaYoung Kim – Site ID Services Specialist, Quintiles Transnational Korea Co., Ltd., South Korea

CRM *in photos*

NHAM Annual Scientific Meeting 2015,
Hilton Kuala Lumpur, 10th-12th April 2015

27th DIA Annual EuroMeeting,
Palais des Congrès, Paris, 13th-15th April 2015

Visit to the new Sarawak General
Hospital (SGH) CRC building, 31st July 2015

Kedah 1st Research Summit,
19th & 20th August 2015

18th Family Medicine Scientific Conference,
Kuala Terengganu, Terengganu, 13th-16th May 2015

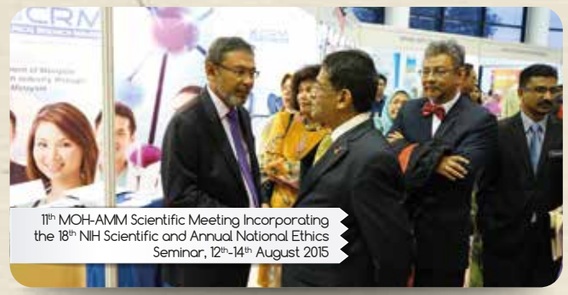
9th National Conference for Clinical Research
(NCCR) 2015, Penang, 27th-29th May 2015

4th KoNSERT Clinical Trial Industry Symposium
Korea, 27th August 2015

Summit on Medical Education, UiTM Sg. Buloh
27th-28th August 2015

26th Annual Scientific Meeting of Malaysian Society
of Neurosciences, Ipoh, 5th-7th June 2015

DIA 51st Annual Meeting 2015, Washington DC, USA
14th-18th June 2015



11th MOH-AMM Scientific Meeting Incorporating
the 18th NIH Scientific and Annual National Ethics
Seminar, 12th-14th August 2015

Visit to CRU Seberang Jaya Hospital, Pulau Pinang
30th May 2015

APHM International Healthcare Cenference
& Exhibition, KLCC ,15th-17th June 2015

SCRS Asia Pac Site Solutions Summit,
Melbourne, Australia, 30th-31st July 2015

BioMalaysia & Asean Bio Economy Conference &
Exhibition, PWTC Kuala Lumpur 17th-19th August 2015

INDUSTRY News

Vaccine Candidate Potentially Effective Against Ebola in Large Trial in Guinea

AMES, Iowa, July 31, 2015 – NewLink Genetics Corporation today announced that the international partnership studying the VSV-ZEBOV (Ebola) vaccine candidate in Guinea has released interim data suggesting that it is effective against Ebola in a large clinical trial. According to the announcement, the interim results suggest that the vaccine candidate demonstrates efficacy within about 10 days of administration to a person without the infection.

Source: NewLink Genetics Corporation

Novo Nordisk to Initiate Phase 3a Development of Oral Semaglutide, a Once-Daily Oral GLP-1 Analogue

Bagsværd, Denmark, 26 August 2015 – Novo Nordisk today announced the decision to initiate a phase 3a programme with oral semaglutide; a once-daily oral formulation of the long-acting GLP-1 analogue semaglutide. The decision follows the encouraging results of the proof-of-concept phase 2 trial announced on 20 February 2015 and the subsequent consultations with regulatory authorities.

Novo Nordisk intends to initiate a global phase 3a programme, named PIONEER, comprising seven trials with approximately 8,000 people with type 2 diabetes. The PIONEER programme will include six safety and efficacy trials and one trial for evaluating the cardio-vascular safety of oral semaglutide.

Source: Novo Nordisk

AstraZeneca and Valeant Pharmaceuticals to Partner on Brodalumab

Tuesday, 1 September 2015 – AstraZeneca today announced that it has entered into a collaboration agreement with Valeant Pharmaceuticals International, Inc. under which it will grant an exclusive license for Valeant to develop and commercialise brodalumab.

Brodalumab is an IL-17 receptor monoclonal antibody in development for patients with moderate-to-severe plaque psoriasis and psoriatic arthritis. Under the agreement, Valeant will hold the exclusive rights to develop and commercialise brodalumab globally, except in Japan and certain other Asian countries where rights are held by Kyowa Hakko Kirin Co., Ltd under a prior arrangement with Amgen Inc., the originator of brodalumab.

Source: Astra Zeneca

Biogen Enrolls First Patient in Global Phase 3 Study of Investigational Treatment Aducanumab (BIIB037) for Early Alzheimer's Disease

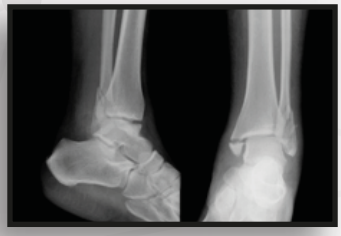
CAMBRIDGE, Mass. September 8, 2015 – Biogen announced today that the first patient has been enrolled in the Phase 3 clinical program for its investigational treatment aducanumab. The Phase 3 program includes two global, placebo-controlled studies named ENGAGE and EMERGE, which are designed to evaluate the efficacy and safety of aducanumab in slowing cognitive impairment and the progression of disability in people with early Alzheimer's disease (AD).

Source: Biogen

Vitamin C: The exercise replacement?

Exercise improves health in overweight and obese adults but can be hard to incorporate into a daily routine. New findings show that taking vitamin C supplements daily instead can have similar cardiovascular benefits as regular exercise in these adults.

Source: American Physiological Society (September 4, 2015)



Diabetes drug boosts bone fat, fracture risk; exercise can partially offset the effect

Inside our bones there is fat. Diabetes increases the amount of this marrow fat. And now a study shows how some diabetes drugs substantially increase bone fat and thus the risk of bone fractures.

The study, published in the journal Endocrinology, also shows that exercise can decrease the volume of bone fat caused by high doses of the diabetes drug rosiglitazone, which is sold under the brand name Avandia.

Source: University of North Carolina Health Care (September 8, 2015)

How the 'heat' compound from chili peppers could help kill cancer cells

Capsaicin, the compound responsible for chilis' heat, is used in creams sold to relieve pain, and recent research shows that in high doses, it kills prostate cancer cells. Now researchers are finding clues that help explain how the substance works. Their conclusions suggest that one day it could come in a new, therapeutic form.

Source: American Chemical Society (September 9, 2015)

Struggles with sleep may affect heart disease risk

Young and middle-aged adults who get too much or too little sleep or have poor quality sleep are at higher risk for the early signs of heart disease than those who get adequate, good quality sleep, research shows.

Source: American Heart Association (September 10, 2015)

Yoga improves arthritis symptoms, mood, study finds

Yoga can be safe and effective for people with arthritis, a randomized trial of people with two common forms of arthritis has found. The researchers report that eight weeks of yoga classes improved the physical and mental well being of people with two common forms of arthritis, knee osteoarthritis and rheumatoid arthritis. The study is believed to be the largest randomized trial so far to examine the effect of yoga on physical and psychological health and quality of life among people with arthritis.

Source: Karolinska Institutet (10 February 2015)

Antibacterial soap no more effective than plain soap at reducing bacterial contamination

Scientists in Korea have discovered that using antibacterial soap when hand-washing is no more effective than using plain soap, according to a paper published today in the Journal of Antimicrobial Chemotherapy. he study examined the effect of triclosan (the most commonly used active antiseptic ingredient used in soap) on bacteria.

Source: Oxford University Press (September 16, 2015)

About CRM
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.

Publish in the CRM bulletin

We welcome submissions of feature articles, write-ups and events related to industry sponsored clinical research for publishing in the CRM bulletin. 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.

2015 UPCOMING NATIONAL & INTERNATIONAL EVENTS

National
International

OCTOBER

- 2nd ISMINS Educational Meeting and 15th Neurosurgical Association of Malaysia Annual Scientific Meeting & Annual General Meeting | 1st – 5th Oct, Kuala Lumpur
- Negeri Sembilan State Research Day: Clinical Relevance over Statistical Significance | 7th Oct, Negeri Sembilan
- Wilayah Persekutuan Kuala Lumpur and Putrajaya State Research Day 2015 | 8th Oct, Putrajaya
- CPhI Worldwide, Madrid, Spain | 13th – 15th Oct, Spain
- 3rd Sabah Medical Research and Scientific Conference 2015: Collaborative Research for Benefit of Community/Sabah State Research Day | 15th – 16th Oct, Sabah
- Bringing Anatomy Alive | 17th Oct, IMU Clinical School Seremban
- 2015 Malaysian Oncology Society (MOS) Annual Scientific Meeting | 17th – 18th Oct, Kuala Lumpur
- The International Congress on Clinical Trials for Medical Devices (CTMD2015) | 21st – 22nd Oct, Austria
- 4th International Conference and Exhibition on Biologics and Biosimilars | 26th – 28th Oct, USA
- 30th Anniversary of Hospital Tengku Ampuan Rahimah Klang in conjunction with Selangor State Research Day 2015 | 29th Oct, Selangor
- East Oncology Updates 2015: "Present Status of Clinical Research in Oncology in Malaysia" | 30th Oct, Kelantan
- Asia Pacific NeuroEndocrine Tumour Society (APNETS) 2015 | 30th – 31st Oct, Penang
- Haematology Updates Meeting: Next Generation Haematology | 31st Oct, Selangor

NOVEMBER

- Taiwan: Asian Conference for Emergency Medicine 2015 | 7th – 10th Nov, Taipei

DECEMBER

- 20th Congress of the Asian Pacific Society of Respirology 2015 | 3rd – 6th Dec, Kuala Lumpur
- European Society for Medical Oncology (ESMO) Asia Congress | 18th – 21st Dec, Singapore

Disclaimer: This list does not include all events that will be held in Malaysia or international.

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