BY CLINICAL RESEARCH MALAYSIA

CRM bulletin

OF CLINICAL RESEARCH AND THERAPY

ISSUE 21
JAN 2021 - JUN 2021

RECOGNIZING CLINICAL RESEARCH ACHIEVEMENTS IN MALAYSIA

Special Coverage

Clinical Trials Day 2021

Rising Stars in Nephrology

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Hospital Pulau Pinang

Research Personality

DR TEH CHENG LAY

About Clinical Research Malaysia

Clinical Research Malaysia (CRM) exists to advance global health solutions for a brighter, more hopeful future for the people by providing speedy and reliable end-to-end clinical research support for quality studies. As these studies unfold, we work together with our partners to create an impetus in delivering better treatment to our end consumers, while at the same time creating high-skilled job opportunities.

The strength of our operation lies in our innate understanding of the local clinical research landscape and implementation of international standards. This, when considered in parallel to the fundamental backing of the government ministries, provides us with an incomparable advantage, as we work hand-in-hand with our partners from the nascent stages of development to materialisation of the end product.

In the journey towards a brighter and better future, we facilitate the entry of industry-sponsored research into Malaysia, working closely with the government and relevant authorities to ensure that all regulations and best practices are met.

In CRM, we credit the outstanding performance to the team we have anchored from within our organisation. Their endless pursuit of innovation and continuous improvement have propelled CRM forward to optimise the opportunities that come our way. In tandem with our passion for the clinical research landscape, we ensure core values of transparency, honesty, accountability, and trustworthiness resonate throughout CRM. These qualities are also cascaded to our principal investigators and Study Coordinators, who act as the catalysts of the clinical research process.

As CRM vouches for an aspiring future in the clinical research industry, we have implemented mechanisms to expand hospital capacity for clinical trials and tests. This is possible by tapping into our vast talent pool consisting of principal investigators and medical assistants

CRM
CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

From The CEO's Desk

Welcome to CRM Bulletin Issue 21. In a blink of eye, we have passed the first half milestone of year 2021. It has been a challenging period for everyone, with the unsparing wave of Covid-19 pushing us back into a total lockdown since end of May. Despite this, CRM remains steadfast in pursuing and conducting its operations, including training and awareness programs and stakeholder engagements. In the two dialogues CRM organised earlier this year, we have noted a growing need to enable decentralized trial practices in Malaysia with clearer transparency. This outcome has been highlighted to the National Committee for Clinical Research which in turn has supported the setup of a working committee to study the gaps and opportunities in conducting decentralized clinical trials in Malaysia.

Malaysia has continued performing in multinational clinical trials, to the credit of our investigators and study coordinators. In five of the global sponsored trials conducted this year, we were the first global/ APAC recruiter, and even topped the global recruitment leaderboard in a non-small cell lung cancer study. One that deserves special mention is the First-in-Patient study conducted in Sarawak General Hospital. Led by Dr Chew Lee Ping, this study is the first to be reviewed by our First-in-Human Scientific Review Panel, and upon site initiation, Dr Chew's team were the first to enroll ahead of the other global sites in this study. In addition, we have seen two Covid-19 vaccine trials initiated in the country this year, one by the Institute of Medical Biology Chinese Academy of Medical Sciences, and another involving a vaccine developed by BioKangtai. We view these accomplishments as a great indicator on the capabilities of our clinical researchers and will continue to highlight these achievements to our stakeholders and interested parties.

CRM has always placed emphasis on operational excellence in performing the work we do to continue supporting our clinical researchers and industry stakeholders. In addition, later this year, the organisation will be embarking on its re-certification of ISO 9001:2015 Quality Management System as well as in obtaining the Anti Bribery Management System accreditation, further solidifying our position as a global trusted research management organization.

Finally, I wish you all safe and well as we continuously adhere to the standard operating procedures set to bring our nation forth in recovery.

Dr. Akhmal Yusof
CEO, Clinical Research Malaysia

www.clinicalresearch.my

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HIGHLIGHTS

CRM Virtual National Conference 2021

11 January 2021 – CRM held its very first virtual National Conference. During the event, CEO of CRM, Dr Akhmal Yusof shared CRM goals & opportunities to all CRM employees. The CRM CEO Awards and Long Service Awards were also presented during the program.

IMBCAMS Phase 3 Covid-19 Vaccine Clinical Trial Officiation

27 January 2021 – The Minister of Health, YB Dato' Seri Dr Adham bin Baba, officiated Phase III Covid-19 vaccine trial, developed by Institute of Medical Biology Chinese Academy of Medical Sciences, China. It's the 1st Covid-19 vaccine trial in Malaysia, which involves 9 trial sites and 3000 trial volunteers.

1st Board of Director's Meeting

18 March 2021– CRM held its 1st Board of Directors Meeting. The virtual meeting was chaired by CRM's Chairman, YB Dato' Sri Dr Adham Baba. Clinical research updates and progress of the company was presented to the board members.

Industry Dialogue 2021/1

23 April 2021 – CRM successfully conducted its first industry dialogue in 2021, discussing on decentralised clinical trials in Malaysia. Participated by the sponsor and CRO representatives, the session fuelled much input from relevant stakeholders to the present challenges and arising opportunities with DCT practices

Training to Improve Performance of Study Coordinator (TIPS)

12 May - 4 June 2021 – CRM carried out its annual TIPS program, which was initiated since 2019. As before, the aim of TIPS is to further improve study operations and to share good practices amongst CRM study coordinators.

GCP Refresher Workshop 2021 Series

4 May & 24 June 2021 – CRM successfully conducted two GCP refresher workshops, each addressing pertinent topic in clinical research conduct. The 1st of the series was on Informed consent process, with the next workshop focused on IP Management in clinical trial.

Malaysia to Participate in Phase 3 Vaccine Trial by BioKangtai

5 June 2021 – Malaysia will be carrying out a Phase 3 Covid-19 vaccine trial, involving 3000 volunteers. The trial is on a SARS-CoV-2 (Vero Cells) inactivated vaccine developed by Shenzhen Kangtai Biological Products Co Ltd.

Investigator Dialogue 2021

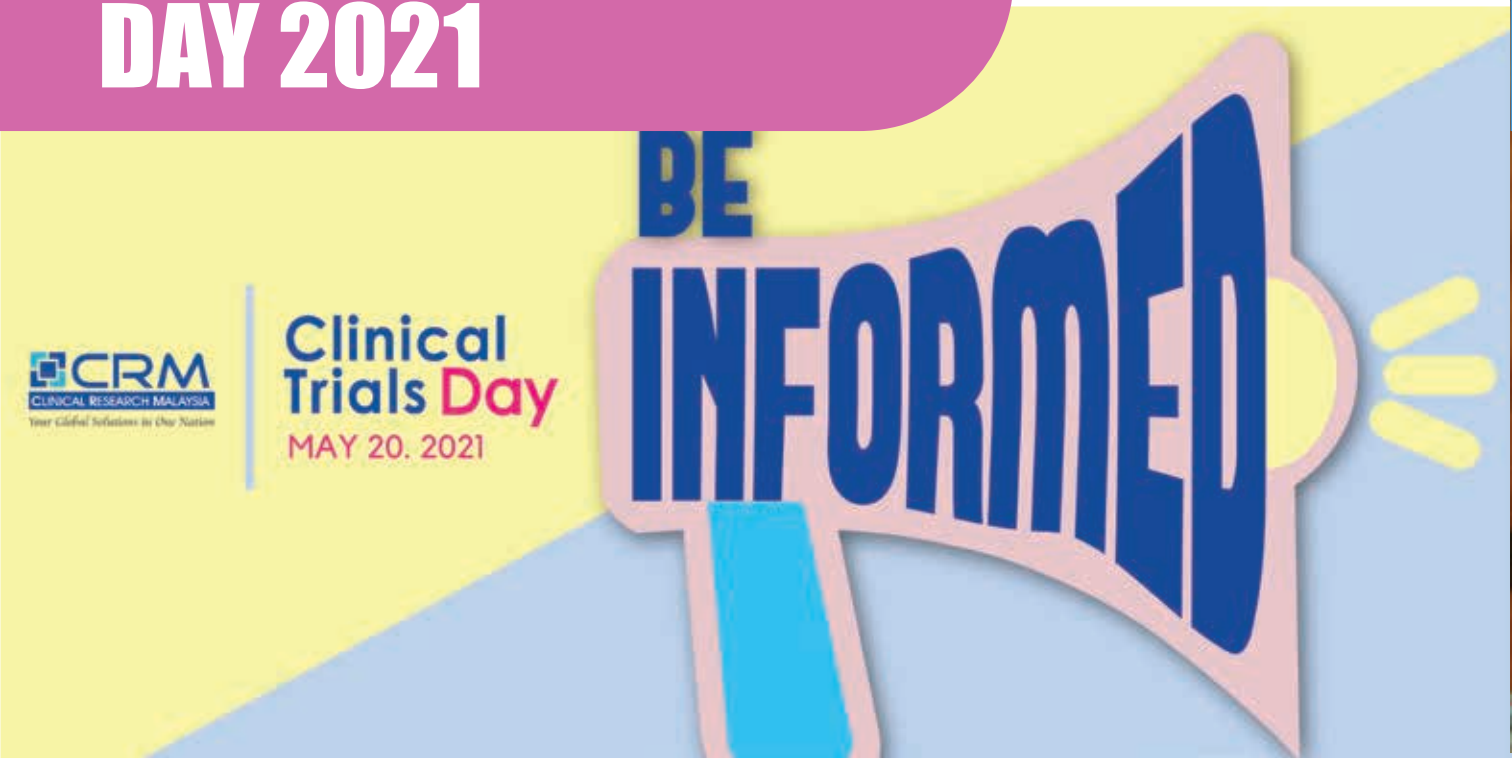
16 June 2021 – Ensuing the footsteps of Industry dialogue, CRM investigator dialogue was held to facilitate the discussion on decentralized clinical trial implementation at study sites.

Protocol Compliance Workshop

30 June 2021 – CRM conducted virtual Protocol Compliance Workshop virtually, which was attended by investigators, study coordinators, pharmacists and clinicians. Program facilitators from IQVIA & MREC shared their knowledge and experience in managing and preventing protocol deviations.

In The News

CLINICAL TRIALS DAY 2021



'BE INFORMED' is a campaign by Clinical Research Malaysia, in conjunction with International Clinical Trials Day. It is aimed to raise awareness of clinical trials by providing accurate information to the public

KUALA LUMPUR, MAY 2021 - Clinical Research Malaysia ccelebrated International Clinical Trials Day, aimed in recognising and honouring the contributions of the clinical research community in Malaysia and the world.

Conducted virtually, CRM shared pertinent information & facts on clinical trial via CRM's social media platforms throughout the month of May. Our stakeholders also took part in our program, by sharing personal messages to the clinical trial community in Malaysia.

To acknowledge the contribution of medical professionals in sponsored clinical research, a small presentation ceremony was held live on Facebook. The Minister of Health, YB Dato' Sri Dr. Adham bin Baba, who is also the Chairman of CRM's Board of Directors, presented the CRM Sponsored Research Award to six recipients in recognition of their significant contribution in clinical research, as well as to spur and encourage more of such efforts.

Message from
Minister of Health Malaysia

Clinical trial information

Sharing of patient's journey (video)

Clinical trial information by
investigator (video)

SPECIAL COVERAGE

CLINICAL RESEARCH MALAYSIA ACHIEVES FORMATION GOALS AND STRENGTHENS INDUSTRY SPONSORED RESEARCH LANDSCAPE IN MALAYSIA

KUALA LUMPUR, 31 MAY 2021 – Clinical Research Malaysia (CRM) has successfully achieved its formation objective in 2020, as highlighted in its Annual Report 2020 which was launched by Minister of Health, YB Dato' Sri Dr Adham Baba in CRM's Facebook Live event.

The event which was held in conjunction with International Clinical Trials Day, also saw the announcement of the six recipients of CRM Sponsored Research Awards 2021, in recognition of their significant contribution in clinical research achievements. Clinicians who received the award include Dr. Soo Hoo Hwoei Fen (Clinical Oncologist) from Hospital Pulau Pinang and Associate Professor Dr. Lim Soo Kun (Nephrologist) from University of Malaya Medical Centre (UMMC) for contributing towards good clinical trial patient recruitment and high number of sponsored research uptake respectively. UMMC and Hospital Kuala Lumpur were both recognized as Clinical Trial Site of the Year for being among the top sites in the nation that conducted high number of sponsored studies in 2020. Janssen (Pharmaceutical companies of Johnson & Johnson), received Sponsor of the Year award for bringing in the highest value of new trials in 2020, while IQVIA Malaysia received CRO of the Year award for contracting the highest number of new clinical trials in 2020.

Clinical Research Malaysia was established in 2012 as an Entry Point Project under the Healthcare National Key Economic Area. The vision was to drive more sponsored research into the country, contributing towards the economy and societal gains. By end of 2020, CRM have succeeded in all its formation goals which saw 1591 new sponsored research, with more than 2000 skilled jobs created and RM 608 million Gross National Income (GNI) generated, making it one of the few successful government-owned organizations that have delivered the targets it was set to achieve.

To date, Malaysia has over 200 hospitals and health care centers that have conducted sponsored research, "Clinical trials bring hope and potentially offer better treatment options to patients as they may benefit from receiving the latest and innovative treatment options that may not yet be available in a country," said Dr. Adham.

CRM's aim to strengthen the clinical research ecosystem in the country have also contributed to intangible benefits on public healthcare access. Through CRM and MOH's collaborative work with Drugs for Neglected Diseases Initiative (DnDi), new affordable treatment regimens are now made available to Hepatitis C patients, paving the way for the nation to eradicate the disease by year 2030.

Since the advent of Covid-19 pandemic in 2020, CRM has participated in multiple engagements with companies as well as inter-ministerial discussions, consulting on the opportunities to conduct COVID-19 treatment and vaccine trials in the country, such as the SOLIDARITY trial by World Health Organisation (WHO) and in Malaysia's first Covid-19 vaccine trial by the Institute of Medical Biology Chinese Academy of Medical Sciences (IMBCAMS).

CRM have also completed its Phase 1 Realization Project (P1RP) which was initiated to build the nation's early phase clinical research capability and thus enabling patients' access to more innovative treatment trials at an early phase of clinical development. Culmination from this groundwork, the National Pharmaceutical Regulatory Agency (NPRA) and the Medical Research & Ethics Committee (MREC) have recently approved a First-in-Patient hematology study in Sarawak General Hospital.

CRM remains steadfast in ensuring deliverance of speed, quality, and reliability in the services it provides. The organisation has been certified with ISO 9001:2015 Quality Management System since early 2019 and has completed its second subsequent year of SIRIM surveillance audit with recommendation for continual of certification. In 2019, the audit report from the National Audit Department recognized CRM as being efficient in managing clinical research.

This year, CRM will pursue the ISO 37001: 2016 Anti-Bribery Management System, pledging its commitment towards being a global trusted research management organization. Moving forward, CRM looks to expand its business into home health nursing, study material destruction and using social media to attract more research opportunities. Within the CRM team, the management and employees will continue to embrace teamwork, empowerment, and communication by further escalating on the company's endeavours of its four key strategies, delivering operations excellence with the continued progress of clinical research in Malaysia.

RECIPIENTS OF SPONSORED RESEARCH AWARDS

RESEARCH PERSONALITY

Dr Teh Cheng Lay

Consultant Rheumatologist,
Sarawak General Hospital

Graduated from Universiti Kebangsaan Malaysia in 1997 and obtained MRCP in 2000. Underwent Rheumatology training in Tan Tock Seng Hospital, Singapore (2001 to 2003) and Royal Perth Hospital (2004 to 2005).

Returned to Sarawak General Hospital in 2006 and started Rheumatology unit in 2006 providing Rheumatology services. Since then, Rheumatology unit has grown to 3 consultants and 4 trainees in Sarawak General Hospital.

Started conducting clinical trials, including self-initiated research projects since 2006 and have published numerous articles in medical journals.

Can you tell us how and when were you first involved in clinical trials?

I started clinical research during my training in Tan Tock Seng Hospital as my mentors there encouraged all doctors to do clinical research. I gained experience in starting and maintaining cohort studies in Rheumatology and also writing medical papers.

While in Royal Perth Hospital, I participated in numerous clinical trials investigating biologics in Rheumathoid Arthritis. The Goatcher Clinical Research Unit of the Rheumatology department in Royal Perth Hospital was a good learning centre for clinical trials.

How has clinical trials change your practice and management of patient care?

Clinical trials provided excellent opportunities for both patients and doctors. Patients are able to gain access to new but costly medications that might provide help in their conditions. Patients also received more comprehensive care and monitoring as clinical trials are very strigent in patient care.

Doctors receive extra training and education on the latest medications and developments in their field of specialities. Rapid developments in Rheumatology through clinical trials have brought paradigm shifts in management of patients with rheumatic diseases. Overall, clinical trials provide positive input to both patients and doctors.

What are the main challenges you encounter when conducting a clinical trial and how do you overcome them?

The main challenges of conducting a clinical trial are patient factors and clinical support for clinical trials. When I started clinical trial in Rheumatoid Arthritis way back in 2006, I needed to convince patients to join the clinical trial and to encourage them to continue in the trial. Apart from patient factors, I need to find my own study coordinator and manage the clinical trial by myself. Nowadays, CRM provide support in term of administration of trials and providing study coordinators. This make clinical trials much smoother in KKM.

What drives or motivates you to conduct clinical trials?

Curiosity and passion to improve patient care in my field have been the 2 main forces that motivates me to conduct clinical trials.

What one word best describes your career as a clinical researcher or investigator? Why?

Serendipity. My career as a clinical researcher was by exposing myself in clinical research during my training time and participating in clinical trials after coming back to SGH. I find that I enjoy clinical research.

Where do you wish to see Malaysia in the field of clinical research in the future?

Malaysia has great potential for clinical research. We have a multi-ethnic population with different diseases that is fertile ground for clinical research.

We need to have epidemiological data on common diseases and start phase 2 and even phase 1 clinical trials in our country.

What needs to be changed for Malaysia to further excel in clinical research?

Policy makers should allocate more incentives for clinicians to be involved in clinical research. Protected time for research even sabbatical for research should be considered for those clinicians who are excellent in clinical research.

Timely recognition of outstanding researchers in the organisation will also provide clinicians motivation to excel in clinical research. Clinicians should be open minded and actively support clinical research as a way to improve patient care.

Standing (L-R): Dr Teh Cheng Lay, Sub-I Dr Sharifah Aishah Bt Wan Mohamad Akbar, Sub-i Dr Cheong Yaw Kiet, Senior SC Chong Tuang Siang and ARM Tan Sia Hong

RISING STARS IN NEPHROLOGY

Dr Norleen binti Zulkarnain Sim
Consultant Nephrologist

Hospital Tengku Ampuan Rahimah

I was first roped into clinical trials by my previous Head of Department, Dato Dr. Tan Chwee Choon, when I was a Medical Officer. I found it interesting and different from my daily routine at that time although it was considered extra work. I was involved in more trials over the years as a sub-investigator when I was training to be a nephrologist. The nephrology fraternity in Malaysia has always been heavily involved in both investigator-initiated and industrial sponsored trials.

Subsequently, I took over the reins as principal investigator from Dato Dr. Tan. There are many benefits when participating in clinical trials as an investigator. The success of trial recruitment starts with good communication and a good understanding of the illness and treatment being investigated. Therefore, it improves your knowledge and communication skills. I have become more meticulous with my cases, and this has made me a better clinician. You learn to appreciate good documentation. You are also giving an opportunity to patients under your care to be involved with new therapies that can improve their prognosis and quality of life.

I have made many good and long-lasting relationships with my patients and their families, my trial team especially my study coordinators (they are my trial life-savers). I believe the work we do is very important for the future of our patients. I hope to recruit more investigators under me and groom them, just as Dato Dr. Tan has done with me, and increase more interest in clinical research amongst junior doctors.

Dr Fariz Safhan Mohamad Nor
Consultant Nephrologist & Head of CRC

Hospital Tengku Ampuan Afzan

I was first involved in doing clinical trials many years ago since I was in medical department in Tengku Ampuan Afzan Hospital as a general physician. The few first studies that I was involved in then were diabetics study, in which I functioned as co-investigator. Subsequently, after being a nephrologist in Nephrology Department, I started to participate as principal investigator in Nephrology clinical trials. I became principal investigator in a few nephrology trial mainly in IgA Nephropathy and Chronic Kidney Diseases.

What motivate me was the desire to be a part of the team exploring new or advanced treatment which will potentially benefit patients care. Patients should participate in trials because these may benefit in their current treatment or future treatment. Clinical trials also have high potential to benefit other patients in the future as there are some diseases which are lacking in suitable or appropriate treatment.

With all these trials, we can potentially develop new treatment which is beneficial in those areas in need of advancement. This will have the chance of changing the outlook of disease. Overall, we have the opprotunity to offer something that have the potential to benefit patients in short term or long term.

I would recommend my other peers to take up clinical trials since this is one of the excellent options to assist our patients to access innovative new treatments. Clinical trials also can empower clinician with knowledge, experience and skills throughout the journey in doing research either as principal investigator or co-investigator. In addition, we gain opportunity to connect and collaborate with global peers alike.

Dr Wan Hasnul Halimi B Wan Hassan
Head of Nephrology Department & Head of CRC Kelantan

Honorary Lecturer & Visiting Consultant physician & nephrologist

Hospital Perempuan Raja Zainab II & Hospital Unversiti Sains Malaysia

My clinical research journey started more than 20 years ago, when I was doing my dissertation study during my Masters in Internal Medicine. I became more interested in clinical research during my work as a junior physician in 2004 when I was asked to join few clinical trials as a sub investigator. The difficulties and challenges at that time further encouraged me to venture more in clinical trial as I find the results rewarding. In 2009 when I started working in HRPZII Kota Bharu as a nephrologist, my Boss and mentor, the only consultant nephrologist then, took me in to be involved in many ISR as well as IIR. My research pursuit then enabled me to win the Young Investigator award in one of the national conference a year later.

At current, despite more responsibilities, I'd still passionate in conducting research. Few of the multi center landmark trial like the study of renal and heart protection (SHARP), SHARP Extended review (SHARP-ER), Fish oil and Aspirin in Vascular access in renal Outcome study (Favored) SONAR and FIGARO diabetic Nephropathy study, to name a few had my involvement as Sub and principal investigators. It was very rewarding to contribute to such large landmark trials that had change management policy. Being able to pass down this passion to the younger generations of researcher and upgrading the level and standards of clinical research also has been my ultimate goal and passion.

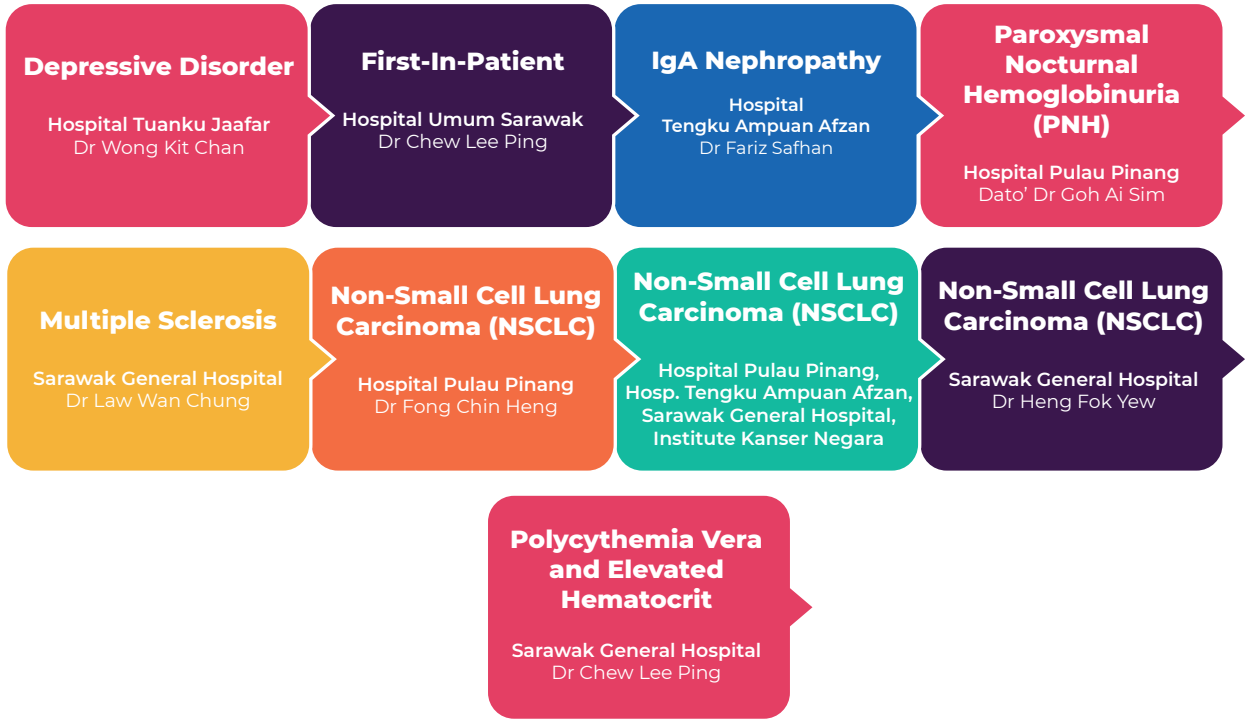
Many have been my role models throughout my journey in clinical research. My Senior Mentor in Nephrology and research, Dato Dr Zaki Morad and Dr Goh Pik Pin, both being the head of CRC in their own time, influenced me a lot in clinical research. My peer group as well as the younger generations of clinical researchers also provide great influence for me. A lot of my clinical practice are based on my research findings. In Kelantan, following our research findings, we have stopped the practice of 'stab Peritoneal dialysis' and replace it with IPD via tenckhoff catheter, provide a 24 hours acute dialysis service and expand dialysis service to Klinik Kesihatan.

Many more, including the way we manage our diabetic nephropathy and CKD patients are based and incorporated from our research findings. I definitely believed that everyone should take up clinical research. The level of research can be at any step depending on their capabilities, interest and commitment. This is because in every aspect of clinical practice, regardless the field, there are still so many unanswered questions that we need to explore. In order to fulfill our responsibilities to provide the best care and treatment for our patients, clinical research is the key essential elements needed.

> **"The difficulties and challenge at that time further encourage me to venture more in clinical trials as I find subsequent result were rewarding"**
>
> *Dr Wan Hasnul*

INFOGRAPHIC

RECRUITMENT ACHIEVEMENTS IN GLOBAL SPONSORED RESEARCH 2021



APAC Top Recruiter | Global Top Recruiter | Overachiever

1st Recruiter APAC | 1st Recruiter Malaysia | 1st Recruiter Global

FEATURED SITE

Hospital Pulau Pinang

Clinical Specialties in HPP:

- Neurology
- Dermatology
- Psychiatric
- Respiratory
- Cardiology
- Oncology & Radiotherapy
- Rehabilitation medicine
- Orthopedic
- Ophtalmology
- Endocrinology
- Otolaryngology
- Urology
- Plastic & reconstructive surgery
- Anesthesiology
- Dental
- Obstetrics & Gynecology
- Pediatrics

Hospital Pulau Pinang was built in 1882, and is the largest public hospital in the state of Penang. The vision of Hospital Pulau Pinang is to establish an excellent referral center in every aspect of healthcare service in the northern region of peninsular Malaysia. The mission of Hospital Pulau Pinang is to provide an efficient, effective, and quality curative, diagnostic and rehabilitation services that emphasize the training and research aspect as well as ensuring that corporate cultural values are incorporated in all the healthcare staff with the slogan of "All for Quality, Quality for All".

Hospital Pulau Pinang consist of 5 main departments which are Women and Children Services, Surgery, Diagnostic and Clinical Support, Medical and Management department.

Doctors
1,156

Pharmacists
215

Nurses
1,762

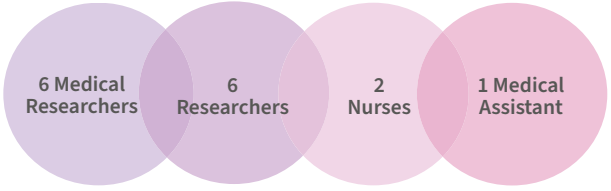
Beds
1,159

Other supporting staffs
1,716

CRC Hospital Pulau Pinang

In accordance with Ministry of Health's desire to form a network of Clinical Research Centres (CRC) under the 7th Malaysia Plan, CRC Hospital Pulau Pinang (CRC HPP) was established. The establishment of this center was proposed in 2001 and commenced operations at the end of 2003. CRC was then placed in Level 1, Ambulatory Care Centre (ACC) building and commenced operations in April 2007. The main objective of CRC Hospital Pulau Pinang was to encourage, promote, support as well as provide facilities to conduct clinical research among the staff of the Ministry of Health Malaysia, Penang. This in addition also creates a group of skilled talents in the field of research, that would conduct and produce quality research.

CRC Hospital Pulau Pinang




CRC Seminar Rooms


CRC Laboratory

CRC HPP Main Functions

Headed by Dr Yoon Chee Kin, the research focus of CRC HPP is in:

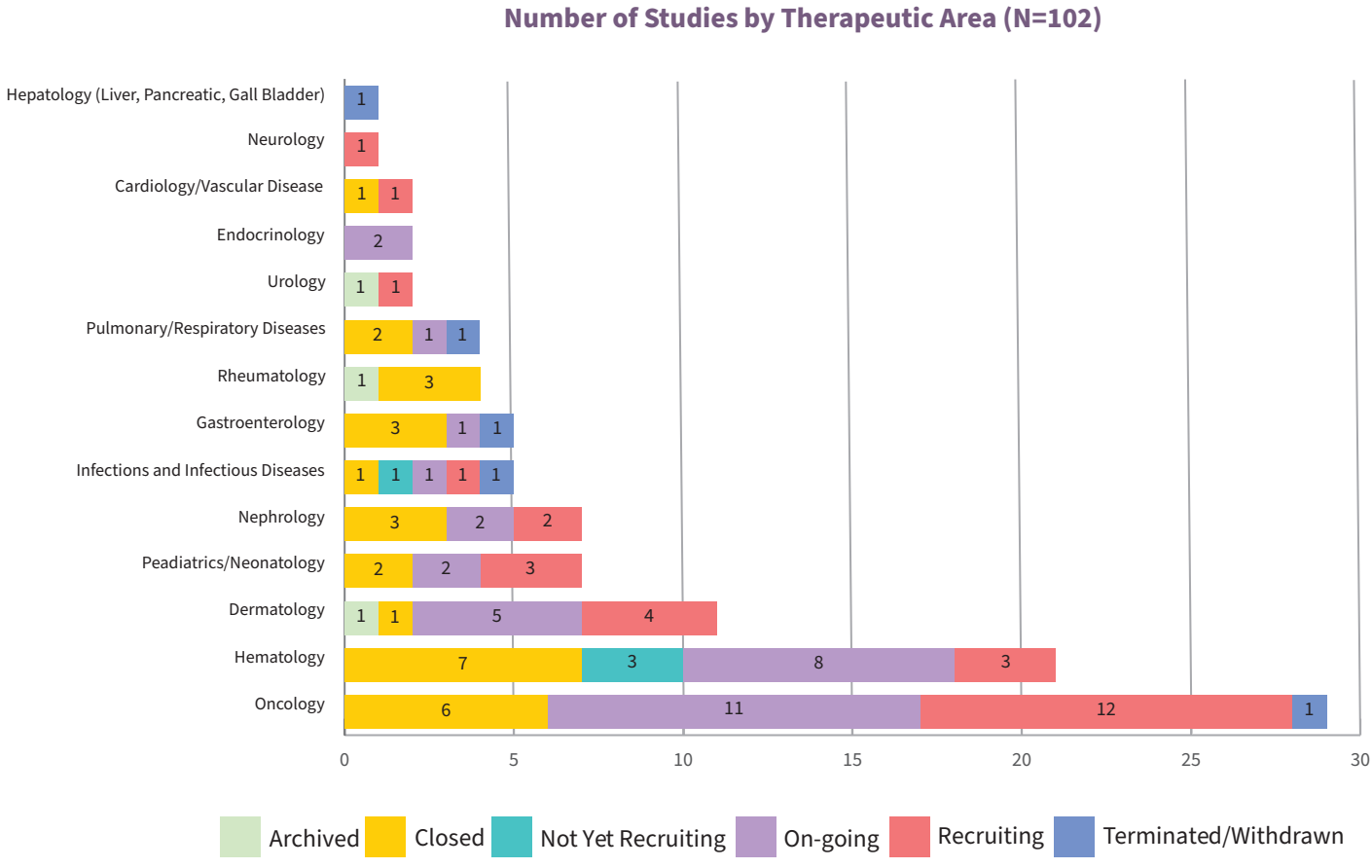
- Clinical Trials
- Disease Treatments and Registers
- Health Outcomes
- Evidence-based Medicine

Conduct research

Provide research related service

Provide research related training

Clinical Trials in Hospital Pulau Pinang



Site Accomplishments in Sponsored Research

2020 → Successfully randomized 4 subjects in 8 months for NSCLC trial - Dr. Irfan Hyder Ali
→ CRM Sponsored Research Award (Top Recruiter) - Dr. Soo Hoo Hwoei Fen

2021 → Top enroller for NSCLC trial - Dr. Fong Ching Heng
→ 1st patient screened in Malaysia for MARIPOSA trial - Dr. Soo Hoo Hwoei Fen
→ Publication on Peritoneal Dialysis International Journal - Mr. Mak Wen Yao

UP CLOSE

Dr Kalairasu Peariasamy

Director of Institute for Clinical Research & Head of Vaccine Selection Technical Working Group

> What would help is by working with teams , networks, institutions that have well-established expertise and abilities to translate results quickly into a well-defined paper. We also need to be progressive with adapting to technology, be it to correct medical misinformation or in application of digital technology in research.

Do share with us your journey in being first involved in clinical research and with CRC / ICR?

My journey started in my course of becoming a professional in medical field, where an academic input in research means gaining some form of evidence in practice. During my attachment at Royal London Hospital, I have benefited from having trained and worked with some of the best clinicians in my field, one on them being Professor Jim Elliot who introduced me to clinical research. Much of my work then was on cleft lips and palate, looking into associated risks, and basis of formation. Later, when I was in Sungai Buloh Hospital, I was privileged to be introduced to very eminent people in clinical research, namely, Dato' Dr Khalid Ibrahim, Datuk Christopher Lee, Dato' Dr Suresh, and Dr Sevapriya. I became more involved in the Clinical Research Centre there, where I eventually became the deputy head and subsequently the head of CRC.

You took over the role as the Director of ICR at a challenging time, when the nation is still grappling with Covid-19 pandemic. Do share with us your foremost challenge as a Director of ICR and your experience in resolving/ managing it.

When I took over the mantle from Dato' Dr Goh Pik Pin, as the Director of ICR, I had some big shoes to fill as Dato' Goh has been in ICR for many years and have been instrumental to many of the initiatives in the network. To me, the strength of the network was very important, especially as the country was battling the pandemic then. Many of our network had elite clinicians and subject matter experts who were in the frontline of managing COVID-19, hence together with infectious diseases specialists and clinicians at hospitals, we quickly set up a database of Covid-19 cases, gathering data that could help us better manage the patients and hospitals. We were very much in favor on the approach of evidence-based medicine, hence we participated

in some of the local and international trials exploring off-label drugs as therapy against Covid-19. It helped that we already had the strength and network setup, in addition to the support by Clinical Research Malaysia (CRM).

Personally, the most challenging task was being appointed the head of the technical working group for the national vaccine selection. There was limited information on the virus then, and we had to review stringently the available clinical trial data before articulating any outcome to the Joint Cabinet Committee. I was fortunate to work with many respected clinicians and experts, including Dr Akhmal, the CEO of CRM, during then. That committee has took its ground very well and we are fortunate that the decision made through this was well received.

What were the significant achievements so far in your time leading this institute?

Firstly, was in the work leading to global Covid-19 vaccine trials in Malaysia. Despite the challenges managing the pandemic, it was important to organize and manage the study team network to enable the uptake of vaccine trials. With these trials, we could have pertinent research data on vaccine efficacy amongst Malaysia population and contribute to the vaccine development globally.

Secondly is in having Malaysia be a part of the SOLIDARITY trial by World Health Organization (WHO). As many were navigating in the search for the best therapy in treating and managing Covid-19 infected patients, Malaysia with the support of CRC network, participated in this global study, to gather evidence in search for safe and effective treatment. Finding from this global project has now proven these studied drugs have little or no effect to improving the care of patients.

Thirdly and most importantly was the work ICR together with its CRC network conducted in the pivotal Covid-19 clinical characterization study in Malaysia. We studied almost 6000 cases from 18 hospitals, which were captured during the first and second wave of the pandemic. Many parameters were investigated, to further understand risk factors, predict disease severity and identify working therapies. These findings were also published in the peer-reviewed medical journal, Lancet, further cementing the quality work our researchers have led with.

What's your aspiration on the path of ICR and the clinical research in Malaysia in the years to come?

Well, Covid-19 has changed the pathway of clinical research, especially in the acceleration of vaccine development to address global need. It has also affected the way we approach high-burden environment within healthcare, and the need to generate evidence quickly. The future for ICR is to look into conducting studies that could provide evidence/ data in making informed decisions and changes to policies. We need to move past fundamental research and undertake impactful research.

The direction of research is also heading towards virtual approaches such as remote management and application of digital technology. We see a need now to have researchers that are tech-savvy with the ability to undertake digital platforms such as big data analytics and even AI. These skill sets are what we hope to develop in our future CRC doctors, pharmacists, practitioners, and researchers.

There is also a need to generate and synergise local data in global repositories (such as ISARIC) so that global research community could access to well-analysed information. But this would need to be explored with caution, especially with effect to data privacy and security, as well as data governance.

Do you have any advice for our healthcare professionals and future researchers who are interested in pursuing clinical research?

Publish your findings. It is very important to synthesize research information quickly and then published immediately. We are often behind in the pace and number of publications, and this should change.

What would help is by working with teams, networks, institutions that have well-established expertise and abilities (ie: analytics, biostatistician), to translate results quickly into a well-defined paper. We also need to be progressive with adapting to technology, be it to correct medical misinformation or in application of digital technology in research.

PUBLICATIONS

What does it Take to Have a Good Experience of Recrutiment in Clinical Research Malaysia

Article published in Journal for Clinical Studies, Volume 12 Issue 5, 16 October 2020

By Aina Farhana Binti Zulkipli & Joanne Yeoh, Clinical Research Malaysia

Introduction

A staggering number of clinical trials fail to meet recruitment goal, which lead to delays, early termination, or inability to draw conclusion at trial completion due to loss of statistical power. It is estimated that roughly 80% of clinical trials fail to meet enrollment timelines and approximately 30% of phase III study terminations are due to enrollment difficulties[1].

In separate analysis of more than 100 trials showed that less than a third and half were awarded an extension[2]. The impact of failure to enroll patients and meeting with timeline can delay product launch that could translate into huge financial losses to the pharma company.

Patient Recruitment: Asia vs Europe & USA

Traditionally, industry-sponsored research has been conducted in high-income countries of Europe and U.S due to established research infrastructure and the birthplace of major pharma companies3. However, globalization resulted in shifting this research outside these countries and reaching out to Asian countries. The key thing that attracts the pharma company to venture Asian population is due to the availability of treatment-naïve patients resulted in speedy recruitment. The large treatment-naïve population including Japan, Malaysia, Thailand and China, presents a significant opportunity [4]. One of the barriers conducting clinical trials in US and western Europe is participant recruitment and retention.

In US and western Europe, racial and ethnic minorities, women and the elderly often underrepresented in enrollment. One trial for HIV-associated cryptococcal meningitis recognized low US patient enrolment and subsequently added Thailand as a trial site, where it recruited 99 patients in 5 sites. The trial added an average of 4 patients per site in Thailand over 3 months compared with 1 per site in the United States[5].

Malaysia have a strong research ecosystem in every healthcare facilities provided by Ministry of Health (MoH), Ministry of Education (MoE) and private hospitals. In MoH, the responsible unit for conducting clinical research is Clinical Research Centre (CRC) which located at every public hospital. To date, there are 35 CRC distribute in peninsular and east Malaysia. Under MoH, there are also government health clinic or 'klinik kesihatan' which also support the work of clinical research in Malaysia.

Besides facilities provided by MoH, there are also teaching hospital under the purview of MoE that actively conducting clinical research, namely University Malaya Medical Centre (UMMC), Universiti Kebangsaan Malaysia Medical Centre (UKKMC), Hospital University Sains Malaysia (HUSM) and International Islamic University Malaysia Teaching Hospital (IIUM Teaching Hospital). And last but not least, there are also several private hospitals conducting clinical research and supported by private clinic. In 2018 and 2019, there are about 330 trials conducted in Malaysia in all healthcare facilities with 235 was conducted in MoH facilities, and the remaining were conducted at MoE and private facilities.

Clinical Research Malaysia

CRM is a non-profit company wholly owned by the Ministry of Health. CRM was established in June 2012 to position Malaysia as a preferred global destination for research and to function as an enabler and facilitator to the industry and medical fraternity for the conduct of clinical trials.

CRM plays an important role to improve the local ecosystem to support growth in industry-sponsored research, 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 this research. CRM is committed to work on three important key strategies; quality, speed and reliability, to ensure satisfaction of relevant stakeholders.

With the controversial challenges in patient recruitment globally, CRM has set key performance index (KPI) to support the recruitment performance of the trials supported by CRM. One of the parameters that we are monitoring is on recruitment achievement for all sites that completed recruitment and we are going to discuss this parameter (result from year 2018 and year 2019) in this article.

Methods

Trial sites identification

In CRM, we have the database to capture the recruitment data on the clinical trials handled by our study coordinators at each trial sites across Malaysia started from year 2012. The database includes important information regarding patient recruitment number for each key therapeutic area. Every month, CRM SCs will update the database and the recruitment specialist will then analyze the data according to different parameters.

The following criteria were included for the analysis:

- Recruitment started on 1st January 2012 onwards (this cut-off was chosen as the database was established in 2012); and
- Recruitment closed on or before 31st December from year 2018 to year 2019

Note: Trials which were terminated earlier or withdrawn are not included in the analysis.

Data Extraction

Data was extracted from 4 major fields in the database which includes 1) trial details (e.g. title, site, region and therapeutic area); 2) study timelines (e.g. site initiation visit (SIV) date and site activation date); 3) recruitment summary (e.g. recruitment target, number of patients randomized); and 4) description of barriers and strategy used related to each trials.

The data were further categorized into regional across Malaysia i.e. northern (Perak, Kedah, Perlis and Pula Pinang), central (Kuala Lumpur and Selangor), southern (Putrajaya, Negeri Sembilan, Melaka and Johor), east coast (Pahang, Terengganu Kelantan and east Malaysia (Sabah and Sarawak).

Data Analysis

Data were analysed using the Microsoft Excel version 10. Descriptive statistics (frequencies and percentages) were used to present information and patterns of trials in 2018 and 2019. The $\chi 2$ test was used to compare the number of trials in 2018 and 2019 with respect to different characteristic of the trials.

Results

Characteristics of the trial sites

From our database, a total of 241 trial sites fulfilled the inclusion criteria and were included in the analysis. Table 1 summarize the characteristic of the trial sites that completed recruitment in 2018 and 2019. Most of the trial sites were involved in oncology trials (26.6%), followed by nephrology trials (10.4%) and pediatric trials (8.7%). Moreover, most of the trial sites were from central Malaysia (25.7%), with 57.7% of the trial sites with the target recruitment of 5 subjects and below and majority of the recrutiment period falls under one year (51.9%).

Comparison of the trial sites from the year 2018 and 2019

There were significant differences in the recruitment target and recruitment achievement as shown below for year 2018 as compared to year 2019 (Table 1). In 2019, most of the recruitment target are more than 5 subjects and most of the trial sites have achieved the recruitment target of 100% and more (p-value <0.05). In 2018, the percentage of sites that achieved recruitment target is 41%, and it increases to 62% in year 2019. (Figure 1)

Discussion

Failure to enroll and retain an appropriate number of participants into a clinical trial results in reduction of statistical power to prove the hypothesis, prolongs study duration time, drains scarce research resources and threatens the validity of research results[6].

There are many barriers of patient recruitment in clinical trials as reported in other literature; complexity of study protocol, lack of awareness about clinical trials in patients, and sociocultural issues related to trial participation[7]. Despite barriers reported, from our analysis, we found that the recruitment rate was improved from year 2018 to the year 2019. It is believe that the following active initiatives taken by CRM have supported the recruitment performance at the trial sites:

1. Active Monitoring and Constant Communication with Relevant Stakeholders

CRM, through the support of the study coordinators placed at the hospital and the Recruitment Specialist whom monitors centrally of the recruitment data has shown improvement of the recruitment performance at the trial sites. Active communicate to discuss possible new recruitment strategies with the relevant stakeholders (i.e. Investigators and Sponsors/Contract Research Organization) kicks in whenever there are recruitment challenges seen at the trial sites.

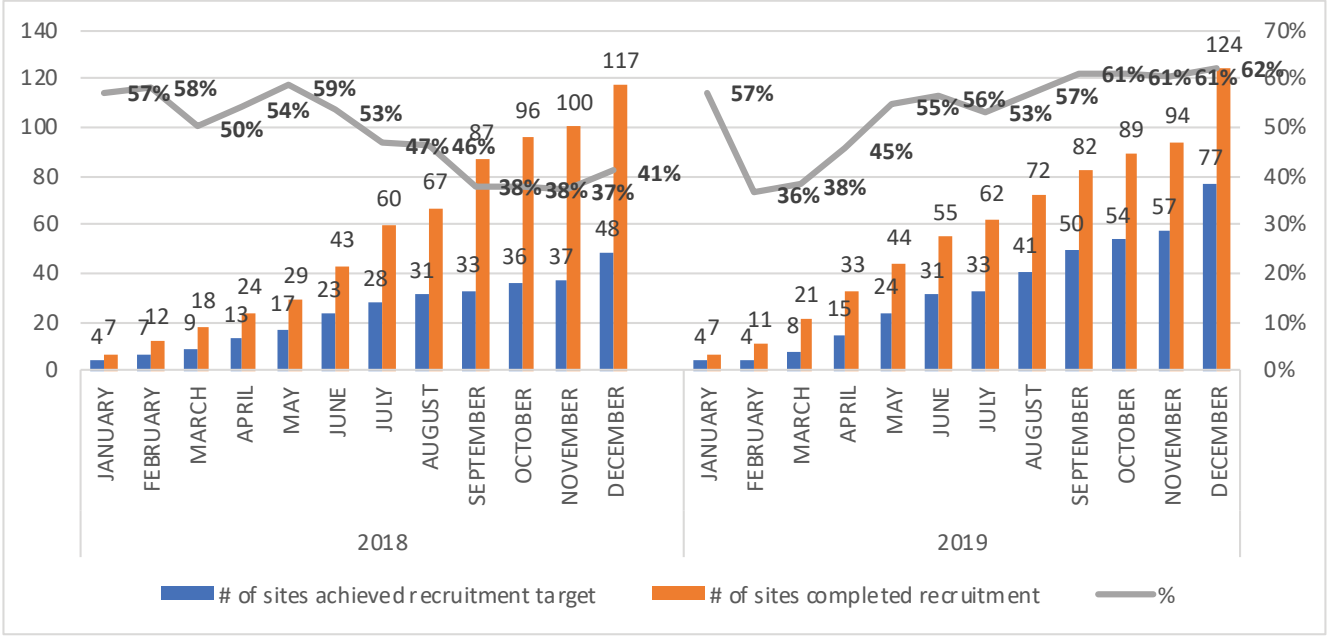
CRM believes this is a shared responsibilities on recruitment and our strategy is in line with a study conducted by Rashmi Ashish Kadam[7], where he suggested that it is best to build a relationship with the players involved in the specific trials and always keep a regular contact with the site staff. Lou Shapiro[8] also reported that in order to ensure success in recruitment, communication with medical doctors and support site staff is important.

Table 1 : Characteristics of trial sites

Characteristics	Total N=241	2018 Total (n): 117	2019 Total (n): 124	p-value
Therapeutic Area		n (%)	n (%)	
Oncology	64 (26.6%)	32 (27.4%)	32 (25.8%)	
Cardiovascular	20 (8.3%)	11 (9.4%)	9 (7.3%)	
Endocrinology	3 (1.2%)	3 (2.6%)	-	
Rheumatology	10 (4.1%)	7 (6.0%)	3 (2.4%)	
Nephrology	25 (10.4%)	16 (13.7%)	9 (7.3%)	
Haematology	7 (2.9%)	4 (3.4%)	3 (2.4%)	
Gastroenterology	16 (6.6%)	10 (8.5%)	6 (4.8%)	
Infectious Disease	4 (1.7%)	3 (2.6%)	1 (0.8%)	
Paediatric	21 (8.7%)	6 (5.1%)	15 (12.1%)	
Neurology	12 (5.0%)	4 (3.4%)	8 (6.5%)	
Psychiatry	3 (1.2%)	3 (2.6%)	-	
Respitatory	7 (2.9%)	7 (6.0%)	-	
Others	50 (20.7%)	11 (9.4%)	39 (31.4%)	
Region				0.34
Northern	62 (25.7%)	32 (27.4%)	30 (24.2%)	
Central	73 (30.3%)	36 (30.8%)	37 (29.8%)	
East Malaysia	43 (17.8%)	15 (12.8%)	28 (22.6%)	
East Coast	24 (10.0%)	14 (12.0%)	10 (8.1%)	
Southern	39 (16.2%)	20 (17.1%)	19 (15.3%)	
Recruitment Target				<0.005*
≤5	139 (57.7%)	80 (68.4%)	59 (47.6%)	
>5	116 (48.1%)	49 (41.9%)	67 (54.0%)	
Recruitment achievement				
Not achieved	116 (48.1%)	69 (59%)	47 (37.9%)	
Achieved 100%	62 (25.7%)	29 (24.8%)	33 (26.6%)	
Overachieved >100%	63 (26.1%)	19 (16.2%)	44 (35.5%)	

*Significantly difference with *p-value* <0.05

Figure 1 Comparison of recruitment achievment in the year 2018 & 2019 (cumulative data from previous month)



2. Create Awareness of Clinical Trials among Public

CRM fully supports on educating the publics on clinical trials and create awareness of such to the nation. A series of clinical trial promotion namely 'I am Aware' and 'Clinical Trial Day' were conducted to support this. The activities were done in either hospitals or public or private institutions where clinical trial information were shared to the public through our staffs.

The volunteers with the interest to participate in the clinical trials (healthy volunteer or patients) may also fill up the consent form for trial mapping through our internal database later i.e. the information of the volunteers will be forwarded to respective trials sites with active recruitment for possible participation if eligible. In 2019, we have conducted 8 campaign at different hospitals, with more than 600 volunteers registered and we have seen the positive outcome where patients were successfully randomized into trials.

In addition to this, CRM has also put up an online platform in our website for the public to register if anyone is interested to join a clinical trial. This is called the 'Find a Clinical Trials' (FACT) and the followings are included the website:

1. The disease of interest in active recruitment stage
2. The location of the trials being conducted

The participants can register themselves through FACT and the relevant information will be shared to the participating sites as to determine further on their eligibility for participation. In 2019, we have received more than 20 volunteer's registration and we have seen the positive outcome of patient enrolment into the study. With the positive progression observed, CRM has also started to reach out to relevant patient support group to advertise the FACT website hoping to attract more targeted patient population in patient recruitment.

3. Training

CRM conducts training in "Recruitment and Retention" to the Investigators and health professional with interest at the hospitals. The training was done through lectures and interactive case scenario among the participants to discuss on the recruitment challenges and new recruitment strategies. In 2019, we have conducted 7 trainings at the trial sites across Malaysia with more than 200 participants.

Conclusion

The recruitment performance for the studies handled by CRM SCs have improved from year 2018 to year 2019. Several key initiatives taken by CRM started in year 2018 including active engagement with the relevant stakeholders, close monitoring and create awareness of clinical trials among the public, training has brought positive progression to the recruitment status in Malaysia.

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Important Clauses in Clinical Trial Agreement

Article published in CLJ Bulletin, Issue 54/2020, 31 December 2020

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Introduction

An agreement plays a vital role in any transaction including, Clinical Trial. It must be made in writing and is voluntarily entered into by the parties involved. The Agreement that governs a Clinical Trial is known as Clinical Trial Agreement (CTA). CTA is an essential document that must be negotiated in detail, finalized, and signed before any Clinical Trial/ Study can commence at the selected Clinical Trial/Study sites. This article emphasizes some of the necessary provisions or clauses that should be included in the Sponsored Research CTA to address the Clinical Trial/Study, and clear expression of the Parties' rights and obligations under the CTA.

Parties to Clinical Trial Agreement & Related Concerns

CTA is a legally binding document that regulates the relationship between the Pharmaceutical Company as the Sponsor of the Study Drug or the Medical Device, or an organization which initiates the Clinical Trial/Study along with financial support to do so, the Institution as the Clinical Trial/ Study Site where its equipment and facility shall be utilized in furtherance of a Clinical Trial/Study and the Principal Investigator (PI) who plays the most prominent role that determines the success of a Study in terms of providing reliable study data and results. In some cases, the Sponsor may authorize or hire a Contract Research Organization (CRO) to enter a CTA with the Institution and the PI. This is usually captured in a separate written agreement between the Sponsor and the CRO of which the contents are not inconsistent with the CTA entered into by the CRO with the Institution and the PI. In the event, the CRO is contracted, and if the CRO is responsible for the monitoring of the Study and accountable for making payments to the Institution and the PI on behalf of the Sponsor, it must be reflected accordingly in the CTA itself so that the Institution or the PI has a contractual remedy against the CRO in case of any non-payment.[1] One important thing to note when the CRO is signed on behalf of the Sponsor, a Clause on Third-Party Beneficiary Law may be included and the CRO may be signed on behalf of the Sponsor under a Power of Attorney or Letter of Authority and the like, and the Sponsor is now the Third Beneficiary under the CTA under which the Sponsor may sue to enforce obligations under the CTA if the Sponsor is not a Party to the CTA. However, with the presence of the Third-Beneficiary Law clause, it is best practice to either have the Sponsor's indemnity clause in the CTA or in the absence of Sponsor's indemnity clause, there must be a separate written Letter of Indemnification signed by the Sponsor and addressed directly to the Institution and PI so that Institution/ PI can claim directly against the Sponsor for any acts or omission. Indemnification is explained in greater detail below. Apart from that, it is also worth noting that the Parties to the CTA in the Malaysian Ministry of Health (MOH) site setting must be local entities. In complying with this requirement, the Foreign Sponsor may authorize its Malaysian entity (if any) or hire a Malaysian CRO to enter the CTA on its behalf.

Description of Clinical Trial/Study

Any Clinical Trial/Study must be identifiable with the Clinical Trial/Study Protocol ID and the Clinical Trial/Study Name. As such, at the beginning of the CTA, it shall provide a brief overview of the Clinical Trial/Study design, which includes but is not limited to, the Clinical Trial/Study therapeutic area, phase of the study, type of study intervention, and how the data analysis is to be performed. This Clause will generally depend on the Sponsor's preference, and it usually depends on the nature of the Clinical Trial/Study. Some require a more detailed Study background, such as the objective and outcome desired from the Study Conduct, estimated time where the Study team shall complete the Clinical Trial/Study, and the number of participants to be enrolled. The description of the Clinical Trial/Study is ideally to be limited to one (1) page as the full Study Protocol duly approved by the relevant Ethics Committee shall be incorporated as an attachment in the CTA for ease of reference and guidance.

Clinical Trial Governance

The Clinical Trial Governance clause sets the minimum compliance requirements in respect of the applicable laws and regulations in the country such as policy and procedures laid down by the relevant Ethics Committee or Institutional Review Board, the principles laid down by the
18th World Medical Assembly (The Declaration of Helsinki, 1964), the Malaysia Guidelines for Good Clinical Practice ("MGCP"), the Guidelines for Application to conduct Drug-Related Clinical Trials in Malaysia (Trial Guidelines) and the Guidelines for Good Clinical Practice of the International Conference of Harmonization ("ICH"), the Malaysian Sales of Drugs Act, the Control of Drugs and Cosmetics Regulations, and other regulations, and any amendments to it, and applicable local and foreign laws, rules, regulations and standards governing the performance of clinical investigations, including but not limited to the rules of the FDA and comparable foreign agencies.

Other than the above, compliance with the approved Protocol shall be another essential note to be added under the Clinical Trial Governance Clause. The Protocol is a document that describes how a Clinical Trial shall be conducted in terms of the design, methodology, statistical considerations, and organization of a clinical trial. The Protocol must lay down specific procedures designed by the Sponsor for conducting the Clinical Trial to ensure the safety of the Clinical Trial Subjects and the integrity of the data collected.[2]

This Clause should also include other regulatory representations and obligations of the Institutions and the PI, including a non-debarment and non-disqualification representation, as well as commitments to report adverse events.

Obligation of Sponsor

Obligations of Sponsor is a pertinent clause in a CTA. CTA shall state the Sponsor's obligations in detail to ensure the Sponsor's accountability. The Sponsor must ensure that each PI shall be qualified by training, i.e., GCP, and should have adequate resources to properly conduct the Study for which the PI is selected. Once the necessary regulatory approval is obtained, the Sponsor's primary obligation is to supply the study drug or medical device (as applicable) in sufficient quantity free of charge to the PI/Institution in a timely manner.

In all events, all study drugs or medical devices supplied shall be owned by the Sponsor. Other than the Study Drug or Medical Device, the Sponsor is also responsible for providing some further study-related information and documents, which include, but is not limited to, the Protocol, the up-to-date Investigator Brochure, and the Case Report Form (CRF) or Electronic Case Report Form (e- CRF). The Sponsor's obligation in monitoring the study conducted shall also be stated in the CTA as monitoring is a crucial activity to verify that the rights and well-being of human subjects are protected, the reported trial data are accurate, complete, and verifiable from source documents and the conduct of the trial is following the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s). The Obligations of Sponsor clause will also revolve around the Sponsor's duty to notify the relevant Ethics Committee or Institutional Review Board of any non-compliance that could impact the Study Subjects' safety and well-being.

Although claims are infrequent, when things go wrong, the impact on human health can be significant; thus, the provision of Clinical Trial Insurance shall also be included as part of the Obligations of Sponsor. It must state that the Sponsor has the Certificate of Clinical Trial Insurance in place, evidencing that the Sponsor has adequate coverage consistent with Clinical Trial industry standards. Insurance is discussed further under the Indemnification heading below.

Clinical Trial/Study Conduct

Clinical Trial/Study Conduct is one of the compulsory clauses in a CTA. This Clause is crucial because it indicates how the Clinical Trial/Study should be conducted where it will be mentioned that the study conducted by the appointed PI and the Study team must comply with the Protocol and any amended Protocol, International Conference on Harmonization Harmonized Tripartite Guideline for Good Clinical Practice ("ICH GCP"), the principles laid down in the Declaration of the Helsinki, governmental and regulatory authorities' regulations, any conditions imposed by a competent Institutional Review Board/Ethics Committee ("IRB/EC"), applicable Law, and such other guidelines as may be introduced for the safe and proper implementation of the study/trial. Further, this Clause will also highlight that any changes or any amendment of the Protocol must obtain the regulatory bodies' approval. The Clause will generally define the investigational product that belongs to the Sponsor and describes whether the Sponsor may provide or arrange other drug products, if applicable, to be used in the trial following the Protocol. It will also detail the products shall not be used for other purposes and describe the custodian/ storage of the products and the right of returning or dispensing the investigational product after the end of the Study. This Clause will also indicate the subject cannot participate in other ancillary Study without the Sponsor's approval. Informed consent shall be obtained from the subjects before enrolling them in the Study, and a separate consent may be needed for future research/ biobanking (if necessary) and suitable to the Protocol. Under the Clause, it will also describe the scenario if the appointed PI is no longer with the Institution, where usually the Institution will be responsible for notifying Sponsor and CRO, in writing, immediately upon learning that the PI appointed is no longer at the Institution and will use its best efforts to identify a substitute PI acceptable by the Sponsor within a reasonable period and the substitute PI must agree in writing to be bound by all obligations, terms, and conditions of the Agreement.

Study Monitoring

Sponsor, Ethics Committee/Institutional Review Board, and regulatory authorities may monitor, inspect, and audit documents, medical records, licenses, work products, etc., at the respective Institution. Thus, under the Study Monitoring Clause, the relevant parties who should be informed when there is an audit or inspection shall be mentioned; for example, PI shall notify Sponsor via email or by telephone if there is a request for permission to inspect Institution's and/or PI's facilities or research records by the regulatory authority. Cooperation of the Parties is needed during the monitoring, audit, and inspection to ensure that all standard procedures and policies are adhered to. Further, if there are any issues during the monitoring, audit, or inspection and corrective actions are needed, reasonable revisions must be taken.

Obligation of Principal Investigator

Obligations of the PI is one of the crucial Clauses that will be inserted in the CTA where it will be mentioned that the PI shall use his best efforts and lead the team to comply with GCP and the Protocol in conducting the trial.

The PI also must not conduct other research that is not required by the Protocol and not conduct other trials that may adversely affect the Protocol. The PI also shall recruit only valid subjects that meet the Clinical Trial/Study criteria and enroll the number of duly qualified subjects according to the Protocol. All subjects must be thoroughly counseled regarding the Study, and legally valid informed consent must be obtained. Besides that, the PI also shall complete the Case Report Form (CRF) or other relevant documents provided by the Sponsor promptly and accurately. The PI must forward the completed CRF and make available any source documents related to the Study to the Sponsor at periodic monitoring visits or promptly upon request with assistance provided to the Sponsor to resolve any discrepancies, errors, or missing information in the CRF and to assist the Sponsor in conducting audits of original case records, laboratory reports and or raw data sources underlying data recorded in the CRF. Such audits shall be conducted with due regard to patient confidentiality. When performing a blind Study, the PI shall maintain the blinding of the Investigational Product, and the randomization codes shall only be released upon completion of the Study and should a medical emergency occur requiring the PI to break the code for a specific valid subject, the PI agrees to notify the Sponsor immediately. It is also mentioned in the CTA that the PI shall obtain all requisite approvals from the Ethics Committee and regulatory authority on the Protocol, Informed Consent, Study advertisements (if any) and any alteration to, or waiver of, any Valid Subject authorization permitting the disclosure of Valid Subject's confidential information in connection with the Study before the commencement of the Study. The Institution and PI shall inform Sponsor promptly in writing about all changes impacting the Trial Staff and/or facilities.

Insurance and Compensation

In the Malaysian GCP, section 5.8.1 mentions that, "if required by applicable regulatory requirement, the sponsor should provide insurance or should indemnify the investigator/ the institution against claims arising from the trial except for claims that arise from malpractice and/or negligence." Usually, a sponsor must obtain and maintain the Insurance throughout the Study/Trial. Meanwhile, the Institution will need to preserve Insurance as required by local state/federal laws, and if needed, the Principal Investigator will only maintain his medical professional indemnity insurance. The clinical trial insurance coverage of the Sponsor would cover claims arising from the use of the investigational product or any related procedure in conducting the trial in which the Sponsor must compensate for medical treatment for subjects who have sustained injuries due to participation in the Study/Trial. However, Sponsor's clinical trial insurance does not include the claims arising from the negligence by the Institution or Investigator.

Indemnification by Institution/PI

The indemnification clause is significant as it protects and secures the parties from anticipated liability, harm, damage, or loss. Generally, this Clause indicates that a party agrees to protect the other against any potential damage, injury, or losses that the other party may occur in performing the obligations. Thus, in drafting the indemnification clause in the clinical trial agreement, we will first identify which parties need to be indemnified and ensure that all the rights of the parties involved are protected. Under the indemnification clause, the Sponsor is entitled to indemnify, defend and hold harmless the Principal Investigator/Institution against any loss, liability, or costs incurred in connection with the Study/ Trial due to the usage of the Investigational product, and usually, the Agreement provides the circumstances in which the Sponsor will not need to indemnify the Institution, in which the exception is only allowed to the extent that injuries are caused by the Institution's negligence and willful misconduct.

Term and Termination of the Agreement

In general, the term and termination clause stipulates the length of the Agreement and the parties' rights to end the Agreement prior to the end of the term of the Agreement. In the context of the CTA, the PI/Institution and Sponsor shall have the right to terminate the CTA under certain circumstances specified in the termination clause, such as termination for default. However, early termination by any of the parties shall be notified to the other party effectively. In the event of premature termination, the pro-rated payment shall be made payable to the Principal Investigator for actual work performed and costs incurred prior to the termination. Besides, the PI shall immediately return to the Sponsor any unused Investigational Product/ Medical Device, confidential information, and other proprietary materials provided by the Sponsor once the CTA is terminated.

Governing Law

The Clause is to determine which state law will govern the terms of the Agreement. It is important to protect the interests of the PI/Institution and the study subjects whereby the CTA's governing Law and jurisdiction must be in accordance with the country or territory in which the Principal Investigator practices. In the Malaysia MOH site setting, the governing Law of the CTA must be Malaysian Law. In reviewing this Clause, we may also consider contractual silence regarding this issue but cannot negotiate any other terms.

Dispute Resolution

Ideally, the parties shall attempt to resolve the dispute through mediation. If mediation fails, then the dispute shall be resolved through arbitration. In Malaysia, The AIAC Mediation Rules and Malaysian Mediation Act 2012 govern the process of Mediation and Arbitration to aid parties in resolving both international and domestic disputes. The venue shall be conducted at The Asian International Arbitration Centre (Malaysia) ("AIAC"), Kuala Lumpur, Malaysia. Alternatively, if agreeable by the Parties, Parties may also resolve the dispute through litigation in the Malaysian courts. Mediation is usually cost saving. Eventually, it is up to the parties' preference.

Payment Terms and Conditions

It is fundamentally important for the financial budget of the Clinical Trial/Study to be negotiated thoroughly. In constructing and negotiating the Clinical Trial/Study budget, the parties must ensure that the payment reflects fair market value for the work performed. In structuring the Sponsor's payment obligation for the Clinical Trial/Study, care should be taken to ensure that the payment structure does not create a financial conflict of interest for the PI or is contrary to any other regulatory laws or requirements. The payment terms and conditions must also indicate that the Sponsor is responsible for paying any taxes assessed in connection with the transaction. Therefore, the Sponsor needs to adhere to the local taxation system. For example, Malaysia has implemented Sales and Services Tax (SST) effective from 1 September 2018 to replace the previous tax system, Goods and Services Tax (GST). Other costs, including the costs associated with the study personnel involved (i.e., investigator, nursing staff, study coordinator) and the costs of all services conducted during the Clinical Trial/Study shall be clearly provided for and agreed upon by all parties in the CTA.

It is also important to identify the financial arrangement on the payment for the PI/Institution, such as invoicing details and the requirements/documents needed to disburse the study payment.

Publication

This Clause will determine the Parties holding the rights to publications on new findings or results from that Clinical Trial/Study. In a Clinical Trial/Study, it is common for the Sponsor to grant the Institution/PI the rights of publication but subject to prior Sponsor's review and approval. Prior to submitting a manuscript or other materials relating to the Clinical Trial/Study to a publisher or organization, the PI shall submit a copy of the manuscripts or materials to the Sponsor for review. The Sponsors should have the right to require the removal of the Sponsor's confidential information to protect their proprietary information and require delayed publication to obtain patent protection.

Intelectual Property

Generally, the Intellectual Property clause discusses the rights of intellectual property (IP) of the IP Owner. It allows the owner of the patents, trademarks, or copyrighted works to protect their works from any use or implementation without consent. In a clinical trial, there are several matters that are important to be addressed in this Clause. For any intellectual property rights that pre-exist before the effective date of the Agreement, each party will retain its pre-existing IP ownership. All IP rights to any discovery or invention developed in the study/trial performance shall belong exclusively to the Sponsor. Therefore, it is also essential to include an IP assignment to assign the sole and exclusive ownership to the Sponsor. Besides that, the Clause shall state that the PI shall retain ownership of any IP they develop during the trial that involves any clinical procedures and related improvements from the trial. For example, during the performance of the Study, if the PI enhances the Sponsor's instrument, the ownership of the IP remains with the PI/Institution.[3]

Confidential Information & Personal Data

The Confidentiality clause addresses the information that will be considered confidential and the obligations to secure and maintain its confidentiality. From the Sponsor's perspective, they need to ensure that any information provided in the performance of the Study will be kept as the Sponsor's confidential information. Meanwhile, the PI/Institution will not accept the confidentiality obligations with unacceptable limitations that will jeopardize their academic interest in promoting research and public welfare.[4]

By addressing the Parties' interests, it is important to ensure that the definition of confidential information must be clearly written in the Agreement and the specific uses of confidential information that are allowed must also be indicated.

There are typical exceptions to the definition of confidential information, which are information that has been made publicly available, information that is in the receiving party's possession prior to receipt from the disclosing party, information independently developed by the receiving party, information lawfully received from the third party, and information disclosed due to any court or administrative ordered for disclosure. In Malaysia, the use and disclosure of the confidential information such as medical information and personal data of Study Subjects are subject to compliance with applicable national privacy laws and regulations, including the Malaysia Personal Data Protection Act 2010.

Conclusion

It is crystal clear that knowing the important provisions or clauses in a CTA is crucial to avoid unnecessary delay in the negotiation of the CTA between Parties. When any of the Parties breach the term of the CTA, the written Agreement, i.e., the CTA will be used as a reference on what the Parties have agreed on to determine who is really at fault. With the CTA's clear wordings, Parties can resolve any future dispute or contractual issues quickly and efficiently.

End Notes

1. Model Clinical Trial Agreement (mCTA) and Clinical Research Organisation Model Clinical Trial Agreement (CRO-mCTA) https://www.myresearchproject.org.uk/Help/Help%20Documents/mCTA-CRO-mCTA-Guidance-March-2020.pdf.
2. https://hub.ucsf.edu/protocol-development Clinical Trial Protocol Development (Last Revised 10/02/2017).
3. R. Leibowitz, Katherine. (2005). The Business of Clinical Trials, Part 1: Negotiating Confidentiality, IP, and Publications. Medical Device and Diagnostic Industry. Retrieved from https://www.mddionline.com/stub/business-clinical-trials-part-1-negotiating-confidentiality-ip-and-publications.
4. Ibid.

CRM IN PHOTOS

Meeting with Major Dato Huan Cheng Guan and Encik Abu Baharin

5 Feb

Delegation from Pharmaniaga Berhad led by Datuk Zulkarnain Md Eusope (Group Managing Director) and En Mohamed Iqbal (Group Deputy Managing Director)

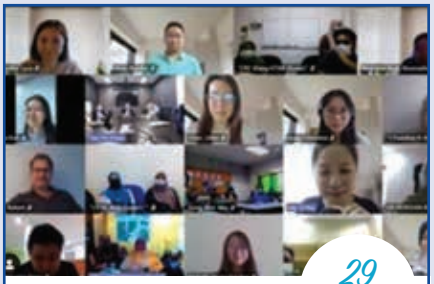
11 Mar

CRM's 1st Board of Director's Meeting

19 Mar

Meeting with Mr Philip Ting & Dato' Seri Dr Chen Chaw

22 Mar

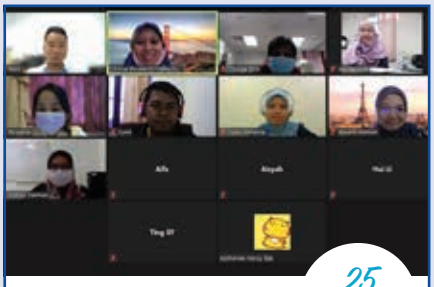


1st Prime Site Joint Steering Committee Meeting (JSC)

29 Mar

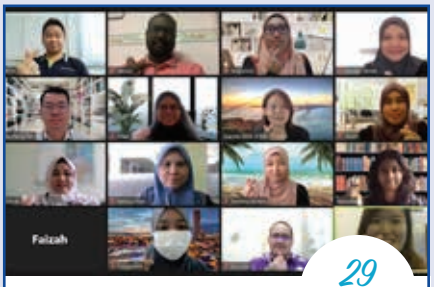
Met with Mr Chong Boon Seng (Everspring Co Ltd)

30 Apr



Subject Recruitment & Retention Workshop

25 Mar



CRM TIPS Training

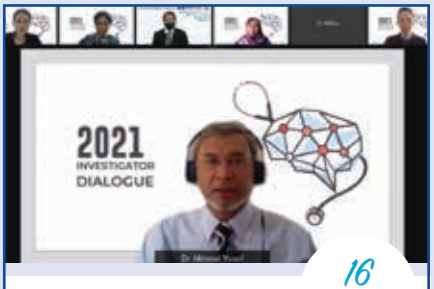
29 Apr

1ST CRM GCP Refresher Workshop

5 May

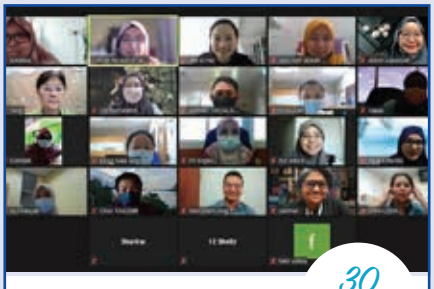
Training to Improve Performance of Study Coordinators

21 May



Investigator Dialogue 2021

16 Jun



Protocol Compliance Workshop

30 Jun

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