Growing the Pool of Clinical Research Investigators in Malaysia

Introduction

The Malaysian government has continuously strived to improve and expand its clinical research ecosystem for the past ten years. The primary goal is to provide a competitive landscape with internationally recognised clinical trial hubs as more pharmaceutical companies continue shifting their clinical trial bases to Asia.

One of the strategies implemented with success by the Malaysian Ministry of Health (MoH) is the establishment of Clinical Research Malaysia (CRM). CRM is a non-profit company acting as a "one-stop" centre to facilitate the growth of industry-sponsored research (ISR). Since the launch of CRM in 2012, it has successfully closed the various gaps within the clinical research ecosystem and continues to address and improve existing unmet needs.

Since early 2000's, Asia-Pacific has seen the benefits of increasing interest by pharmaceutical industries in conducting clinical trials in the region. The cumulative volume of clinical trial densities of selected countries in the South East Asian (SEA) region has almost tripled from 2016 to 2020.[1,2] The clinical trial density in Malaysia doubled from 2016 to 2020, i.e. from 8 to 17, and this is reflected in the increasing numbers of ISRs conducted in the country.[1–4] The number of sponsored research conducted in Malaysia is growing steadily from 162 studies in 2019, 191 studies in 2020 and 215 studies in 2021 despite the COVID-19 pandemic.[3,4] A crucial aspect in conducting high quality clinical trials is the availability of qualified and experienced investigators. Hence, Malaysia will need to increase the pool of available clinical investigators to match the demand and interest of sponsors and contract research organisations in conducting trials here. This article focuses on the current status of Malaysian investigators and the future perspectives for CRM and the MoH in growing the country's clinical investigators pool.

Global Perspectives on Principal Investigators (PI)

Although the day-to-day tasks of a clinical trial are performed by various study team members, PI is pivotal in ensuring the proper conduct of the clinical research and patient safety.[5]

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH E6) Good Clinical Practices (GCP) details the roles and responsibilities of clinical research investigators, including that of the PI.[6] All investigators must be GCP certified and have experience in conducting quality trials. Investigators need to demonstrate the ability to recruit the targeted subjects, supervise and complete the trial within the study timelines, as well as to train the support staff. The investigator and institution (clinical trial site) must ensure there are adequate medical facilities to support the clinical trial, especially when adverse events caused by the investigational product occur.

The number of PIs worldwide varies widely depending on the source of information.[7] Separate databases set up by different clinical research organisations (CROs) and clinical trial organisations estimate between 40,000 to 500,000 PIs globally. Some of these databases reveal that the largest proportions of PIs are in Europe (40%) and North America (32%). Asia-Pacific has the third-highest proportion at 18%. Based on the ClinicalTrial.gov and the DrugDev network databases, an investigator engages with one to three trials per year on average.[7] The IMS Health database, however, shows that 32% of investigators undertook only one trial in five years.[7]

Clinical Studies in Malaysia

The Malaysian healthcare system encompasses healthcare facilities under three large categories, i.e. the MoH, the Ministry of Higher Education (MoHE; that includes teaching hospitals) and the private sector. Clinical trials can be conducted in any healthcare facility within the three categories provided they fulfil the regulatory and ethical criteria set by the Malaysian GCP, as well as local regulations and guidelines.

From 2017 until 2021, the majority of sponsored research studies were conducted in the MoH public hospitals and health clinics, followed by the MoHE teaching hospitals (Figure 1).[4]

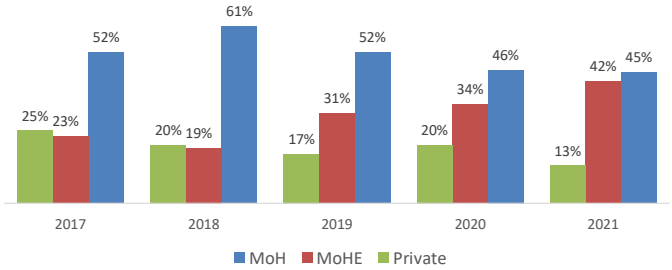

Figure 1. The percentage of approved sponsored research conducted in the three healthcare systems in Malaysia.[4]

Note: For multi-centre studies, the same trial could involve multiple sites from different sectors. However, only a single value will be captured under the site sector, irrespective on the number of site(s) within the sector.

The extensive utilisation of the MoH and MoHE hospitals as clinical trial sites is not surprising. Though there are 45% more private hospitals than public hospitals in Malaysia,[8] the official bed capacity is 260% more in public hospitals. The vast difference in the patient population can also be seen in the number of admissions and outpatient attendance between the two healthcare sectors. The public sector has approximately twice the number of admissions (2.3 million vs 1 million) and seven times more outpatient attendances (21.4 million vs 3 million).[8] The major reason for such high patient volumes in the public sector hospitals is that patient management is heavily subsidised by the government. At a nominal fee, patients

receive consultation, investigations and treatments for all minor and most major conditions/disease. Hence, the patient capacity and potential subject recruitment are significantly higher within the public hospital setting.

The Need for More Clinical Investigators

In 2018, there were 11,686 registered specialists in Malaysia from both the public and private sectors and across various specialities.[9] The public hospitals held more total specialists (58.4%) than the private sector (41.6%).

The majority, if not all, of the PIs conducting clinical research are specialists, and the top five number of new ISRs by therapeutic areas between 2015–2021 were oncology, cardiology, infectious disease, endocrinology and haematology (Figure 2).[4] In 2020, there were a total of 300 cardiologists and 133 oncologists, of which only 10% and 26% were working in the MoH hospitals, respectively.[10] Not all specialists have received Good Clinical Practice (GCP) training and are experienced in conducting or leading clinical trials. Therefore, the discordance created between the number of available specialists and principal investigators as well as the growing number of clinical trials in the top 5 therapeutic areas indicate the pressing need to grow the pool of investigators, especially in those mentioned therapeutic areas. These gaps have led to current investigators being saturated with conducting clinical trials and thus a limitation with accepting more ISRs, and the opportunities to explore new treatment for the population.

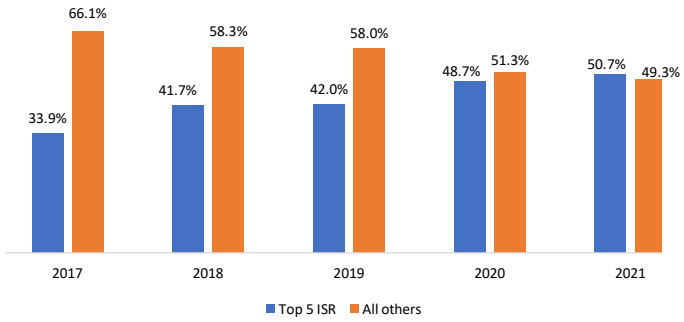

Figure 2. Proportion of the top five ISRs based on speciality (oncology, cardiology, infectious disease, endocrinology and haematology) over a 5-year duration compared to the proportion of ISRs conducted in all other therapeutic areas (22 other therapeutic areas such as Immunology, Gastroenterology, Neurology, Paediatric/Neonatology and more). Source: Clinical Research Malaysia.

Addressing the Gaps – Plans and Perspectives

In recognising the need to increase the pool of investigators across the public and private sectors in Malaysia, CRM together with the MoH have embarked on several initiatives to create awareness among investigators on the value and importance of clinical research.

Since 2017, the CRM Sponsored Research Award is given annually to recognise top investigators who achieved excellent recruitment of study subjects, as well as those who have successfully published research articles in high impact peer reviewed journals. To date, a total of 26 awards have been given to top investigators, trial sites, sponsors and CROs in recognition of the contribution to the clinical research industry in Malaysia. Another initiative is through the conduct of a series of seminars and webinars to attract potential and interested specialists to be involved in clinical research. This complimentary programme which started in 2017, includes multiple roadshows in different regions of the country and online webinars that are open to all Malaysian healthcare professionals. To date, over 20 of such roadshows and webinars have been conducted. CRM also publishes biannual bulletins featuring investigators, sharing their experience in clinical research with the objective to motivate up and coming investigators to embark on clinical research. These initiatives carried out indirectly supported the growth of new investigators involved in ISR in the country (Figure 3).

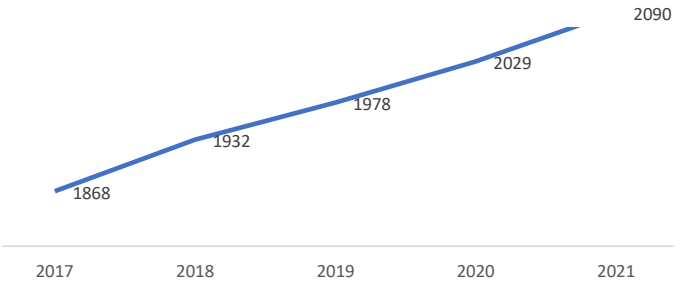

Figure 3 The cumulative growth of new investigators involved in ISR from 2017 to 2021.[4]

Additionally, to bolster the attractiveness of participating in clinical research as investigators, the Malaysian government continuously strives to improve existing policies that support clinicians. Teaching hospitals within the MoHE allocate sabbatical leave and/or research leave for clinicians to conduct research, participate in clinical research fellowships at global centres of excellence and training attachments at international research institutions. Other than inculcating interest in clinical research, these policies encourage formation of international networking collaborations in clinical research through exposure to high quality research programs and encouraging interactions with other like-minded clinicians.

Meanwhile, the MOH in 2017, had allocated one day a week for clinicians within their facilities to conduct ISR in line with its efforts in increasing the number of clinician researchers in the public sector. CRM also continuously enables and encourages investigators in the MOH to take up clinical research on top of their daily clinical service. CRM supports these clinicians by managing the clinical trial budget and reviewing clinical trial agreements on behalf of the investigators.[11] Additionally, CRM also recruits and trains Study Coordinators to be GCP certified, proficient in trial site related duties and comply to CRM's standard operating procedures, before placing them at trial sites throughout Malaysia to support the investigators. These financial, legal and human resource support provided by CRM is vital as it allows the investigators to solely focus on the conduct and delivery of clinical trials, and manage their time between clinical service and clinical research activities.

The growth of the Malaysian clinical trial ecosystem should also consider planning for the future. Hence, as the country gears up for an increase in the number of clinical trials, strategies for career development in clinical research will be needed. This includes creating new career pathways for the physician-scientist for those interested in focussing on research, and to develop and train support staff with accredited courses for research nurses, clinical trial coordinators and data managers. The rationale is to create pools of qualified and quality members of a clinical research team within established and upcoming clinical trials sites to enable and support the principal investigators. With a well-trained team, the potential for investigators to take on more research activities will increase.

Conclusion

With the establishment of CRM and its collaborative efforts with the MoH and other government entities, Malaysia has made great strides in enhancing its presence in the global clinical research scene. The gaps in the quantity of qualified clinical investigators, mainly PIs, are being addressed to ensure a sustainable pool of investigators. These steps include programs and policies to improve the clinical

investigators' time resources, training and mentoring more specialists, and creating an attractive clinical research pathway.

REFERENCES

1. Frost & Sullivan. Asia: Preferred destination for clinical trials. 2017. Available at: https://frost-apac.com/BDS/whitepaper/Asia-Pacific%20Clinical%20Trials%20-%20White%20Paper%20-%20Frost%20&%20Sullivan.pdf. Accessed February 2022.
2. Frost & Sullivan. Asia: Preferred desitination for clinical trials. 2020. Available at: https://frost-apac.com/BDS/whitepaper/Asia-Pacific%20Clinical%20Trials%20-%20White%20Paper%20-%20Frost%20&%20Sullivan.pdf. Accessed February 2022.
3. Clinical Research Malaysia. Annual report. 2020. Available at : https://clinicalresearch.my/wp-content/uploads/2021/04/210427_CRM_AR2021_FA4- Digital-low-res.pdf.
4. Clinical Research Malaysia. Annual report. 2021. Available at: https://clinicalresearch.my/annual-report/
5. Feehan AK, Garcia-Diaz J. Investigator Responsibilities in Clinical Research. Ochsner J. 2020;20(1):44-49.
6. European Medicines Agency. Guidelines for good clinical practice E6(R2). 2016. Available at: https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice#current- version---revision-2-section. Accessed February 2022.
7. CentreWatch. Number of global clinical PIs remains a mystery. 2015. Available at: https://www.centerwatch.com/articles/15859. Accessed October 2021.
8. Ministry of Health Malaysia. Health facts 2019. Planning Division, Health Informatics Centre 2019; MOH/S/RAN/152.19(PT)-e. Available at: https://www.moh.gov.my/moh/resources/Penerbitan/Penerbitan%20Utama/HEALTH%20FACTS/Health%20Facts%202019_Booklet.pdf. Accessed February 2022.
9. Ministry of Health Malaysia. Human resources for health- Country profile 2015-2018. Available at: https://www.moh.gov.my/index.php/pages/view/1919?mid=626. Accessed February 2022.
10. CodeBlue. Minister: 10% of cardiologists, quarter of oncologists serve MOH hospitals. Avaialble at: https://codeblue.galencentre.org/2020/10/22/minister-10-of- cardiologists-quarter-of-oncologists-serve-moh-hospitals/. Accessed February 2022.
11. Clinical Research Malaysia. A unique model to accelerate industry-sponsored research in Malaysia. Available at: https://clinicalresearch.my/a-unique-model-to- accelerate-industry-sponsored-research-in-malaysia-journal-for-clinical-studies/. Accessed February 2022.

Nur Ain binti Amir

Nur Ain currently works at Clinical Research Malaysia as a Feasibility Specialist. She has been liaising with doctors, pharmaceutical companies, and Clinical Research Organization to conduct feasibility study for clinical trial. She has experienced with IIR study. She is a graduate of Universiti Putra Malaysia.

Email: nur.ain@clinicalresearch.my

Cheng Shu Hui

Shu Hui is currently a Feasibility Specialist at Clinical Research Malaysia. She has the experience in diagnostic as well as research and development field. She has her degree with honors in Medical Biotechnology from Sunway University Malaysia.

Email: shuhui@clinicalresearch.my

Audrey Ooi

Audrey Ooi is the Head of Business Development at Clinical Research Malaysia. She has over 8 years of experience in the clinical research field, with cross-functional roles in marketing, project management, stakeholder engagement and medical writing. She is a graduate of Monash University and holding master degree.

Email: audrey.ooi@clinicalresearch.my