2024

Second Edition

A guide to conducting

CLINICAL TRIALS

in Malaysia

Foreword by Minister of Health Malaysia

Clinical research stands as a cornerstone of the healthcare system, playing a vital role in providing patients access to innovative and life-changing therapies. In Malaysia, this field has witnessed remarkable growth, positioning the nation as a leader in Southeast Asia for global industry-sponsored trials. This achievement reflects not only Malaysia's dedication to advancing healthcare but also the confidence of the international research community in our capabilities.

As the Minister of Health, I am deeply committed to fostering a healthcare system built on research, evidence-based practices, and the principles of precision medicine. I firmly believe that by leveraging cutting-edge research and personalized care, we can transform healthcare delivery, improve patient outcomes, and elevate Malaysia’s standing in the global medical community.

Since 2021, Malaysia has made significant strides in the early-phase research ecosystem, including First-in-Human (FIH) studies. Accredited centers like Sarawak General Hospital and Ampang Hospital have successfully conducted multiple FIH studies sponsored by leading pharmaceutical companies. These accomplishments have solidified trust in Malaysia’s ability to deliver high-quality clinical trials, as evidenced by numerous publications and presentations of multi-regional trial findings co-authored by Malaysian investigators.

The success of Malaysia’s clinical research landscape stems from the collaboration of key stakeholders. Regulators such as the National Pharmaceutical Regulatory Agency (NPRA) and Medical Device Authority (MDA) ensure safety and quality. Ethics committees safeguard the integrity of studies, while industry sponsors, Contract Research Organisations (CROs), and trial sites provide innovation and infrastructure. Clinical Research Malaysia (CRM), as a Global Trusted Research Management Organisation, plays a pivotal role in streamlining research processes and positioning Malaysia as a hub for trials with speed, quality, and reliability.

Between 2012 and 2024, the clinical research industry contributed RM1.5 billion to Malaysia’s Gross National Income, supported by over 2,500 sponsored studies and the creation of more than 2,700 skilled jobs. As Malaysia continues its trajectory as a regional hub for clinical research operations, the demand for skilled professionals in this sector has grown. CRM’s Center of Excellence is addressing this need by nurturing local talent, aiming to expand the industry workforce to 4,000 by 2033.

Beyond economic contributions, clinical research has directly benefited over 26,000 patients, granting access to advanced and innovative therapies. These achievements underscore the transformative potential of clinical trials in driving healthcare innovation and economic growth. Moving forward, I am committed to ensuring that clinical research remains central to our healthcare strategy, underpinned by a strong foundation of research and innovation. Together, with the dedication of professionals and organisations like SCRPM, we will continue breaking barriers, setting new standards, and delivering on the needs and hopes of our patients.

DATUK SERI DR. DZULKEFLY AHMAD
MINISTER OF HEALTH

A Note from the President of the Society of Clinical Research Professionals Malaysia (SCRPM)

It is with great pleasure that I present the second edition of "A Guide to Conducting Clinical Trials in Malaysia." The clinical trials industry in Malaysia is rapidly advancing, positioning itself as a powerhouse in the region. Malaysia has become exemplary and a leader in this field, setting high standards for others to follow.

Over the years, Malaysia has made significant strides in clinical research, achieving numerous milestones that have paved the way for its current status. The environment in Malaysia continues to evolve, keeping pace with global trends and technological advancements. This dynamic industry faces numerous challenges, making it essential to have comprehensive guidance to support its growth and development.

As we look to the future, we envision Malaysia further strengthening its position as a leader in clinical trials, driving innovation and excellence. The Society for Clinical Research Professionals Malaysia (SCRPM) has been instrumental in fostering this growth. By providing a platform for networking and knowledge sharing, SCRPM plays a vital role in supporting industry professionals.

I would like to extend my heartfelt thanks to all who contributed to the review of this guide. Special appreciation goes to the task force members whose dedication and hard work have made this second edition an invaluable resource for the industry. Additionally, I acknowledge the support of government bodies, healthcare institutions, and industry partners, especially Clinical Research Malaysia (CRM), who have been pivotal in our journey.

As we continue to navigate this dynamic field, I encourage all readers to actively engage with this guide and contribute to the ongoing growth and success of the clinical trials industry in Malaysia. Together, we can achieve remarkable advancements and improve the lives of many.

Goh Tse Seng

President

Society of Clinical Research Professionals Malaysia (SCRPM)

Interested and want to be an SCRPM member?

Please email scrpmalaysia@gmail.com for more information and on being a member

Acknowledgements

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SCRPM would like to acknowledge the below parties who have been instrumental in contributing time and effort in the review of the handbook and making it a reality.

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1. Overview of Clinical Trials in Malaysia

Background and Overview

Malaysia occupies a unique position in Southeast Asia with a population size of approximately 34.1 million (estimated) as of second quarter of 2024. The ethnic composition of Malaysia is diverse and composed of ethnic Bumiputra (70.4%), Chinese (22.4%), Indians (6.5%) and others population (0.7%)[1].

The number of live births recorded in 2023 was 455,761, with an increase of 7.1 per cent compared to 2022 (423,124). The crude birth rate declined from 15.7 (2022) to 14.4 (2023) births per 1,000 population. The total fertility rate rose from 1.6 births per woman in 2022 to 1.7 in 2023. From 2014 to 2019, life expectancy rose by 0.3 years. However, between 2020 and 2022, it fell by 0.9 years due to excess deaths during the COVID-19 pandemic. The good news is that life expectancy is on the rise again, with an anticipated increase of 1.2 years in 2023 and 2024, driven by a decrease in mortality during those years.

Overall, the annual population growth rate in Malaysia remains stable at approximately 1.09% in 2023. Notably, this marks the first increase in population growth observed during the analyzed period.

These demographic factors combined with high literacy rates of 95.71% (2021) amongst Malaysians[2] and proficiency with the use of English as the key medium of instruction amongst medical practitioners should, in theory, make Malaysia an attractive venue for clinical research. Additional factors that enhance Malaysia's appeal for conducting clinical trials are:

1. Cost efficiency: Malaysia offers competitive costs and an established healthcare system compared to other regions.
2. Specialized infrastructure: The country boasts excellent facilities and expertise in various medical specialties.

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[1]Department of Statistics Malaysia

[2]Data from worldbank.org

3. Healthcare trends: The rising standards of living have led to an increase in lifestyle diseases, along with ongoing challenges from communicable diseases, particularly in rural areas.
4. Regulatory Environment: Supportive government regulations make Malaysia a preferred destination for clinical research.
5. Qualified investigators: Investigators in Malaysia are required to be trained and certified in Malaysian Good Clinical Practice.
6. Phase 1 Clinical Trial Guidelines: The introduction Phase 1 trials enables effective early-phase drug discovery and development in Malaysia.

In July 2024, IQVIA published research highlighting that Malaysia ranks 28th worldwide in country readiness scores for global clinical trials, with Indonesia as the only other Southeast Asian country making the top 30 (Figure 1). The top three countries are the United States, Germany, and Japan. The rankings are based on scores in three key dimensions: patient availability, clinical infrastructure, and operating infrastructure, each of which is further broken down into specific sub-metrics[3].

The Clinical Research Malaysia (CRM) annual report 2023 highlighted that there were 276 newly sponsored clinical research studies in Malaysia, the highest since the CRM founding in 2012 (Figure 2). Since 2012, these efforts have contributed a cumulative Gross National Income value of RM1.16 billion from sponsored research.[4] Per CRM Bulletin Issue 28, Malaysia ranked number one in Southeast Asia for the number of global industry-sponsored studies for 2023-2024[5].

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[3] Rethinking Clinical Trial Country Prioritization - IQVIA

[4] 29-Apr-Website_CRM_AR2023.pdf

[5] https://clinicalresearch.my/wp-content/uploads/2024/08/Website-CRM-Bulletin-28.pdf

Figure 1: Readiness algorithm scores and readiness score allocation trials by country – all industry interventional Phase I-III trials

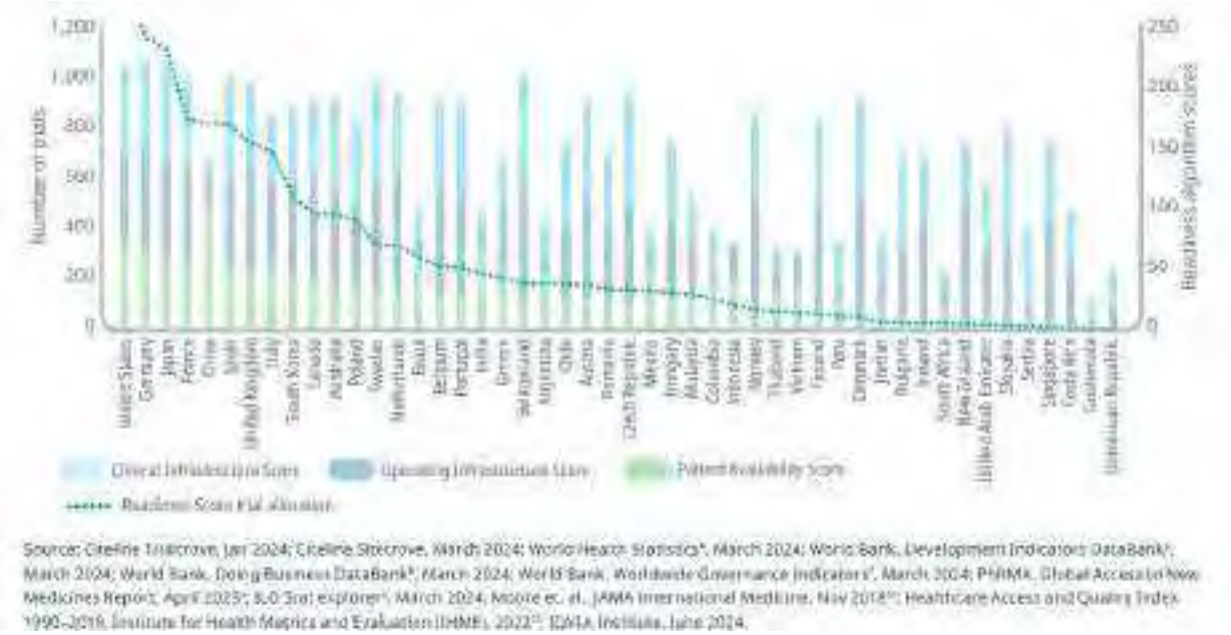

Figure 2: Number of Sponsored Research in Malaysia from 2012-2023

The Total Expenditure on Health for Malaysia during 2011-2021 ranged from RM35,953 million in 2011 to RM78,220 million in 2021. The health spending as a share of Gross Domestic Product (GDP) for the same period ranged from 3.94 percent to 5.06 percent of GDP. Health spending in the public sector was higher than the private sector throughout the years. Overall, the per capita spending on health ranged from RM1,237 in 2011 to RM2,401 in 2021. The total General Government Health Expenditure (GGHE) as percentage of General Government Expenditure (GGE), increased from 6.5 per cent in 2011 to 8.67 per cent in 2021. Despite the increase, healthcare spending as a share of GDP is still relatively low compared to developed countries.[6]

The impetus as such has been for the government of Malaysia to grow research and create a conducive ecosystem to support a healthy and robust clinical research industry in Malaysia.

Launched on 25 September 2010, the Economic Transformation Programme (ETP) was formulated as part of Malaysia's National Transformation Programme. Its goal was to elevate the country to developed-nation status by 2020, targeting Gross National Income (GNI) per capita of US$15,000. This would be achieved by attracting US$444 billion in investments which will, in turn, create 3.3 million new jobs.

Industry Sponsored Trial was mooted as part of the ETP initiative under Entry Point Project (EPP) 2: Creating a Supportive Ecosystem to Grow Clinical Research. The aim of this project was to achieve GNI of RM578.4 million and the creation of 905 new jobs by 2020. While acknowledging that Malaysia was indeed lagging behind its peers, steps were being implemented to change this, and a target had been set to achieve at least 1,000 clinical trials by 2020. This EPP therefore focused on developing a supportive clinical research ecosystem that allows for more efficient and higher quality trials. Per CRM annual report 2020, CRM have successfully attained its formation goals that was to create 1000 new skilled jobs, conduct 1000 sponsored research and produce a GNI of RM 578 million by 2020[7].

The following are some of the government initiatives taken to promote and develop industry sponsored trial:

- Development of Malaysian Good Clinical Practice Guidelines in 1999 and mandating Good Clinical Practice (GCP) certification for all investigators participating in clinical research. The guidelines have been updated in 2004, 2011 and 2018 (as aligned with the ICH-GCP (R2 addendum).

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[6]Malaysia National Health Accounts Health Expenditure Report 2011-2021

[7]210427_CRM_AR2021_FA4-Digital-low-res.pdf (clinicalresearch.my)

- The formation of a National Committee for Clinical Research (NCCR) in 1997 focusing on Policy Shaping. The committee meets at least twice annually and is chaired by the Director General of Ministry of Health (MOH). The NCCR, Ministry of Health, is spearheading various initiatives to enhance and regulate the quality of biomedical research and clinical research practice in Malaysia. The NCCR is made up of member representatives and experts from the Ministry of Health, various national Universities, the Malaysian Pharmaceutical Society (MPS), the Pharmaceutical Association of Malaysia (PhAMA), the Malaysian Organisation of Pharmaceutical Industries (MOPI), as well as other Non-Governmental Organisations.

  This composition of member representatives reflects the ongoing "smart partnerships" amongst the various stakeholders with interests in quality clinical research in Malaysia. The secretariat for this committee is the Investigational Product Evaluation and Safety Section, based at the National Pharmaceutical Regulatory Agency. As of June 2008, the hosting duties became the responsibility of the Institute of Clinical Research, Ministry of Health Malaysia.

- Clinical Research Malaysia, a global trusted research management organization established by the Ministry of Health in 2012. CRM assists research organizations, sponsors and investigators by:

  - Providing a one-stop centre for the conduct of feasibility assessments (and access to the public hospital network of investigators)
  - Assisting in an advisory capacity and acting as a resource centre for interested stakeholders. Providing Study Coordinator support to facilitate investigators with the conduct of the clinical research.
  - Providing financial management support to sponsors and investigators.
  - Improving public and patient awareness.
  - Providing training related to clinical research.

- Strengthening the regulatory framework to support ethical research and increase regulatory oversight. The Investigational Product Evaluation and Safety Section, National Pharmaceutical Regulatory Agency, has issued clear guidelines for the conduct of research and inspection guidelines in consultation with industry stakeholders to support this end. The agency oversees clinical trials in Malaysia through the granting of Clinical Trial Import Licence

(CTIL)/ Clinical Trial Exemption (CTX) and through the conduct of regulatory inspections of sites, sponsors, Contract Research Organization (CRO) and Institutional Review Boards (IRB) in Malaysia. The agency has also developed Malaysian Guideline for Application of Clinical Trial Import License and Clinical Trial Exemption, Guidelines for Good Clinical Practice Inspection, the Malaysian Guideline for Bioequivalence (BE) Inspection, Guideline for Phase 1 Unit Inspection and Accreditation Program and Guideline for Independent Ethics Committee Registration and Inspection.

- Adding research as an area of prioritisation under the New Industrial Plan (NIMP) 2030. NIMP 2030 is a strategic framework aimed at positioning Malaysia as a leading economic powerhouse in the region. A key focus of this plan is the pharmaceutical industry, where clinical trials play a crucial role in advancing research and development (R&D) efforts. By prioritizing these initiatives, the NIMP aims to accelerate Malaysia's economic growth and enhance its competitive edge in the global market.

Generally, research is conducted in Malaysia at teaching institutions/ university hospitals such as University Malaya Medical Centre, Hospital Canselor Tuanku Muhriz, Hospital Universiti Sains Malaysia; government hospitals (MOH) institutions; the National Heart Institute and increasingly at private medical centres across the country. The wide network of local MOH health clinics represents a unique opportunity for access to a previously untapped, primary care patient pool.

The Regulatory body that oversees clinical research is the Investigational Product Evaluation and Safety Section, National Pharmaceutical Regulatory Agency. Regulatory submissions are made in parallel with IRB submissions. The agency has an informative website that is user friendly with easy navigation for quick access to information and resource material.

The IRB structure in Malaysia depends on the location or type of facility conducting the research. Most teaching institutions have their own local IRB/Independent Ethics Committee (IEC), while research conducted at Ministry of Health hospitals fall under the purview of the central IRB, Medical Research and Ethics Committee (MREC). In 2012, a circular was issued by the Drug Control Authority (DCA) that required all IRB in Malaysia that approve drug related trial to be registered with the DCA. The list of registered IRB's can be found on the National Pharmaceutical Regulatory Agency (NPRA) website.

2. Differences between International Council on Harmonization - Good Clinical Practice (ICH-GCP E6 R2) & Malaysian GCP guidelines (Fourth Edition, 2018)

Malaysian GCP is derived from the core principles of ICH-GCP though there are some differences as cited in the table below to accommodate local regulations/ requirements and cultural practices.

Section	Malaysian GCP	ICH-GCP
Definitions: Section 1 Malaysian GCP includes several additional definitions that are not cited in ICH-GCP Section 1, definition differs slightly from ICH-GCP	1.6 Approved Training in Good Clinical Practice Training which is approved by the National Committee for Clinical Research (NCCR). The content of the training must incorporate the curriculum as stipulated by the committee.	Does not have a corresponding definition.
	1.14 Clinical Trial Exemption (CTX) An approval by the DCA authorising the applicant to manufacture any local product for the purpose of clinical trial.	Does not have a corresponding definition.
	1.15 Clinical Trial Import Licence (CTIL) A license in Form 4 in the schedule of The Control of Drugs and Cosmetics Regulations of 1984, authorising the licensee to import any product for purposes of clinical trials,	Does not have a corresponding definition.

	notwithstanding that the product is not a registered product.	
	1.27 Drug Control Authority A regulatory authority established for the purpose of regulating the Control of Drugs and Cosmetics Regulations, 1984.	Does not have a corresponding definition.
	1.30 Herbal /Animal Medicinal Products Plant/animal-derived materials or products with therapeutic or other human health benefits which contain either raw or processed ingredients from one or more plants/animals.	Does not have a corresponding definition.
	1.39 Investigational Product A pharmaceutical form of an active <u>ingredient including plant/ animal-derived medicinal products</u> or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication (off-label use), or	ICH-GCP does not include plant/animal-derived medicinal products as part of the definition. 1.33 Investigational Product A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different

	when used to gain further information about an approved use.	from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
	1.48 National Committee for Clinical Research (NCCR) A committee established for the purpose of coordinating and promoting clinical research in Malaysia, chaired by the Director General of Health, Ministry of Health Malaysia.	Does not have a corresponding definition.
Section 3: Institutional Review Board/ Independent Ethics Committee 3.2 Composition, Functions and Operations	An addition Section 3.2.7 allows the Central IRB for the Ministry of Health Malaysia to provide a review for research for any institution that does not have its own IRB.	No corresponding clause.
	3.2.7. An institution without IRB/IEC may request IRB/IEC of Ministry of Health, Malaysia to make decisions on behalf of the said institution.	No corresponding clause.
Section 4: Investigator Section 4.1 Investigator Qualifications	Malaysian GCP stipulates that the investigator(s) training in GCP has to be **approved training** as per definition Section 1.6. 4.1.1	Does not stipulate specific requirements for approved GCP training. 4.1.1 The investigator(s) should be qualified by education,

	The investigator(s) should be qualified by education, approved training in Good Clinical Practice, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB/IEC, and/or the regulatory authority(ies).	training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB/IEC, and/or the regulatory authority(ies).
4.8 Informed Consent by illiterate subjects	Section 4.8.9 pertaining to illiterate subjects/ or legally acceptable representative permits the use of thumbprint. 4.8.9 If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any	ICH-GCP has no reference as to the use of a thumbprint for illiterate subjects or legally acceptable representative. 4.8.9 If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be

	other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and/**or thumb printed** and dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and appropriately understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.	provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.
Section 4.8.10 Elements of the Informed Consent Form	For cultural considerations, Malaysian GCP requires the disclosure of the source of the investigational product that	No corresponding clause.

	may be culturally unacceptable. 4.8.10 (u) The source(s) and component(s) of the investigational product(s) that may be culturally unacceptable.	
Section 5: Sponsor 5.6.1 Investigator Selection	The sponsor is responsible for selecting the investigator(s)/institution(s). Each investigator should be qualified by training (including approved GCP training) and experience and should have adequate resources (see 4.1, 4.2) to properly conduct the trial for which the investigator is selected. If organization of a coordinating committee and/or selection of coordinating investigator(s) are to be utilized in multicenter trials, their organization and/or selection are the sponsor's responsibilities.	The sponsor is responsible for selecting the investigator(s)/institution(s). Each investigator should be qualified by training and experience and should have adequate resources (see 4.1, 4.2) to properly conduct the trial for which the investigator is selected. If organization of a coordinating committee and/or selection of coordinating investigator(s) are to be utilized in multicenter trials, their organization and/or selection are the sponsor's responsibilities.
Section 5.14 Supply and handling of Investigational Product(s)	Malaysian GCP cites the regulatory requirements for importation of the IP stipulating the requirement for the Clinical Trial Import License and customs clearance process.	5.14.2 The sponsor should not supply an investigator/institution with the investigational product(s) until the sponsor obtains all required documentation (e.g.

	5.14.2 The sponsor should not supply an investigator/institution with the investigational product(s) until the sponsor obtains all required documentation (e.g. approval/favourable opinion from IRB/IEC and regulatory authority(ies). <u>All importation of clinical trial drugs should go through customs even though a clinical trial import licence has been obtained.</u>	approval/favourable opinion from IRB/IEC and regulatory authority (ies)).
Section 5.20 Non-Compliance	Malaysian GCP includes a clause concerning the enforcement powers of the Drug Control Authority (DCA) 5.20.3 The DCA will enforce the rules and punitive action will be decided by the DCA.	No corresponding clause.

3. Drug Control Authority (DCA) and National Pharmaceutical Regulatory Agency (NPRA)

The National Pharmaceutical Regulatory Agency (NPRA) acts as a secretariat to the Drug Control Authority (DCA), Ministry of Health Malaysia (MOH).

NPRA has been designated as a World Health Organization (WHO) Collaborating Centre for regulatory Control of Pharmaceuticals and it is also a participating authority in the Pharmaceutical Inspection Cooperation Scheme (PIC/S).

Effective from 29th March 2013, Malaysia is officially a non-member with full adherent to the Organisation for Economic Cooperation and Development (OECD) Council Acts related to Mutual Acceptance of Data (MAD) in the Assessment of Chemicals on Good Laboratory Practice (GLP). At present, thirty-eight (38) OECD countries and seven (7) non-member countries i.e. Argentina, Brazil, India, Malaysia, Singapore, South Africa and Thailand adhere to the system.

NPRA had been designated as the Malaysian Compliance Monitoring Authorities (CMAs) by the Malaysian Government. NPRA is the CMA for the non-clinical safety testing of test items contained in pharmaceutical products, cosmetics products, veterinary drugs, food additives and medical devices.

Any party interested in conducting clinical trial/s in Malaysia must retrieve up to date comprehensive information/regulations from the official portal (Clinical Trial - Guidelines). The NPRA are constantly engaged with relevant stakeholders and these information/regulations are being updated by the NPRA on an ongoing basis. Content in this handbook is non-exhaustive. Current Malaysia Guideline for Application of Clinical Trial Import Licence (CTIL) and Clinical Trial Exemption (CTX) should be referred for matters related to CTIL and CTX.

3.1 Overview

Before commencing any clinical trial, the sponsor (or the sponsor and the investigator), must submit an application to the NPRA for review, acceptance, and/or permission to begin the trial. The applicant must apply for a Clinical Trial Import License (CTIL)/Clinical Trial Exemption (CTX) prior to importation/ manufacturing the products locally for the study.

The Regulatory Guideline for the application of CTIL is Malaysian Guideline for Application of Clinical Import Licence (CTIL) and Clinical Trial Exemption (CTX).

In addition, other Regulatory Guidelines that governs the conduct of Clinical Trials in Malaysia, are the following: -

- Malaysian Guidelines for Good Clinical Practice
- Guidelines for Good Clinical Practice (GCP) Inspection
- Malaysian Guideline for Independent Ethics Committee Registration and Inspection
- Malaysian Guideline for Phase I Unit Inspection and Accreditation Programme
- Malaysia Guideline for BE Inspection

3.2 Products that Require CTIL/CTX

The following products will require a CTIL/CTX:

- An unregistered product, including a placebo, imported/manufactured locally for the clinical trial.
- A product with a marketing authorization when assembled (formulated or packaged) in a way different from the approved form; AND when used for unapproved indication or when use to gain further information about an approved use, for clinical trial purposes.
- A traditional product with a marketing authorization with an indication for "traditionally used", when used for unapproved therapeutic claim in a clinical trial.

3.3 Application Formalities for CTIL/ CTX

3.3.1 Who can apply for CTIL/CTX

- An investigator
- An authorized person from a locally registered pharmaceutical company/ sponsor/CRO with a permanent address in Malaysia.

3.3.2 Submission and screening of CTIL/CTX application

- Request online screening from the Head of Investigational Product Evaluation and Safety Section (IPESS), Centre of Product and Cosmetic Evaluation (CPCE)
- Screening officer from IPESS will notify applicant of document receipt date via email.
- The IPESS officer will check for completeness of the CTIL application dossier and compliance with regulatory requirements. Submission checklist is available as a general guide.
- Results of screening will be provided to the applicant within 7 working days.
- Upon successful online screening, make payment at Finance, Account & Revenue Section.
- Submit hardcopy dossier and official receipt for verification to the screening officer for application acceptance and evaluation.

3.4 Documents to be submitted in a new application for CTIL/CTX

	Documents
3.4.1	**Table of Contents** A template can be found in Appendix A of the CTIL/CTX guideline.
3.4.2	**Cover letter** The subject line should contain the full NMRR Registration Number (if available), protocol number and title of the trial.
3.4.3	**CTIL/CTX application form** Download from NPRA website.
3.4.4	**Receipt for processing fee (**if applicable) CTIL application processing fee is RM 500.00 per product. The processing fee can be paid using a credit card, debit card, bank draft/money order/postal order payable to *'Bahagian Regulatori Farmasi Negara*'. Application for CTX is free of charge.
3.4.5	**Company Registration Certificate** (if applicable) Not required for investigator-initiated trial.

3.4.6	**Letter of Authorization** (as applicable) Format as per Appendix B1 of CTIL/CTX guideline.
3.4.7	● Poison Type A License for pharmacists in private sector **OR** ● Annual Retention Certificate (ARC) for public pharmacists **OR** ● Malaysia National Registration Identify Card for other applicants.
3.4.8	**EC approval letter**
3.4.9	**Clinical trial protocol**
3.4.10	**Declaration by investigator/ PI of each trial site** Format as per Appendix D2 of CTIL/CTX guideline. Original copy must be provided.
3.4.11	**GCP certificate (**from recognized/ approved GCP course by NCCR, Ministry of Health Malaysia) **and CV for investigator/ PI of each trial site.**
3.4.12	**Informed consent form (Initial version only)** Either in English or *Bahasa Melayu*.
3.4.13	**Pharmaceutical data for all products** Format as per Appendix D of CTIL/CTX guidelines following types of investigational product.
3.4.14	**Label for all products**
3.4.15	**Evidence of Good Manufacturing Practice (GMP) Compliance** from the manufacturer of investigational product and final batch releaser. *Lesen Pengilang* if local manufacturer.
3.4.16	**Investigator's Brochure**
3.4.17	**Overall risk and benefit assessment**

3.4.18	**A copy of scientific advice from other regulatory agencies (if available)**
3.4.19*	**Evidence of Phase 1 Unit Accreditation by NPRA**
3.4.20*	**Insurance Cover**
3.4.21*	**Declaration by Sponsor for CTIL/CTX Application Involving FIH Clinical Trial**
3.4.22	**Electronic copy of application in CD/DVD-ROM**
3.4.23	**Other or additional documents** e.g. published clinical data if applicable.

*For First-in Human Trial only

3.5 Additional requirements

The CTIL/CTX holder shall inform NPRA of any information that casts doubt on the continued validity of the data that has been submitted to NPRA.

NPRA may request for further supplementary data and/or additional documents, including GLP certification and GLP final report, for application of CTIL/CTX, where necessary.

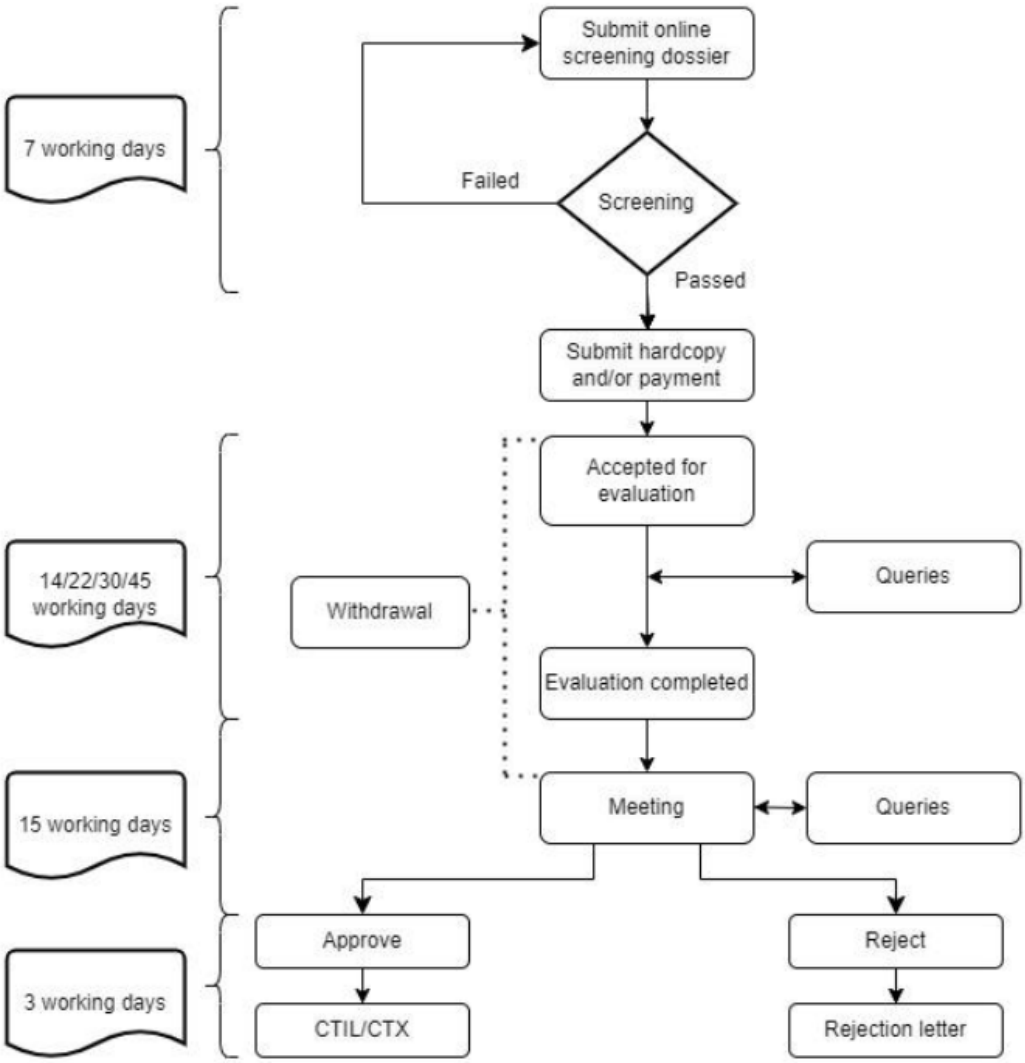
Type of Products	**Requirements**
Non-modified, registered comparator/ auxiliary product	Approved package insert or equivalent document (e.g. summary of product characteristics) from the country of origin can be submitted in place of pharmaceutical data, Certificate of Analysis, certificate of GMP Compliance and IB.
Modified registered comparator/auxiliary product	For modified products (e.g. repackaging, encapsulation), Appendix D2 and certificate of GMP Compliance for the manufacturer involved in the modification are required, along with the

	approved package insert from the country of origin.
Biosimilar product	Full quality dossier including comparability exercises and nonclinical studies between the biosimilar and reference product is required. A stepwise approach should be applied during nonclinical development.
Vaccines	Quality documents for vaccine products should meet format specifications in Appendix D6. The CTIL/CTX guideline should be read in conjunction with other guidelines including guidelines from WHO, EMA, USFDA.
Cell and Gene Therapy Products (CGTPs)	Application for CTIL/CTX is applicable for CGTPs that fall under Class II, in conjunction with Guidance Document and Guidelines for Registration of CGTPs in Malaysia 2016.
FIH Clinical Trials in Malaysia	CTIL/CTX applications for FIH trials will be accepted in stages for new chemical entities, herbal products, and biologics (except CGTP). Clinical trials with generic products, biosimilar products, or registered herbal products for "traditionally used" indications are not considered FIH trials.
Investigational product(s) containing psychotropic substance or dangerous drug	Import Authorization from the Pharmacy Enforcement Division, Ministry of Health Malaysia is required after obtaining CTIL.
Manufacturing product(s) solely for clinical trial(s) in foreign country	EC’s approval letter, Declaration by investigator/PI, GCP certificate and CV of investigator/PI, and registration with NMRR are

	not necessary as the product is for trials outside Malaysia.

3.6 Processing of CTIL/CTX Application

3.6.1 Flow Chart



3.6.2 Timelines

Type of Applications	Timeline for assessment by NPRA
Under normal Circumstances all CTIL/CTX application will be assessed within the following timeline: - For FIH clinical trials, clinical trial involves biological/ biotechnological, CGTPs as well as herbal product with therapeutic claim. Note: For FIH clinical trials, this timeline includes the review time taken by external Panel of Expert(s)	45 working days
- For all products except those products mentioned above	30 working days
Fast Track Fast-track reviews can be considered for application of new IP used for treatment/ prevention in pandemic/ epidemic situations in the interest of public health except for FIH clinical trials. Fast-track CTIL/CTX application will be assessed within the following timeline:	
- For clinical trial involves biological/ biotechnological, CGTP and herbal product with therapeutic claim.	22 working days
- For all products except those products mentioned above.	14 workings days

3.7 Guidance for the Application of Variation

Any variation application can only be submitted once the application of CTIL/CTX has been approved. Valid CTIL/CTX is required for all variation applications. Thus, the applicant should ensure the CTIL/CTX is valid throughout the whole study, i.e. until the last site closure in Malaysia, although there is no importation and manufacturing of IPs.

All variation applications will be assessed within 15 days. Variation application may be rejected if NPRA does not receive satisfactory response for the queries or information requested by the evaluator after 15 working days.

No.	Variation Application	Documents Required
3.7.1	Additional Quantity of IP	• Justification of additional quantity • Calculation of quantity • Information of previously approved quantity for investigational product. • IP Accountability, if applicable
3.7.2	Additional/Change of Trial Site	• Declaration by investigator/ PI of each trial site (original copy) • GCP certificate for investigator/ PI of each trial site. • CV for investigator/ PI of each trial site • Information of previously approved quantity for investigational product. • EC approval, if available *Note: EC approval letter should be submitted to NPRA as soon as possible once it is available. Parallel submission to NPRA and EC is allowed.*

3.7.3	Change of CTIL/CTX holder	Change of CTIL/CTX holder within the **same company** a. Reason for the change of CTIL holder b. Poison Licence Type A / ARC of the new holder Change of CTIL holder to a **different company** a. Reason for the change of CTIL holder b. Poison Licence Type A / ARC of the new holder c. Company registration certificate of the new licence holder d. Letter of Authorisation for Transfer of CTIL Holder. A format of this letter in Appendix C1 of CTIL/CTX guidelines may be used as a reference. **e.** Statement of Acceptance. Format for Statement of Acceptance can be found in Appendix C2 of CTIL/CTX guidelines.
3.7.4	Additional Investigational Product, e.g. Different strength Different dosage form Different vial size Different final volume Auxiliary product Comparator Placebo	• Justification for additional investigational product • Calculation of quantity • Pharmaceutical data • Certificate of Analysis • IP Label • Evidence of GMP Compliance • Official Receipt for processing fee • Information of previously approved quantity for investigational product.

3.7.5	Additional or Change Manufacturer	Evidence of GMP Compliance.
3.7.6	CTIL/CTX Renewal	● Official receipt for processing fee ● Information of previously approved quantity for investigational product.
3.7.7	Change in the name and address of the applicant's company	● A copy of Company Registration Certificate ● A copy of the applicant's Poison Licence Type A for pharmacist in the private section or AR for a public pharmacist, whichever applicable
3.7.8	Change of investigator/PI	● Declaration by investigator/PI (original copy) ● GCP certificate for investigator/PI ● CV for investigator/PI ● EC approval, if available *Note: EC approval letter should be submitted to NPRA as soon as possible once it is available. Parallel submission to NPRA and EC is allowed*
3.7.9	Other variation e.g. Change in pack size/type of packaging	Justification of variation Supporting document

3.7.10. Interim Report

In cases of trials lasting for more than six months, an interim report must be submitted in hard copy annually no later than one year after the initial approval date until end of trial. It is acceptable for a report to be submitted within the month that it is due. An interim report should be submitted for each trial site.

3.7.11 Protocol Deviation

All significant protocol deviation(s) related to inclusion or exclusion criteria, the conduct of the trial, patient management or patient assessment and the corrective action/ preventive action taken, in Malaysia, should be reported to NPRA at an interval determined by the CTIL/CTX holder. Such report must be submitted no later than one year after the initial approval date and continue until end of trial. The CTIL/CTX holder is expected to follow the timeline specified for the interim report.

Any deviation(s) from the protocol that significantly affect the credibility of study data or subject safety must be reported to the NPRA immediately upon Sponsor's awareness.

3.7.12 Reporting Amendment/ Update after CTIL/CTX Approval

- Amendment/ update to the clinical trial protocol, pharmaceutical data (including shelf-life extension), IB and other related document are required to notify NPRA.
- For the protocol amendment, NPRA must be notified after a favourable opinion from EC has been obtained for each site involved.
- The applicant shall notify the NPRA if there is any change in the sponsor for the clinical trial.

3.7.13 Trial Discontinuation

	Timeline for CTIL/CTX holder/sponsor to notify DCA	**Documents to be submitted by CTIL/CTX holder at the end of the trial**
End of Trial	Within 3 months from the last site closure in Malaysia.	• End of Study Summary Report pertaining to the site conducting the trial within 3 months from site closure. The report should be submitted for each trial site. Please refer to Appendix F of the CTIL/CTX guideline for the format of the report.
Early Trial Termination/ Temporary halt	Within 15 working days of temporary halt or early termination of the clinical trial. The reasons shall be	

	clearly explained, and any follow-up measures taken for safety reasons shall be described.	● Drug Accountability and Disposal Report must be submitted to NPRA within 3 months from the last site closure unless otherwise justified. ● Confirmation on the local drug disposal or return of unused drug supplies to the country of origin or regional depot. Note: For local disposal, all investigational products should be disposed of by the authorized bodies/ authority and documented. Destruction certificate should be provided as the evidence of destruction.

3.7.14 Clinical Study Report

Shall be submitted within 1 year after the completion of the full trial or within 1 year from frozen file or data lock date for international multicentre studies.

NPRA must be informed of any possible delay in submission of the report, particularly where the delay is unavoidable as in multicentre studies.

3.8 Safety Reporting

The CTIL/CTX holder shall be responsible for ensuring all Suspected Unexpected Serious Adverse Reactions (SUSARs) arisen from clinical trials conducted in Malaysia with CTIL/CTX and other multicentre overseas (from the same protocol) are reported to NPRA:

SUSARs	**Report Type**	**Timelines for reporting**
Fatal or life-threatening events	Initial Report	Submit as soon as possible but no later than 7 calendar days
	Follow-up Report	A complete report as possible within 8 additional calendar days.
Non-fatal or life-threatening events	Initial Report	Report as soon as possible but not later than 15 calendar days
	Follow-up Report	Follow up information should be actively sought and submitted as it becomes available.

Start reporting: Date notification of CTIL/CTX approval is received from NPRA
End reporting: CTIL/CTX has expired or the End of Study Summary Reports have been submitted for all trial sites in Malaysia, whichever is later.

3.8.1 Safety Decision Arising from Report Analysis / by Other Regulatory Authority

The sponsor/CTIL/CTX holder is required to inform NPRA within 48 hours of the occurrence of any new, significant safety events that may jeopardise the safety of the subjects, which have arisen from an analysis of overseas reports or action concerning safety which has been taken by another country's regulatory agency.

The sponsor should inform all Malaysian investigator(s) and through the investigator, the EC of this information.

The sponsor/ CTIL/CTX holder is also required to be able to provide promptly clinical details of any individual overseas adverse drug reaction reports if requested by NPRA.

3.9 Inspection by NPRA

An inspection may be conducted by NPRA at the trial site, at the sponsor's and/ or CRO's facilities, or at other establishments deemed appropriate by NPRA. The aims are to ensure the rights, safety and well-being of study subjects have been protected, to determine the validity of the data submitted to NPRA, to assure the integrity of scientific testing, and to ensure the legislation/ regulation, GCP principles and the Declaration of Helsinki (Appendix I) are complied with. Failure to allow NPRA to inspect may result in regulatory action such as product will not be registered or de-registered, and the investigator/ trial site will be disqualified.

4. IRB/IEC

An IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects. (Malaysia GCP 3.1.1).

It is the responsibility of the investigator and/or institution where the medical research is to be conducted, to apply via the Principal Investigator (PI) or Principal Coordinating Investigator (for studies with more than one MOH site) to the MREC to seek approval for the conduct of a proposed medical research by the investigator. The investigator and/or institution may delegate the responsibility for MREC submission to the sponsor or sponsor's representative, but the ultimate responsibility for the integrity of the submission always resides with the investigator and/or institution.

4.1 Types of IRB/IEC

In Malaysia, submission to the Ethics Committee and National Pharmaceutical Regulatory Agency (NPRA) can be conducted in parallel. There are 2 types of Ethics Committees:

Central Ethics Committee: A Central Ethics Committee called the Medical Research and Ethics Committee (MREC), reviews and approves all clinical trials to be conducted at all MOH hospitals as well as institutions without a Local Ethics Committee.

Local Ethics Committee: Non-MOH hospitals may have their own Ethics Committees. The registered ECs with NPRA are available on the NPRA website.

4.2 IRB/IEC Application Process and Documents Required for IRB/IEC Submission

4.2.1 Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia

4.2.1.1 Submission to Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia

- The application process for the MREC is conducted on-line through the National Medical Research Register (NMRR) website. Users must register on the National Medical Research Register (NMRR) website to create a user account that can be used for all future submissions. All relevant information is available under the User Manual/Documents section in the NMRR website (National Medical Research Register).

- NMRR is a web-based tool designed to support the implementation of the National Institute of Health (NIH) guidelines on the conduct of research in the Ministry of Health Malaysia (MOH). NMRR enables online research registration and online submission, as well as ethical review and approval of MOH research.

- The register constitutes a publicly accessible database of ongoing and completed medical research and clinical trial projects in MOH and Malaysia. As for now, it is compulsory for all clinical trials conducted in Malaysia to register their clinical trial prospectively with NMRR (requirement by the National Pharmaceutical Regulatory Agency (NPRA) for clinical trials requiring CTIL/CTX licenses). Also, registration in NMRR is required for all research related to MOH (undertaken by MOH personnel or conducted in MOH facilities or using MOH data/patient/personnel as subject or funded by an MOH Research Grant) as stated in NIH Guidelines for Conducting Research in Ministry of Health Institutions & Facilities.

- Currently NMRR V2.0 is being used to replace the previous NMRR V1.0. The upgrading is for system improvement and to comply with all specified international requirements. The research initiated using NMRR V1.0 will continue to use V1.0 until the system transition to NMRR V2.0 is completed.

- Before the submission process is started, the Principal Coordinating Investigator (for studies with multiple sites submitted to MREC) needs to be appointed to act as the main investigator in the study. The Principal Coordinating Investigator/ a designated Corresponding Person is responsible for submitting the relevant study documents in NMRR.

- Studies submitted to the MREC are initially assessed to determine the type of review required, based on the level of risk associated with the study. For clinical research, most studies involving more than minor increase over minimal risk will typically require a full board review by the MREC.

- The PI or Principal Coordinating Investigator is generally not required to attend MREC full-board review meetings unless specifically requested by the MREC reviewers. If attendance is necessary, the Secretariat will notify the PI or Principal Coordinating Investigator at least 2 working days in advance. In cases where the PI or Principal Coordinating Investigator is unable to attend, the Secretariat will arrange a teleconference.

- The PI or Principal Coordinating Investigator will be notified of the decision within 10 working days after the meeting. If there is a delay due to the need for additional review or clarifications following the meeting, the MREC Secretary will promptly communicate the details to the PI or Principal Coordinating Investigator.

- The scheduled panel meeting dates are published on the NMRR website. The review team is divided into 2 panels: the Red Panel and Blue Panel. Each month, 2 MREC meetings are held, one by each panel, except in January and December.

- Please refer to the User Manual/Documents in the NMRR website but not limited to:
    - Manual for Initial Research Registration Submission and Other Submission Purposes (this is a comprehensive guide to demonstrate how to navigate and complete submission in NMRR)
    - Manual for Revision Submission and Deletion of Submission
    - Data Elements and Parameters for NMRR Submission

4.2.1.2 Work Process and Documents Required for MREC Submission

Initial Submission for MREC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	A formal, signed cover letter from Principal Coordinating PI addressed to the Chairperson of MREC is required. The letter should: - List all investigators and their respective roles - Specify all participating sites - Provide a complete list of documents submitted for MREC approval, including their version numbers and version dates. The cover letter must be printed on the official hospital letterhead of the Principal Coordinating Investigator.
Protocol	Yes	To be submitted in the English Language. Malay Language may be accepted if complete.
Protocol Review Checklist	Refer comments section	Required to be submitted for interventional research
Investigator's Brochure	Refer comments section	Required to be submitted if there is an investigational product
Patient Information Sheet (PIS) & Informed Consent Form (ICF)	Yes	Required to submit in English & Malay Language. Other languages (Simplified Chinese, Tamil etc) are optional depending on site needs.
Patient Information Sheet (PIS) Review Checklist	Refer comments section	Required to be submitted for interventional research
Patient Materials	Refer comments section	Not mandatory, however need to be submitted if it will be used in the study. Mandatory languages are Malay and English. Simplified Chinese and Tamil are optional.

Subject recruitment procedures/Advertisements	Refer comments section	Not mandatory, however need to be submitted if it will be used in the study. Mandatory languages are Malay and English. The Simplified Chinese and Tamil are optional
Case Report Forms	Yes	
Insurance Certificate	Refer comments section	Required to be submitted if study is industry sponsored.
PI and Sub-Investigator CV	Yes	Required to submit updated CV.
PI and Sub-Investigator GCP Certificate	Yes	Required for clinical research.
Investigator Agreement, Head of Department and Institutional Approval (IA-HOD-IA)	Yes	The prefilled form is generated from NMRR. The form to be signed by the Principal Investigator, Head of Department, and Institutional Director. Principal Investigators will only need to complete the form based on their institution and not based on study sites.
Conflict of Interest Declaration Form for Investigators	Yes	This is required to be submitted to MREC at the time of new study submissions (for initial approval) and post-approval amendments involving addition of new investigator/s.
Other Documents including documents related to other site staff, professional indemnity or approval by other ECs	No	
Clinical Trial Agreement	Yes	
Payments to Investigators / Site budget	No	

Payments to Subjects	Yes	The subject travel reimbursement, including the amount per visit and the method of payment, must be clearly specified in the Patient Information Sheet under the subject reimbursement section. The payment should be prorated based on the number of visits completed.
MREC Meeting Fee	No	No submission fee is required.
Online or manual submission	Refer comments section	Online submission via NMRR system.
How to check submission status	Refer comments section	Study Investigators / Principal Coordinating Investigator / Corresponding Person is able to monitor study progress in NMRR once the study is forwarded to MREC. The Principal Coordinating Investigator will receive email notification at each stage of submission. Additionally, the Principal Coordinating Investigator can check the approval status from NMRR Version 2 from time to time.
How study team is informed on the study final decision	Refer comments section	The MREC decision letter is sent via email to the Principal Coordinating Investigator. Additionally, the Principal Coordinating Investigator can check the approval status and download the decision letter directly from the NMRR Version 2 website.
Useful guidance documents	Refer comments section	*Online Submission:* User Guideline for Investigator/Clinical Research Associate (CRA) – New Research Registration & Other Submission Purposes (this is a comprehensive guide to demonstrate how to navigate and complete submission in NMRR)
Useful links	Refer comments section	National Medical Research Register

Subsequent Reporting for MREC

Requirement	**How to Report**	**Timeline for submission/ reporting**	**Timeline for review & approval/ acknowledgment**	**Comments**
Amendments (Amendments in the study documents/ study team/ study sites)	Please refer to the User Manual/ Documents in the NMRR website for: User Guideline for Post Ethical Approval Submission (Amendment)		<u>Substantial Amendments:</u> 20 Working days <u>Non-Substantial Amendments:</u> 10 Working days	Please complete and submit together the MREC specific form for study amendment - **Amendment Application Form**. Decision whether the amendment submitted is substantial/ non-substantial will be decided by MREC. MREC decision letter is provided via e-mail to the Principal Coordinating Investigator.
Ethical Renewal	Please refer to the User Manual/ Documents in the NMRR website for: User Guideline for Post Ethical Approval	Submitted at least 2 months prior to the approval lapse date. (For details on	Within 30 days	Please use the MREC specific form for ethical renewal – **Continuing Review Form**

	Submission (Ethical Approval Renewal)	MREC approval expiry date, please refer to the MREC Initial Approval letter OR MREC Ethical Renewal letter).		MREC decision letter is provided via e-mail to the Principal Coordinating Investigator.
Study Closure/ Termination	Please refer to the User Manual/ Documents in the NMRR website for: User Guideline for Post Ethical Approval Submission (Closure/Termination Notification)	Study Final Report is submitted via NMRR within two (2) months from study completion. Study Termination Memorandum is submitted via NMRR within one (1) month from study termination.	10 working days	The Study Final Report is submitted when the study has been closed at all the MREC approved sites. The Study Termination Memorandum is submitted when the study is terminated prior to completion. Please use the MREC specific form for: Study Closure- **Study Final Report** Study Termination- **Study Termination Memorandum** MREC decision

				letter is provided via e-mail to the Principal Coordinating Investigator.
Notification for Protocol Deviation (PD)	Submission via PD Platform in NMRR. Please refer to User Guideline for Post Ethical Approval Submission (Protocol Deviation Reporting)	30 calendar days from the acknowledgement awareness of incident	Immediate acknowledgement e-mail from NMRR to Study Corresponding Person (CP) /Corresponding Person (CP) Back-up.	CP, CP Backup & Principal Coordinating Investigator are allowed to submit PD for all sites. Site Investigators only allow access and submit PD for their own sites.
Other Notifications (Interim Reports, Site Closure notification, etc.)	Please refer to the User Manual/ Documents in the NMRR website for: ✓ User Guideline for Post Ethical Approval Submission	-	Immediate acknowledgement e-mail from NMRR to Study Corresponding Person (CP) /Corresponding Person (CP) Back-up..	-

4.2.2 Medical Research Ethics Committee University of Malaya Medical Centre (UMMC-MREC)

4.2.2.1 Submission to Medical Research Ethics Committee University of Malaya Medical Centre (UMMC-MREC)

- It is the responsibility of the Principal Investigator to obtain approval from UMMC-MREC before starting the clinical trial/study. Principal Investigator must ensure that no subject undergoes any trial related procedures before the MREC issues its written approval/favorable opinion for the trial.

- The UMMC-MREC meets regularly once a month. The submissions must reach the UMMC-MREC secretariat by the first week of the month and ethics meetings are usually held on the third Wednesday of each month.

- Submission dateline and meeting schedule are available on the UMMC-MREC website at UMMC-MREC Meeting Dates.

- The Principal Investigator will be contacted by phone call and email if the study needs to be presented at the UMMC-MREC meeting.

- For any Interventional Clinical Research, which involves drugs or medical devices, the Principal Investigator must register with the National Medical Research Register (NMRR) before the approval letter is generated. Please provide a proof of the NMRR submission or approval from NMMR.

- Applications for new studies, amendments, notifications, etc. shall be performed via online system as below:

    - Portal Staff MyUMMC – for UMMC/UM Faculty of Medicine staff whom have Single Sign On (SSO) login (e-Service i Research).
    - eService SSO UMMC - for UMMC/UM Faculty of Medicine staff who do not have SSO login.

- The review timeline for MREC's first decision on a new study application is within 60 days from receipt of application by the Secretariat.

- For amendments, notifications or other revisions to an approved study, they shall be reviewed not later than 30 working days after classification (expedited/minor/major) by the Chair.

- The following events require prompt reporting to MREC:

    - Deviations from or changes to the protocol to eliminate immediate hazards to the trial subjects.

    - Changes or observations (including SAEs) that increase the risk to subjects and / or significantly affect the conduct of the trial.

    - New information that may adversely affect the safety of the subjects or the conduct of the trial.

    - Any trial, which is prematurely suspended or terminated.

4.2.2.2 Work Process and Documents Required for UMMC-MREC Submission

Initial Submission to UMMC-MREC

Document for Submission	**Required?**	**Comments**
Cover letter	No	Applicants can provide Cover Letter as optional to supplement the submission.
Application Form	Online submission	MREC Initial Submission via MyUMMC or Portal/UMMC eservices.
Protocol	Yes	English only.
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil (if needed).
Case Report Forms	If Applicable	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	
Clinical Trial Agreement	Yes	Draft would be sufficient.
Payments to Investigators / Site	Yes	Draft would be sufficient.

budget		
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee	Yes	MYR 1000 (Initial Submission) MYR 200 (Subsequent Amendment)
Online or manual submission	Refer comments section	Online submission by PI or site staff.
How to check submission status	Refer comments section	Site to check with EC or contact Clinical Investigation Centre for assistance.
Useful guidance documents / links	Refer comments section	UMMC Medical Research Ethics Committee (MREC)

Subsequent Reporting to UMMC-MREC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Online Submission. PI/SC to upload relevant documents into the submission portal.	PI/SC is able to print out the submission view page once all documents/information is uploaded. Approval letter can be expected within 30-60 days (online) from the completed submission.	Approval will be provided to the Principal Investigator (online).
Notification	Online Submission. PI/SC to upload relevant documents into the submission portal.	PI/SC is able to print out the submission view page once all documents/information is uploaded.	All protocol deviations must be reported.
Interim reporting/progress report/approval renewal	Online Submission. PI/SC to upload relevant documents into the submission portal. Site to complete Annual study report and study closure report form.	PI/SC is able to print out the submission view page once all documents/information is uploaded.	Approval will be provided to the Principal Investigator (online).
Completion of clinical trial	Online Submission. PI/SC to upload relevant documents into the submission portal. Site to complete Annual study report and study closure report form.	Closure report within one month after the study closure or termination. PI/SC is able to print out the submission view page once all documents/information is uploaded.	

4.2.3 Research Ethics Committee, Universiti Kebangsaan Malaysia (RECUKM)

4.2.3.1 Submission to Research Ethics Committee, Universiti Kebangsaan Malaysia (RECUKM)

- RECUKM is responsible for monitoring the conduct of approved research. In addition to the requirements stated in the approval letter from the RECUKM, the principal investigator shall:
  - Conduct the trial in compliance with the approved protocol.
  - Provide reports of the progress of the trial to the RECUKM, at a frequency directed by the RECUKM (6 monthly Progress Report Submission).
  - Duly notify the RECUKM of any protocol deviation during the conduct of the trial.
  - Notify, in the manner and form specified by the RECUKM, any Serious Adverse Events (SAEs) at any trial sites.
  - Inform the RECUKM as soon as possible of any new safety information from published or unpublished studies, or clinical use that may have an impact on the continued ethical acceptability of the trial.
  - Inform the RECUKM, giving reasons, if the trial is discontinued before the expected date of completion.

4.2.3.2 Work Process and Documents Required for Research Ethics Committee, Universiti Kebangsaan Malaysia (RECUKM)

Initial Submission to RECUKM

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	In English.
Application Form	Refer comments section	1. UKM-JEP-SS01 – UKM Research Ethics Committee Document Submission Checklist 2. UKM-JEP-SS02 – Document Checklist (Checklist for Research Involving Trial projects (Sponsor-Industry) only) 3. UKM-JEP- BO01 (UKM Research Ethics Committee Application Form) 4. UKM-JEP-BO02 (UKM Research Ethics Committee Review Form) 5. 5.UKM-JEP-BO08 (UKM Research Ethics Committee Conflict of Interest Form)
Protocol	Yes	English Only.
Protocol Signature Page	No	
Investigator's Brochure	Yes	English Only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional and will not be required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	

PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	
Other Documents Required, including documents related to other site staff, physician indemnity or insurance etc.	Refer comments section	1. Summary of proposal 2. Document Acceptance Checklist
Site contracts with sponsor	Yes	Draft Contract is sufficient.
Payments to Investigators / Site budget	Yes	Draft Budget is sufficient.
Payments to Subjects	Yes	The amount of Subject Travel Reimbursement needs to be mentioned in the ICF.
Slides presentation (10 slides) about the study	Yes	
Online or manual submission	Refer comments section	Manual submission: Required 1 copy for EC, 1 copy for PI. Submission of softcopy via email to EC Secretariat for SSPI initial review and verification. Once approved, prepare the hardcopy of submission and send to *the Sekretariat Penyelidikan Perubatan & Inovasi (SPPI), PPUKM*. Primary reviewer will then review the contents and issue any queries if applicable prior to the scheduled EC meetings. PI may provide responses to the queries prior to the meeting.
How to check submission status	Refer comments section	Investigator to contact EC officers. EC will provide the decision in writing, which will outline the

		necessary changes for proposals requiring modifications, usually within ten (10) working days of the scheduled meeting.
Key contacts	Refer comments section	For the application from Faculty of Medicine UKM, all softcopies of study documents should be sent by email to EC Secretariat for review. Contact information as below and typically it takes no more than one week for the review and response. For Initial submission, please submit to: sepukm@ukm.edu.my Once approved, site to prepare the hardcopy and send to UKMREC, *Sekretariat Penyelidikan Perubatan & Inovasi (SPPI).* Address: Sekretariat Penyelidikan Perubatan & Inovasi Tingkat 2, Blok Pendidikan Pusat Perubatan Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, 56000, Cheras Kuala Lumpur EC Enquiry can be contacted: 1. Ms. Fatimah Binti Mat Zin Email : fatimahz@ppukm.ukm.edu.my c.c to sepukm@ukm.edu.my ● Inquiries regarding the EC meeting. ● Status of proposal after EC meeting. ● Amendment submission for EC meeting. ● Amendment submission after EC meeting. ● Amendment/update after EC approval. ● Notification submission ● Interim reporting/Progress report ● SAE/SUSAR Reporting
Useful guidance documents / links	Refer comments section	UKM Research Ethics Secretariat

Subsequent Reporting to RECUKM

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	1. Prepare EC submission Cover letter 2. To submit a soft copy of amendments along with signed cover letter via email to Ms. Fatimah Mat Zin and prepare 1 hardcopy for manual Submission to EC.	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the dossier.	Approval will be provided to the Principal Investigator. Form: UKM-JEP-BO04_Time Addition Form UKM-JEP-BO05_Change of researcher
Notification	Site to send 1 submission dossier (hard copy) to EC.	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the dossier.	All protocol deviations are required to be reported
Interim reporting/progress report/approval renewal	Once the application is verified as complete, 1 set of hardcopy applications must be submitted to the Secretariat of Medical Research & Innovation, PPUKM (SPPI) and Chairman of Research Ethics Committee UKM. Submit a cover letter with the required information.	Every 6 months, for the duration of the study. Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the dossier. Annual reports and requests for renewals must be sent to the UKMREC thirty (30) days prior to the expiry	

		date of the letter of ethics approval.	
Completion of clinical trial	Once the application is verified as complete, 1 set of hardcopy application must be submitted to the Secretariat of Medical Research & Innovation, PPUKM (SPPI) and Chairman of Research Ethics Committee UKM.	Principal Investigator to provide RECUKM with a final report within 30 days of the expiry date of the letter of ethics approval.	

4.2.4 Human Research Ethics Committee, Universiti Sains Malaysia (JEPeM)

4.2.4.1 Submission to Human Research Ethics Committee, Universiti Sains Malaysia (JEPeM)

- An application for review or for ethical approval to JEPeM-USM should be submitted by a Principal Investigator responsible for the ethical and scientific conduct of the research.

- All initial application to JEPeM-USM should be submitted via JEPeM online submission system at Application System for USM Research Ethics

- Applicants should fill up all the relevant forms in the online submission and upload all the necessary related documents.

- Complete application shall be considered for review in the upcoming JEPeM-USM meeting not more than twenty-five (25) working days upon receipt by the Secretariat.

- The Secretariat will acknowledge the receipt of a complete application. Incomplete application will be returned back to the applicant.

- The Secretariat will verify the completeness of the application by notify the research team via email.

- Tentative dates of JEPeM's meetings are available on the JEPeM website (Date of JEPeM Meeting). In general, JEPeM has 3 meetings a month.

- All medical research involving humans is encouraged to be registered with the National Medical Research Registry (NMRR). However, for research involving drugs (interventional and observational), NMMR registration is mandatory effective from 1 January 2014.

- MREC review and approval is only required for the studies that involve Ministry of Health (MOH) personnel or that is conducted in MOH facilities or funded by MOH research grants.

4.2.4.2 Work Process and Documents Required for Human Research Ethics Committee of Universiti Sains Malaysia (JEPeM)

Initial Submission to JEPeM

Document for Submission	**Required?**	**Comments**
Cover letter	Optional	In English.
Application Form	Refer comments section	All initial Application to JEPeM-USM should be submitted via JEPeM online submission system at System Application for USM Research Ethics Site will submit OBB Form via online application during initial application.
Protocol	Yes	English Only.
Protocol Signature Page	Yes	
Investigator's Brochure	Yes	English Only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional and will not be required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/ advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Refer comments section	To be submitted if applicable
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	

PI and Sub-Investigator GCP Certificate	Yes	
Other Documents Required, including documents related to other site staff, physician indemnity or insurance etc.	Yes (if applicable)	
Site contracts with sponsor	Yes	Draft Contract is sufficient.
Payments to Investigators / Site budget	Yes	Draft Budget is sufficient.
Payments to Subjects	Yes	No need to mention in the ICF. In order to keep the participation really voluntary, the PI needs to mention the honorarium but only after participants have signed the consent form. Once the participant agreed and signed the consent form, all the details about the honorarium including amount, how and when the payment will be made is available in the separate sheet of documents.
Online or manual submission	Refer comments section	Online submission for initial submission, Manual submission via email for post approval submission.
How to check submission status	Refer comments section	Investigator to contact EC officers.
Key contacts	Refer comments section	Mr. Mohd. Bazlan Hafidz Mukrim Secretary of Human Research Ethics Committee USM Division of Research & Innovation, Health Campus USM Health Campus Tel. No.: 09-767 2354 / 09-767 2352 / 09-7672350 Email: bazlan@usm.my / ctfatihah@usm.my
Useful guidance	Refer comments	JEPeM Application Forms

documents / links	section	

Subsequent Submission to JEPeM

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	1. Complete JEPeM-USM FORM 3(A)2021: STUDY PROTOCOL AMENDMENT SUBMISSION FORM *26/07/2021* 2. Manual Submission, all submission can be done via email to the Secretariat staff. Hard copies are not required. 3. Full board review for amendment that (may include but is not limited to): -Additional treatments or the deletion of treatments -Any changes in inclusion/exclusion criteria - Change in method of dosage formulation, (e.g. oral changed to intravenous) - Significant change in the number of subjects - Significant decrease or increase in dosage amounts 4. Site to contact EC to check on the approval status.	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the dossier.	Approval will be provided to the Principal Investigator.
Notification	Submit an email of notification letter to EC and EC will	Site to make a copy of the cover letter and obtain an	All protocol deviations are required to be

	acknowledge receipt. Study Protocol Noncompliance (Deviation or Violation) Report. JEPeM-USM FORM (D)2019: STUDY NON-COMPLIANCE REPORT	acknowledgement stamp when submitting the letter.	reported
Interim reporting/progress report	Ethical clearance or approval is typically granted for a period of one (1) year. Continuing review is required to be done once a year. JEPeM-USM FORM 3(B)2019: CONTINUING REVIEW APPLICATION FORM*26/07/2021*	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the letter. - to be submitted 60 days prior to expiry date.	The frequency of continuing review is indicated in the Study Protocol Approval Letter.
Completion of clinical trial	Final Report Form for Interventional Study. JEPeM-USM FORM 3(C)(i) 2019: FINAL REPORT FORM FOR INTERVENTIONAL STUDY	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the letter.	
Early Study Termination	Early Study Termination Application Form. JEPeM-USM FORM 3(E)2019: EARLY STUDY TERMINATION APPLICATION FORM	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the letter.	Approval of this application would require further completion of JEPeM-USM FORM 3(C)(i) 2019: FINAL REPORT FORM FOR INTERVENTIONAL STUDY

4.2.5 Research Ethics Committee (REC), Universiti Teknologi Mara (UiTM)

4.2.5.1 Submission to Universiti Teknologi Mara (UiTM) Research Ethics Committee (REC)

- The Universiti Teknologi MARA (UiTM) Research Ethics Committee (REC) was established and approved by the Vice Chancellor of UiTM in 2004. The Committee is on Tier 2 (Executive), under the governance of UiTM Research and Innovation, where it reports to the University Research Committee (JKIPU) and to the UiTM Senate. The REC consists of 19 members with various expertise (registered healthcare professionals, a statistician and other experts in research) from UiTM, 2 experts from other academic institutions and 2 lay members. Meetings are held on the third Tuesday every month.

- All research proposals involving human participants must be endorsed by the Faculty / Branch's Research Committee and ethics approval must be obtained from the UiTM REC prior to the data collection. In the case of studies involving researchers other than UiTM staff, or collecting data from participants from other institutions, ethical approval must also be sought from the relevant research ethics committee. For example, if data is to be collected from any governmental bodies under the Ministry of Health (MOH), researchers should obtain the approval from the Medical and Research Ethics Committee (MREC) of the MOH.

4.2.5.2 Work Process and Documents Required for Research Ethics Committee (REC), Universiti Teknologi Mara (UiTM)

Initial Submission to RECUiTM

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	1. Application Form for Ethics Approval (Borang REC 1/ 2016 Rev 1) 2. PART E - Ethical Questionnaire (Borang REC 1E / 2016) 3. Checklist for Applicants for site to fill out (Borang REC 4/2016)
Protocol	Yes	English only.
Protocol Signature Page	No	
Investigator's Brochure	Yes	English Only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English and Malay. Simplified Chinese and Tamil are optional and will not be required to be submitted if PI confirms that the study population would NOT require Chinese and Tamil. (UiTM Template for subject information sheet and consent form- Borang REC2/2016 BM and BI)
Subject recruitment procedures/advertisements	No	
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	

PI and Sub-Investigator GCP Certificate	Yes	
Other Documents Required, including documents related to other site staff, physician indemnity or insurance etc	Not applicable	
Site contracts with sponsor	Yes	
Payments to Investigators / Site budget	Yes	
Payments to Subjects	Yes	Need to be mentioned in the ICF.
Online or manual submission	Refer comments section	Online submission via Research Ethics Depository (RED). The User Manual is available at The Research Ethics Depository (RED) System Manual
How to check submission status	Refer comments section	The submission status is available in RED or Investigator to contact the Secretariat for REC.
Key contacts	Refer comments section	UiTM Research Ethics Committee Department of Research and Innovation Level 3 Bangunan Wawasan 40450 Shah Alam Selangor Darul Ehsan E-mail: recsecretariat@uitm.edu.my Office Number: 03 - 5544 1638/ 2890/ 2846/ 2049/ 2794 03 5521 14251
Useful guidance documents / links	Refer comments section	Research Ethics Committee UiTM

Subsequent Submission RECUiTM

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Send ONE (1) amendment submission dossier (hard copy and soft copy) to the REC Secretariat. i. The amendment form (REC 7) Template for Cover Letter (REC 10)	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the dossier. Submission should be made 2 weeks prior to the REC meeting. Decision will be given within 2 weeks after the REC meeting.	Approval will be provided to Principal Investigator.
Notification for	Send ONE (1) amendment submission dossier (hard copy and soft copy) to the REC Secretariat.	The Secretariat will email the notification or provide an acknowledgement stamp when submitting the dossier.	
Interim reporting/progress report/approval renewal	Send ONE (1) amendment submission dossier (hard copy and soft copy) to the REC Secretariat.	Submission should be made 2 weeks prior to the REC meeting. Decision will be given within TWO (2) weeks after the REC meeting.	Approval will be provided to Principal Investigator.
Completion of clinical trial	Send ONE (1) completion submission dossier (hard copy and soft copy) to the REC	The Secretariat will email the notification or provide an acknowledgement	

	Secretariat. ● The completion form (REC 8) ● Template for Cover Letter (REC 10)	stamp when submitting the form. The submission is within 6 months of study completion.	
Early Study Termination	Site to submit Research-Project-Closure-Report-Form.	Site to make a copy of the cover letter and obtain an acknowledgement stamp when submitting the letter.	

4.2.6 Sunway Medical Centre Independent Research Ethics Committee (SREC)

4.2.6.1 Submission to Sunway Medical Centre Independent Research Ethics Committee (SREC)

- The Sunway Medical Centre Independent Research Ethics Committee (SREC) is a committee established under the authority of Sunway Medical Centre Sdn Bhd (SunMed). It evaluates the ethical aspects of research in SunMed, ensuring that they are reliably conducted in accordance with both international and Malaysian standards of 'Good Clinical Practice' (GCP).

- SREC holds as its primary responsibility the safeguarding of the rights, safety, and well-being of all research subjects. As per GCP requirements, members of the SREC are drawn from medical and non-medical sectors to ensure sufficient objectivity and independence from SunMed clinicians undertaking the research. The Clinical Research Centre (CRC) is the Secretariat to SREC.

4.2.6.2 Work Process and Documents Required for Sunway Medical Centre Independent Research Ethics Committee (SREC)

Initial Submission to SREC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	Initial Application Form is available on website: Research Application Form Requires Research Approval Application Form, Research Approval Application Checklist
Protocol	Yes	English only
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	Mandatory for interventional study. Optional for minimal risk non-interventional study
Clinical Trial Agreement	Yes	Draft is acceptable

Payments to Investigators / Site budget	Yes	Draft is acceptable
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee	Yes	Please refer to the SREC Application guidelines
Online or manual submission	Manual	Manual submission to IEC. Requires 3 copies (1 original and 2 photocopies) of the completed application forms and supporting documents. Submit via secured email also the softcopies of the submissions.
How to check submission status	Refer comments section	To check directly with the secretariat via email.
Useful guidance documents / links	Refer comments section	SunMed Clinical Research Centre

Subsequent Submission to SREC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Manual submission to IEC Secretariat	The application outcome will be notified to the PI.	Requires 3 copies (1 original and 2 photocopies) of the completed application forms and supporting documents. Submit via secured email also the softcopies of the submissions.
Notification	Manual submission		Requires for Protocol deviation reporting, SAE reporting and SUSAR. Safety notifications via web such as DrugDev are also accepted.
Interim reporting/progress report/approval renewal	Manual submission		Submitted via a Cover Letter and Research Progress Report Form (i.e. Form 4).
Completion of clinical trial	Manual submission		Submitted via a Cover Letter and Research Closure Report Form (i.e. Form 5).

4.2.7 Institut Jantung Negara Research Ethics Committee (IJNREC)

4.2.7.1 Submission to Institut Jantung Negara Research Ethics Committee (IJNREC)

- The primary purpose of the IJNREC, a subcommittee of Research Committee, is to protect the rights and welfare of human subjects involved in research activities being conducted in Institut Jantung Negara (IJN).

- Chairman, IJN Research Ethics Committee, shall be responsible for the constitution of IJNREC and has a minimum number of eight (8) members and maximum of fifteen (15) members.

- IJNREC shall meet at least four (4) times a year. Additional meetings will be scheduled as necessary. The meeting dates will be published on the website.

- An application that has been accepted for review and assigned a reference number should not make any revisions, prior to the IJNREC meeting.

4.2.7.2 Work Process and Documents Required for International Institut Jantung Negara Research Ethics Committee (IJNREC)

Initial Submission to IJNREC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	Research Registration Form (CRD-QR-A01) and IJNREC Application Form (CRD-QR-A02)
Protocol	Yes	English only. Requires a summary (as far as possible in non-technical language), synopsis, or diagrammatic representation ('flowchart') of the protocol.
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	Required to submit in English.
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	GCP certificate accredited by NCCR
Clinical Trial Agreement	Yes	Draft is acceptable

Payments to Investigators / Site budget	Yes	Draft is acceptable
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee	Yes	
Online or manual submission	Online Submission	A completed application should be received not later than 10 working days before the next scheduled IJNREC meeting. Requires 15 copies of Research Proposal and supporting documents.
How to check submission status	Refer comments section	All applications shall receive notification in writing of the decision of the IJNREC not later than 90 working days after acknowledgement of receipt of completed application.
Useful guidance documents / links	Refer comments section	REC - Submission - Institut Jantung Negara

Subsequent Reporting to IJNREC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Manual Submission	The application outcome will be notified to the PI.	Amendment Application Form (CRD-QR-A07)
Notification	Manual submission		Requires for Protocol deviation reporting, SAE reporting and SUSAR.
Interim reporting/progress report/approval renewal	Manual submission		Application for Renewal Form (CRD-QR-A10). For ethical clearance or approval approaching the one-year expiry date and requiring a renewal or extension, it is advisable to submit the application 30 days prior to expiry date.
Completion of clinical trial	Manual submission		Notification of Closure Form (CRD-QR-A12)

4.2.8 IIUM Research Ethics Committee (IREC)

4.2.8.1 Submission to IIUM Research Ethics Committee (IREC)

● The IREC, initially known as ethics committee, was first established in 2004. The name was later changed to IREC in February 2012 to reflect its role as the University's ethics committee and this was endorsed by the highest authority of the university, the Senate at its meeting.

● All the application must be reviewed and approved by Kulliyyah Research Committee/ Institution.

● IREC chairperson and secretariat meet on as mentioned in Schedule unless otherwise specified. The meeting schedule is available on website. Meeting will hold at least 4 times annually. Tentative Meeting Date – IIUM Research Ethics Committee

4.2.8.2 Work Process and Documents Required for IIUM Research Ethics Committee (IREC)

Initial Submission to IREC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	Register the application submission at Initial Review – IIUM Research Ethics Committee Please obtain application ID and download link of the submitted form
Protocol	Yes	English only. Requires completion of Protocol checklist
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	
Clinical Trial Agreement	Yes	Draft is acceptable

Payments to Investigators / Site budget	Yes	Draft is acceptable
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee	Yes	For Sponsored Trial: MYR 1,000 (IIUM Staff) and MYR 1,500 (Non IIUM Staff) For Investigator Initiated Trial: Waive (IIUM Staff) and MYR 500 (Non IIUM Staff)
Online or manual submission	Hybrid Submission	The hard copies of submission package and the downloaded application form are submitted to IREC Secretariat.
How to check submission status	Refer comments section	The Full review application should not take longer than 3 months subject to the date of IREC Meeting.
Useful guidance documents / links	Refer comments section	IIUM Research Ethics Committee

Subsequent Reporting to IREC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Online Submission	The Super Expedited and Expedited review should not take longer than 4 weeks, from the date of receipt of the study protocol considering the completed submission package and application queue.	Investigators are required to submit an Amendment form together with every amended document requested. Amendment will take about twenty (20) working days or up to sixty (60) working days if a full-board review is required.
Notification	Online Submission		Requires for Protocol deviation reporting, SAE reporting and SUSAR.
Interim reporting/progress report/approval renewal	Online Submission		Ethics approval by IREC only valid for one (1) year, therefore investigator need to submit request for continuing review. Investigator are required to submit Continuing Review form one (1) month before the current approval expiry. Continuing Review will take about twenty (20) working days or up to sixty (60) working days if a full-board review is required.
Completion of clinical trial	Online Submission		Investigators are required to submit the End of Study Report form together with

			study abstract/summary to IREC after the completion of the study. Review and decision on closing of file shall take 10 working days or up to sixty (60) working days if a full-board review is required.

4.2.9 Jawatankuasa Etika Universiti Putra Malaysia JKEUPM (ETHIC COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECT)

4.2.9.1 Submission to Jawatankuasa Etika Universiti Putra Malaysia JKEUPM (ETHIC COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECT)

- The Ethics Committee for Research Involving Human Subjects (more commonly referred to with its Malay acronym, JKEUPM) was established under the authority of the Senate of Universiti Putra Malaysia on 8 September 2011. JKEUPM is specifically given the task of protecting research participants, and to make researchers be responsible in ensuring that the basic principles regarding the use of human subjects are observed in their research.

- JKEUPM is guided by the National and International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS). JKEUPM recognizes ethical clearance from other Ethics Committees, e.g. from the Ministry of Health and other universities, which are recognized by the National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia. Thus, a research project which has received ethical clearance from any of these other committees does not require a separate clearance from JKEUPM.

4.2.9.2 Work Process and Documents Required for Jawatankuasa Etika Universiti Putra Malaysia JKEUPM (ETHIC COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECT)

Initial Submission to JKEUPM

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	The form is available online. JKEUPM Application Forms
Protocol	Yes	English only.
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP Certificate	Yes	
Clinical Trial Agreement	Yes	Draft is acceptable

Payments to Investigators / Site budget	Yes	Draft is acceptable
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee	Yes	RM1000 fee charge applies to the INDUSTRY with reference to a research project which receives sponsorship from a pharmaceutical company and known as Industry-sponsored Clinical Research. (The research protocol is prepared by the company).
Online or manual submission	Online Submission	PI submits a complete set of documents to JKEUPM Secretariat at jkeupm@upm.edu.my For Full Board Review, PI needs to present the protocol during Full Board Meeting, the decision will be notified to PI through email.
How to check submission status	Refer comments section	Under usual circumstances, the time taken for study protocol approval shall depend on the revision timeline as stated i.e. 60 working days for any revision from the day of first review and 30 working days from the first day of review.
Useful guidance documents / links	Refer comments section	JKEUPM

Subsequent Reporting to JKEUPM

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Online Submission	PI submits a complete set of documents to JKEUPM Secretariat at jkeupm@upm.edu.my	
Notification	Online Submission	PI submits a complete set of documents to JKEUPM Secretariat at jkeupm@upm.edu.my	
Interim reporting/progress report/approval renewal	Online Submission	PI submits a complete set of documents to JKEUPM Secretariat at jkeupm@upm.edu.my	
Completion of clinical trial	Online Submission	PI submits a complete set of documents to JKEUPM Secretariat at jkeupm@upm.edu.my	

4.2.10 Independent Ethics Committee Subang Jaya Medical Centre (IEC SJMC)

4.2.10.1 Submission to Independent Ethics Committee Subang Jaya Medical Centre (IEC SJMC)

- Independent Ethics Committee Subang Jaya Medical Centre is an ethics committee fully registered with the National Pharmaceutical Regulatory Agency.
- This committee is an independent body constituted of medical, scientific and lay members who collectively have the qualifications and experience to review and evaluate the scientific, medical and ethical aspects of a proposed research project.
- Scope of coverage: Subang Jaya Medical Centre, Bukit Tinggi Medical Centre, Ara Damansara Medical Centre, Parkcity Medical Centre
- All clinical trial submissions must be registered with NMRR and obtain NMRR ID prior to the submission to IEC Subang Jaya Medical Centre (IEC SJMC)

4.2.10.2 Work Process and Documents Required for Independent Ethics Committee Subang Jaya Medical Centre (IEC SJMC)

Initial Submission to IEC SJMC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	To retrieve from SJMC Clinical Research Application | Subang Jaya Medical Centre
Protocol	Yes	English only
Protocol Signature Page	No	
Investigator's Brochure	Yes	English only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil.
Subject recruitment procedures/advertisements	Refer comments section	Mandatory to submit if to be used in study. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	Signed and dated
Sub-Investigator CV	Yes	Signed and dated
PI and Sub-Investigator GCP Certificate	Yes	PI and Sub-Investigator GCP Certificate is mandatory for interventional study. This is optional for minimal risk non-interventional study.

Clinical Trial Agreement	Yes	In parallel with ethics review
Payments to Investigators / Site budget	Yes	While the ethics review process is ongoing, you may submit a draft version. Final version must be submitted once ethics approval is obtained.
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Initial Review Fee	Yes	A one-time application fee of RM 1,500 per research study is charged for the services of IEC to review sponsored research. The post approval submission fee can be referred to the application form or website.
Online or manual submission	Manual	Manual submission to IEC. ● One complete Research Application Dossier containing original hard copies of all documents. ● Three sets of Abbreviated Dossier containing Research Application Form, Protocol, Information Sheet/Consent Form, Investigator's Brochure. ● One soft copy of the complete research application documents (via email). All sets must be properly organized in a file with index dividers for easy referencing.
How to check submission status	Refer comments section	Principal investigator will be notified of the date and time of the IEC meeting (at least seven days in advance) where the application is to be reviewed.
Useful guidance documents / links	Refer comments section	SJMC Clinical Research Review Procedure | Subang Jaya Medical Centre

Subsequent Reporting to IEC SJMC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Manual submission to IEC Secretariat	The application outcome will be notified to the PI.	Requires 1 original Cover Letter, Application Form for Amendment and Updates to Research Project and amendment summary of changes. Submission requires 1 complete set of original hard copy documents and 2 abbreviated dossiers. Tracked changes and clean versions must be provided separately. All documents should include index dividers for easy referencing. Soft copy submission should include 1 complete set of documents, with tracked changes and clean versions provided separately.
Notification	Manual submission	Protocol deviation – within 30 days of awareness.	To report Deviations from, or changes of, the protocol To report the changes increasing the risk to subjects and/or affecting significantly the conduct of the trial To report on new information that may affect adversely the safety of the

			subjects or the conduct of the trial To report all adverse drug reactions (ADRs) that are both serious and unexpected affecting the subject.
Interim reporting/progress report/approval renewal	Manual submission	Annual Progress Report at least 30 days before expiry of ethical approval	Cover letter, Annual Progress Report form, any other supporting documents.
Completion of clinical trial	Manual submission	Study Closure Report 90 days after closure of the study	Submission should include: Cover letter Study Closure Application Form Study Closure Report

4.2.11 Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)

4.2.11.1 Submission to Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)

- The Research and Ethics Committee is established by the Board of Management (BOM) of Pantai Hospital Kuala Lumpur (PHKL) based on the ethical guidelines stated in the Declaration of Helsinki (2013). The operation of the REC is guided by the ethical principles outlined in World Health Organisation (WHO) Operation Guidelines for Ethics Committee that Review Biomedical Research, International Council for Harmonisation (ICH) and Malaysian Guideline for Good Clinical Practice, National and International Ethics Guidelines for Biomedical Research Involving Human Subjects (CIOMS).

- The Research and Ethics Committee comprises of both genders and a mix of scientific/ medical members, a legal representative and at least one (1) lay member. To oversee the various specialties of research undertaken at the hospital, the Research and Ethics Committee should consist of a minimum of 7 and maximum of 20 members who collectively have the qualifications and experience to review and evaluate the science, medical and ethical aspects of the proposed research. The Research and Ethics Committee Chairman, Deputy Chairman and Members will be appointed by hospital Person in Charge (PIC) upon the advice of the Medical and Dental Advisory Committee (MDAC). The duration of membership will be two (2) years.

4.2.11.2 Work Process and Documents Required for Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)

Initial Submission to PHKL REC

Document for Submission	**Required?**	**Comments**
Cover letter	Yes	
Application Form	Yes	Available online PHKL Application Forms
Protocol	Yes	English version is sufficient
Protocol Signature Page	Not compulsory but good if available	
Investigator Brochure	Yes	English only.
Informed Consent Form (ICF) and Patient Materials	Yes	Required to submit in English, Malay and Simplified Chinese. Tamil is optional, and not required to be submitted if PI confirms that the study population would NOT require Tamil. Translation certificate is required for ISR Interventional study.
Subject recruitment procedures/advertisements	Refer comments section	Not mandatory, submit if applicable. To be submitted in applicable languages, i.e. English, Malay, Simplified Chinese and Tamil.
Case Report Forms	Yes	
Insurance Certificate	Yes	
PI CV	Yes	
Sub-Investigator CV	Yes	
PI and Sub-Investigator GCP	Yes	Only investigator with certified GCP will be approved.

Certificate		
Clinical Trial Agreement	Yes	Submit at least the draft for the IEC members to review
Payments to Investigators / Site budget	No	
Payments to Subjects	Yes	Must be specified in the ICF under the subject reimbursement section.
EC Meeting Fee (provide details - how much, when & how).	Yes	RM1300 for New Application and RM 250 per amendment. Invoice will be sent to the CRO/Sponsor IEC to waive the application fee for Investigator Initiated Research (IIR). As for non-commercial or non-sponsored research will be upon IEC judgment discussion.
Online or manual submission	Online	Submit a signed electronic copy of the form and all supporting documents to my.phkl.rec@pantai.com.my. Submissions in (CD/DVD/Thumbs drive). All sets must be properly organized in a file with dividers.

Subsequent Reporting to PHKL REC

Requirement	**How to Report**	**Timeline for submission review/meeting & approval**	**Comments**
Amendments	Online submission to IEC Secretariat	The application outcome will be notified to the PI.	Submit a signed electronic copy of the form and all supporting documents to my.phkl.rec@pantai.com.my.
Notification	Online submission		Submit a signed electronic copy of the form and all supporting documents to my.phkl.rec@pantai.com.my.
Interim reporting/progress report/approval renewal	Online submission		Submit a signed electronic copy of the form and all supporting documents to my.phkl.rec@pantai.com.my.
Completion of clinical trial	Online submission		Submitted via a Cover Letter.

4.3 Safety Reporting Procedures and Requirements

4.3.1 Serious Adverse Event (SAE) reporting

Ethics Committee	**Fatal / Life Threatening Events**	**Non-Fatal/ Non-Life Threatening Events**	**Reference**
MREC (involving MREC approved sites)	Initial report as soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.	No later than 15 calendar days from awareness of event by investigator.	Public FAQ SAER | National Medical Research Register Follow up information should be actively sought and submitted to MREC as soon as it becomes available. SAEs involving other Malaysian sites (but not MREC approved sites) need to be reported to MREC but this can be done periodically.
UMMC-MREC	All SAEs have to be reported by the investigator to UMMC-MREC immediately and not more than 48 hours of notification. A written report on the UMMC-MREC SAEs form (BK-MIS-1118) is to be submitted promptly and not more than 7 days to UMMC- MREC.		Medical Ethics Application Standard Operating Procedure (SOP), Section 7.24 (c) FAQ | UMMC-MREC
The Human Research Ethics Committee of USM (JEPeM)	Immediately		Final JEPeM-USM SOP III
RECUKM	***Local serious adverse events:*** A verbal report should be made within 48 hours of event occurrence or	Foreign serious adverse events: OTHER SAE, reports submitted within fifteen (15) calendar days upon receipt	Guidelines for Ethical Review of Clinical Research or Research Involving Human Subjects, Research Ethics Committee (REC), Universiti Kebangsaan Malaysia

	discovery. A written report should be submitted as soon as possible but no later than seven (7) calendar days upon awareness of the occurrence. An updated written report must be submitted within thirty (30) additional calendar days from the initial notification. ***Foreign SAEs:*** ALL FATAL OR LIFE THREATENING SAEs as soon as possible but no later than seven (7) calendar days upon receipt from sponsor or the Contract Research Organization (CRO).	from sponsor or the Contract Research Organization (CRO).	
Universiti Teknologi MARA (UiTM) Research Ethics Committee (REC)	Notification of Serious Adverse Events (SAEs) within 48 hours from the time when the SAEs were made aware of the site.		
Sunway	Both serious and unexpected occurring in the		

Medical Centre Independent Research Ethics Committee (SREC)	Sunway Medical Centre is to be reported to SREC within one working day from first knowledge by the investigator or his research team.	
Institut Jantung Negara Research Ethics Committee (IJNREC)	All incidents must be reported within 7 working days of the investigator's becoming aware of the incident. All SAE(s) must be notified to IJNREC within 24 hours. Fatal and life-threatening events must be reported within 48 hours of notification.	IJNREC SAE Reporting Form
IIUM Research Ethics Committee (IREC)	All internal SAEs (occurring in IIUM PI site) must be reported to the IREC within 72 hours of occurrence using the SAE Reporting form. External SAEs (occurring in participants at other sites) must be reported in a prompt manner if the information impacts the continued ethical acceptability of the trial. This includes cases where the information requires, or indicates the need for, a change in the trial protocol or information statement, including changed monitoring.	Post-Approval Submission – IIUM Research Ethics Committee
JKEUPM (ETHIC COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECT)	Initial report as soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.	No later than 15 calendar days from awareness of event by investigator.
Independent Ethics	Initial report should be submitted as soon as possible, but no later than 7 calendar days from awareness of the event by the	SJMC Clinical Research Review Procedure | Subang Jaya Medical Centre

Committee Subang Jaya Medical Centre (IEC SJMC)	investigator, followed by a complete report within 8 additional calendar days. No later than 15 calendar days from awareness of event by the investigator.	
Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)	Initial report should be submitted as soon as possible, but no later than 7 calendar days from awareness of the event by the investigator, followed by a complete report within 8 additional calendar days. No later than 15 calendar days from awareness of event by the investigator.	

4.3.2 Suspected Unexpected Serious Adverse Reaction (SUSAR) Reporting

<table>
<tr><th>Ethics Committee</th><th>Fatal / Life Threatening Events</th><th>Non-Fatal/ Non-Life Threatening Events</th><th>Reference</th></tr>
<tr><td>MREC (involving MREC approved sites)</td><td>Initial report as soon as possible but not later than 7 calendar days from awareness of SUSAR by investigator, followed by a complete report within 8 additional calendar days.</td><td>No later than 15 calendar days from awareness of event by investigator.</td><td>Public FAQ SAER | National Medical Research Register

SUSARs involving other Malaysian sites (but not MREC approved sites) needs to be reported to MREC but can be done periodically. Same applies for global SUSARs.</td></tr>
<tr><td rowspan="2">UMMC-MREC</td><td>As soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.</td><td>As soon as possible but no later than 15 calendar days from awareness of event by investigator. Follow up information should be actively sought and submitted as it becomes available.</td><td rowspan="2">Medical Ethics Application Standard Operating Procedure (SOP), Section 7.24 (d)
FAQ | UMMC-MREC</td></tr>
<tr><td colspan="2">The following foreign SUSAR do not require reporting:
I) Clinical Trial not conducted in UMMC.
ii) Suspected drug is known to be other than trial drug (e.g. Other treatments, placebo or comparator drug).
iii) SAE and not drug related.
iv) Suspected Expected Serious Adverse Reaction.</td></tr>
</table>

The Human Research Ethics Committee of USM (JEPeM)	Immediately	Final JEPeM-USM SOP III
RECUKM	Overseas SUSAR: Reports are submitted within thirty (30) calendar days upon receipt from the sponsor or the Contract Research Organization (CRO).	Guidelines for Ethical Review of Clinical Research or Research Involving Human Subjects, Research Ethics Committee (REC), Universiti Kebangsaan Malaysia
Universiti Teknologi MARA (UiTM) Research Ethics Committee (REC)	No later than 15 calendar days from awareness of event by the investigator. For more detailed information, please contact the IEC Secretariat.	
Sunway Medical Centre Independent Research Ethics Committee (SREC)	SAEs reported outside Sunway Medical Centre (e.g. Those received via CIOMS reports in Multicenter Studies) are to be notified to SREC within one month of its receipt by the Investigator or his/her research team.	
Institut Jantung Negara Research Ethics Committee (IJNREC)	All other external SAEs need only be submitted if they are suspected or unexpected (SUSAR) and may be submitted as a periodic listing. A periodic listing of SUSARs must be submitted at least six monthly (using Periodic SAE form)	IJNREC SAE Reporting
IIUM Research Ethics	External SAEs (occurring in participants at other sites) must be reported in a prompt	Post-Approval Submission – IIUM Research Ethics Committee

Committee (IREC)	manner if the information impacts the continued ethical acceptability of the trial. This includes cases where the information requires, or indicates the need for, a change in the trial protocol or information statement, including changed monitoring. All other external SAEs (that do not fit the above criteria) need only be submitted if they are suspected and unexpected (i.e. SUSARs) and may be submitted as a periodic listing. A periodic listing of SUSARs must be submitted at least six monthly using the SUSAR Report form.	
JKEUPM (ETHIC COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECT)	No later than 15 calendar days from awareness of event by the investigator. For more detailed information, please contact the IEC Secretariat	
Independent Ethics Committee Subang Jaya Medical Centre (IEC SJMC)	No later than 15 calendar days from awareness of event by the investigator. For more detailed information, please contact the IEC Secretariat.	
Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)	SUSARs involving other Malaysian sites needs to be reported however can be done periodically. Same applies for global SUSARs.	

5 Other Clinical Trial Requirements

5.1 Study Drug Supplies

- The Certified True Copies of the Clinical Trial Import License (CTIL) and Pharmacist License A are required to be with the clearance vendor at the airport for shipment release.

- It is important to note that within the guidelines, there is a requirement that the CTIL holder shall submit to the DCA the Drug Accountability Report for Importation. This would require the CTIL holder to keep track of the quantities of clinical trial drug that is imported within the country and that it does not exceed the quantity approved by NPRA. The format of this report is indicated within the Malaysian Guideline for Application of CTIL and CTX. It is critical that the shipment quantities are being tracked on an on-going basis and to ensure an application of variation is submitted to obtain additional approved quantities, if needed, ahead of time.

5.2 Biological Samples Importation/Exportation

- Governing Acts and Regulations
  - Prevention and Control of Infectious Disease Act 1988
  - Prevention and Control of Infectious Diseases (Importation and Exportation of Human Remains, Human tissues and Pathogenic Organisms or Substances) Regulations 2006

- The import/export permit can be applied for through an online application using the BLESS system version 1.0 (Portal BLESS). The applicant needs to complete the online application form by selecting the respective health office / district health office and provision the following documents: a copy of NRIC or passport of the applicant, information about the tissue or part thereof, a certification or documentation from the importing or exporting country and information or documentation on method of disposal. There are fees to be paid for the private sectors and the amount depends on the risk group category for the specimens that are being exported.

- An import/export permit for the year will be issued upon approval. The copy of the permit needs to be provided together with other shipping documents such as proforma invoices, airwaybills at the time of importing/exporting the specimens. The import/export permit needs to be renewed annually, or if there is any change to the current laboratory(ies), including the relocation address or the entity name.

- However, if the applicant is unable to upload certain documents, the documents could be submitted manually (either via post or to the agency's counter) based on the requirements from the respective agency. For the manual submission, the applicant is required to specify the BLESS submission number in each document for reference.

5.3 Communication, Multimedia and Hybrid Product Importation

- Governing Acts and Regulations for importation of communication equipment.
  - Customs Act 1967 Customs (Prohibition of Imports) Orders 2017

- Communication product: Any network facilities or customer equipment used for connecting to a public communications network or for radio communications using a frequency band of up to 420 THz.

- Hybrid product: Any hardware or device integrated with communication module for connecting to public communication network or for radiocommunications utilizing band up to 420 THz. (i.e.: Wi Fi, Bluetooth, ANT, NFC, Zigbee, WPT, Qi, RFID, LoRA , NB IoT, GSM, 3G, 4G LTE, 5G).

- Both of these product categories must be certified before they can be used or sold in the local market as outlined in the Communication and Multimedia Act 1998. Certification for communication equipment is carried out by SIRIM QAS International Sdn. Bhd. (SIRIM QAS), a registered certifying agency with the Malaysian Communications and Multimedia Commission (MCMC).

- The importer is required to register and submit an application in e-ComM system (eComM - Online Certification for Communication and Multimedia Products) for an approval

process. Once application in e-ComM system is approved, the importer may submit an import permit application in e-Permit system for custom acknowledgement. There are fees associated with the online certification as well as the import permit.

- For more information on application related to communication devices, please contact WhatsApp Hotline +6019-717 2627 or email sirimepermit@sirim.my or visit SIRIM QAS website (Communication, Multimedia and Hybrid Product | SIRIM QAS International Sdn. Bhd.)

5.4 Medical Device Importation/Exportation

Medical Device Authority (MDA)

Medical Device Authority (MDA) is the government agency entrusted to serve the Malaysia medical device's industry. It is a federal statutory agency under the Ministry of Health Malaysia to implement and enforce the Medical Device Act 2012 (Act 737). The main objectives of the Act are to address public health and safety issues related to medical devices and to facilitate medical device trade and industry.

In February 2005, the Cabinet approved the proposal for the development and implementation of medical device regulatory program. Subsequent to the Cabinet decision, Medical Device Authority Act 2012 (Act 738) and Medical Device Act (Act 737) have been published in the Gazette on 9th February 2012.

MDA was established under the Act 738 on 15 March 2012 and has been officially and fully in operation since 16 June 2012.

The exemption from registration for medical devices for clinical research or performance evaluation was initially implemented through MDA Circular Letter No. 3 Year 2014 and later replaced by Medical Device (Exemption) Order 2016. However, this circular letter is no longer effective and shall be referred to as Medical Device Exemption (Order) 2024. Other than clinical research or performance evaluation, medical device that fulfil the criteria for personal use, demonstration for marketing and education, custom made and special access are also eligible for exemption from registration requirement under the specified Order.

A comprehensive information on procedure to notify the Authority for medical device exemption from registration requirement for the purpose of clinical research or performance evaluation can be retrieved from the official portal (www.mda.gov.my).

5.4.1 Guideline documents

The documents as guideline for conducting clinical research or performance evaluation that involves medical devices are:

- Malaysian Standard: Medical Devices - Quality Management Systems - Requirements For Regulatory Purposes (ISO 13485)

- Medical Device Guidance Document (MDA/GD/0016 April 2017) : Notification Of Exemption From Registration Of Medical Devices For The Purpose Of Clinical Research Or Performance Evaluation

- Malaysian Standard: Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155)

- Malaysian Standard: Medical devices - Application of risk management to medical devices (ISO 14971)

- Relevant international standards on specific medical device under investigation of a study.

5.4.2 Notification processes

5.4.2.1 The notification processes consist of 2 routes which are:

- Clinical Investigational Use:

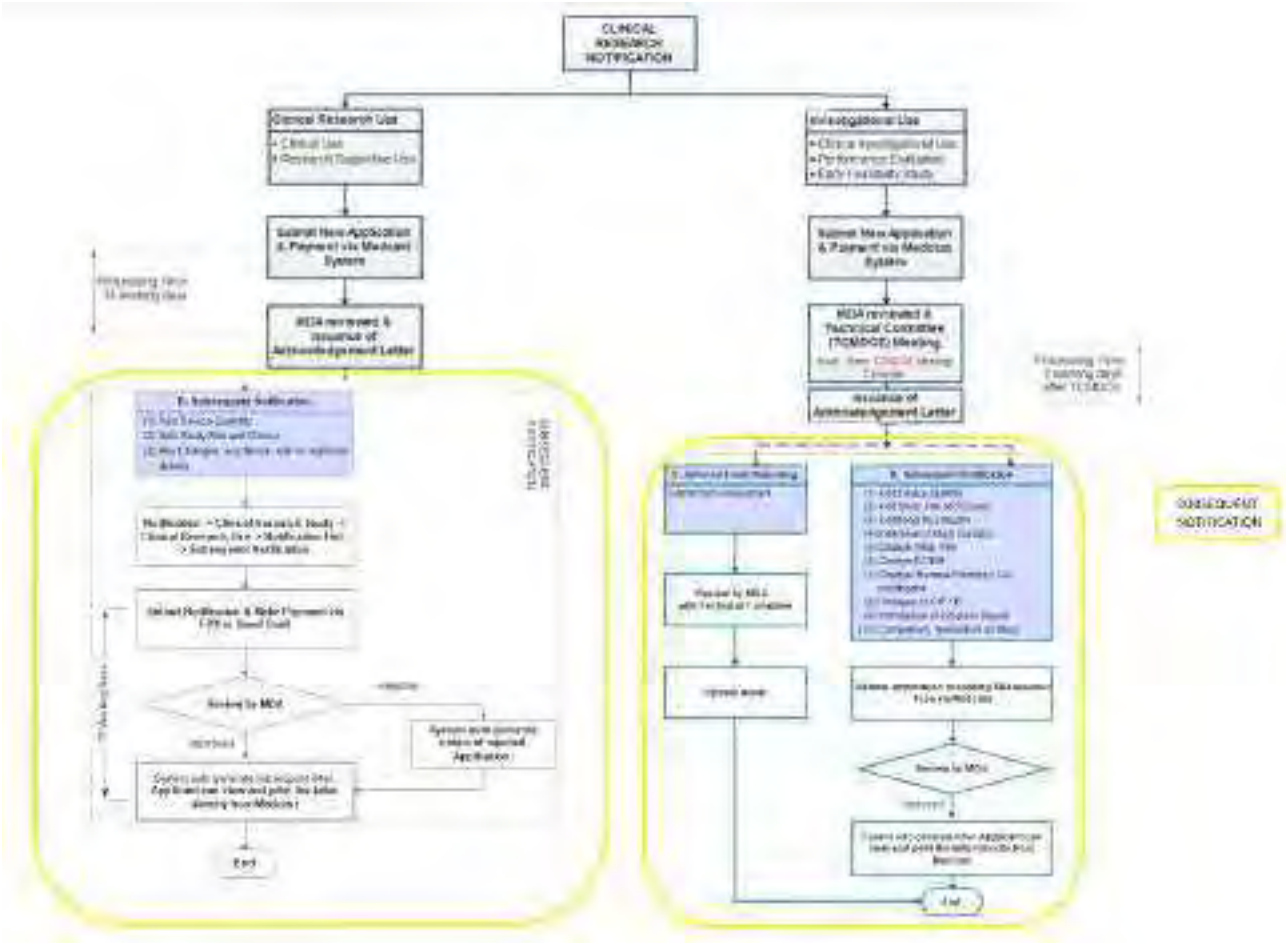
The use of an unregistered device in a clinical investigation designed to generate clinical data on the clinical performance and safety of the device required to support the Pre-Market Approval submission for device registration.

- Clinical Research Use:

(i) The use of an unregistered or registered device to generate clinical experience data that is outside the conduct of a clinical investigation, on the clinical performance and safety of the device required to support the Pre-Market Approval submission for device registration.

(ii) The use of an unregistered device in the context of another health research. The device per se is not under investigation but is required to make the research feasible to be conducted in Malaysia.

Below is the diagram showing the flow of notification:



5.4.2.2 Notification process:

Process	Description	
	Clinical Investigational Use:	**Clinical Research Use:**
Similarities		
Initial Notification	Applicant shall submit to the Authority a Notification of Exemption from Registration of Medical Devices for Clinical Research, using the online form through MeDC@St 2.0 (https://medcast.mda.gov.my)	

Applicant	Application can be made by an investigator, local sponsor, manufacturer, an authorised person from a local organisation (in the case of foreign sponsor) or Contract Research Organisation (CRO).	
Letter of 'Acknowledgement on Notification'	Letter of 'Acknowledgement on Notification' by MDA will be issued to the applicant after approval.	
Subsequent Notifications	Subsequent and changes notification can be made on the study after online submission of notification via MeDC@St 2.0. Additional device or site of study is applicable for both notifications of Clinical Investigational Use and Clinical Research Use.	
Administrative Charge	All new notifications shall be accompanied together with an administrative charge of RM 300 per notification.	
Differences		
TCMDCE Meeting Required	The applicant is required to present on the study proposal in the TCMDCE meeting. The approval for letter issuance is based on the decision made through the meeting. The meeting is to be held once every month and the schedule of meeting is as announced in the TCMDCE calendar in MDA Portal.	Not Applicable
Ethical Approval	The ethic approval can only be obtained after MDA approval.	Ethic approval letter by IRB/IEC shall be submitted together during submission of notification.

Notification of Change	Changes that involve trial sites, Principal Investigator, IRB/IEC, or others such as changes on study duration and changes on CIP / IB need to be notify to the Authority.	only changes of device and trial site need to be notified to the Authority.

5.4.2.3 Supporting documents required for Notification on Clinical Investigational Use:

- Clinical Investigation Plan (CIP)

The clinical investigation plan (CIP), in written form, defines the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation. It contains in particular the information as laid down below. If part of this information is submitted in a separate document, it is referenced in the CIP.

- Investigator's Brochure (IB)

The investigator's brochure (IB) contains the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. Any updates to the brochure or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner.

- The aspects that the CIP and IB should contain is defined in the Medical Device Guidance Document (MDA/GD/0016 April 2017).

5.4.2.4 Supporting documents required for Notification on Clinical Research Use:

- Ethic approval by IRB/IEC
- Packing List for Study-Visits Specific Kits

5.4.2.3 Supporting documents required for Notification on Clinical Investigational Use:

- Clinical Investigation Plan (CIP)

The clinical investigation plan (CIP), in written form, defines the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical investigation. It contains in particular the information as laid down below. If part of this information is submitted in a separate document, it is referenced in the CIP.

- Investigator's Brochure (IB)

The investigator's brochure (IB) contains the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. Any updates to the brochure or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner.

- The aspects that the CIP and IB should contain is defined in the Medical Device Guidance Document (MDA/GD/0016 April 2017).

5.4.2.4 Supporting documents required for Notification on Clinical Research Use:

- Ethic approval by IRB/IEC
- Packing List for Study-Visits Specific Kits

5.4.3 Conditions of notification

The notification of exemption from registration of medical devices for the purpose of clinical research or performance evaluation shall be subjected to the following conditions:

- The unregistered medical devices shall only be permitted for import by the applicant.

- The applicant shall be responsible for ensuring that the quality, safety and performance of the unregistered medical device are not adversely affected during import, storage and distribution of the medical devices.

- The applicant shall ensure that medical devices for clinical investigational use is designed, conducted and reported in accordance to ISO 14155, Clinical research of Medical Devices for Human Subjects – Good Clinical Practice.

- The applicant shall ensure the relevant Ethics Committee approval has been obtained for each investigation site.

- The applicant for Clinical Investigational Use shall inform Medical Device Authority of any incidents arising from the use of the unregistered medical devices for clinical research /performance evaluation that become known to the applicant as according to Form SADE (can be downloaded from MDA portal and submitted manually through email). Any adverse consequence that results from the use of the medical device shall be the responsibility of the applicant. The applicant shall report the incident/problem to the Authority. The incident/problem reporting must be reported to Medical Device Authority within 48 hours of the occurrence of the incident. The applicant shall indemnify against all actions, claims or proceedings in respect of any incidents, problems injury to or death of any person whomsoever arising out of or in connection with the use of the unregistered medical device(s). This condition does not apply to Clinical Research Use.

- The applicant shall maintain records on the distribution of the unregistered medical device at the clinical research /performance evaluation sites.

- Upon completion of the clinical research /performance evaluation, the applicant shall make a declaration using the form: Notification for Export /Disposal of Devices Upon Completion /Termination of Clinical Investigation (can be downloaded from MDA portal). This declaration shall be submitted to the Authority through email within 30 days after the date of completion. However, upon completion of a Clinical Research Use, this declaration is not required.

- Should the clinical research /performance evaluation terminate earlier than the proposed date or temporarily suspended, Medical Device Authority shall be notified of the reasons for termination or suspension within two (2) weeks of the clinical research /performance evaluation being discontinued using the same form as stated above.

- The approved quantity of the unregistered medical devices shall be indicated with—NOT FOR SALE, FOR CLINICAL INVESTIGATION/CLINICAL RESEARCH/ PERFORMANCE EVALUATION PURPOSES ONLY.

- All remaining unused supplies of the unregistered medical device(s) shall be returned to the Sponsor.

- All medical devices involved in clinical research except the used disposables shall be returned to Sponsor.

- Applicant for Clinical Investigational Use shall submit a progress report every 6 months through email, following template as perform in Clinical Investigational Use Progress Report that can be retrieved from MDA portal. This condition does not apply to Clinical Research Use.

- Any other conditions may be requested by the Authority from time to time.

- The medical devices should be labeled accordance with labelling requirement specified by the Authority.

6 Clinical Trial Agreement and Study Budget

Clinical trial agreement (CTA) is a legally binding contract that manages the relationship between the parties involves namely sponsor, the institution and principal investigator/payee. It is an important legal document in clinical trial as it documents and formalizes the understanding between the parties and provides a legal and financial terms relating to the performance of a clinical trial.

In Malaysia, CTA and budget related to employees of Ministry of Health (MoH) Malaysia will be reviewed and endorsed by Clinical Research Malaysia (CRM). CRM is authorized by the Malaysia's government for these purposes representing the clinical research industry in Malaysia. Whereas CTA which involves negotiation with private hospitals and Ministry of Higher Education (MoHE) (e.g. University Hospitals) usually has their own local unit of Clinical Research Centre (CRC) whom will manage, negotiate and finalize the contract.

This includes the clinical trials initiated by the investigators themselves. Investigator Initiated Research (IIR) or Investigator Initiated Trial (IIT) may or may not require CTA depending on the procedures involved as well as the category of clinical trials.

CTA is mentioned in International Conference on Harmonization Good Clinical Practice (ICH-GCP) as well as Malaysian Guideline of Good Clinical Practice (MGCP).

ICH-GCP 1.17: "A contract is a written, dated and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract."

ICH-GCP 4.9.6 & 5.9: "The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator or institution."

MGCP 5.1.4 of the GCP provides that all agreements made by the sponsor with the investigator or any other party in connection with the trial should be in writing, as part of the study protocol or in a separate agreement.

6.1 Clinical Trial Budget

Budget negotiation can be a lengthy and tedious process because each trial has different budget based on the complexity of the clinical trial and the capital of the sponsor. Sometimes, due to insufficient budget, contracting parties could not reach agreement with budget and had to resort to termination of startup of a clinical trial. Also, there could be situation where sponsor faced financial constrain and had to terminate the clinical trial even though it has gone through start up and recruited several subjects.

In general, clinical trial budget should include the following purpose being paid or provided by sponsors:

1. Fair market value of the staff working hours proportionate and complexity to the clinical trial conduct.
2. Hospital charges for consumables, facilities and equipment if not provided by the sponsor.
3. Overhead charges in percentage or fixed price as specified by the trial site if applicable.
4. Adherence to local taxation system (example SST, VAT etc.). Currently, all services will be subjected to 8% SST (or at its prevailing rate) charges as implemented by Malaysia Government in accordance with Service Tax Act 2018 (if applicable).
5. Insurance and indemnity for the sponsor's protocol and IPs.
6. Institutional Review Board (IRB) fees / Regulatory application fees.

Clinical trial budget can be presented in various methods. The budget can be designed to be paid per subject enrolled, monthly fees and/or even on milestone achievements. Therefore, it is up to the contracting parties to negotiate the schedule of payment and method of payments. All the payments made payable to the site by the sponsor, must be clearly written in the CTA and its terms and condition for payment. Payment made to the site must be made in fair market value and also for only the work done related to the clinical trial.

Compensation for the trial subjects must be handled with caution and reasonable limits so that there will be no undue influence to them. In addition, the amount related to subject compensation will need to be approved by the EC. Usually, subject compensation cannot be paid due to loss of wages. This will be specified also in the CTA how much each subject will be paid for transportation or meal allowances. In addition, paid amount will be invoiced by the investigator/institution to the sponsor,

where sponsor may request investigator to provide payment records for the subjects for verification purposes.

6.2 Review and negotiation of CTAs

The requirements for reviewing CTAs lie with the contracting parties and their organizations. Sponsors/CROs usually have their corporate legal department to ensure all the terms specified in the CTA will be sufficient to adhere to the sponsor's local and/or international regulations of conducting clinical trials and the data collected can meet the requirement of their Regulatory Authorities. Whereas for the Investigators and Institutions who are being engaged by the sponsor to perform clinical trial, they will need to ensure the CTA are adhered to the local and/or international governing laws and bodies. Therefore, the negotiation process can be difficult to complete if it is a first working experience for particular Sponsor, Investigator or Institution. The negotiation process may also end with disagreement to certain terms and condition that lead to unsuccessful execution of a CTA.

According to MGCP 5.6.3 provides that the sponsor should obtain the investigator's/institution's agreement:

(a) To conduct the trial in compliance with GCP, with the applicable regulatory requirements(s) and with the protocol agreed to by the sponsor and given approval/favorable opinion by the IRB/IEC;
(b) To comply with procedures for data recording/reporting;
(c) To permit monitoring, auditing and inspection;
(d) To retain the trial related essential documents until the sponsor informs the investigator/institution these documents are no longer needed.

Below are some sections that are generally mentioned in a CTA and what they mean:

1. Definition of the signing parties:
   Sponsor and its affiliates, Investigators legal details and Institution's legal entity are being specified in this section. Usually the contracting parties mentioned will officially sign the CTAs in the signatories section.

2. Study title and Protocol ID:
   Title of the protocol and usually indicates as well to cover its amendments in the life of the clinical trial.

3. Independent Ethics Committee:
   Conditions and requirements of the investigators to follow recommendations of Ethics Committee that review, approve or disapprove the protocol.

4. Trial Conduct:
   Describe how the study will be conducted in accordance to which protocol.

5. Sponsor Drug or Investigational Product (IP):
   Define which drugs are owned by sponsor. Custodian and rights for dispensing, Control and use of IPs are defined as well. In addition, if there is any reimbursement for the IPs or comparator drug will be stated in this section.

6. Research Grant/ Funding:
   Funding or grant that sponsor will agree to pay to Investigator and Institution for conducting the clinical trial.

7. Trial Subject enrollment:
   The agreement of Investigator and Institution to enroll the subject in accordance to the protocol requirements will be defined in this section.

8. Informed Consent:
   Type of consent obtained from the subject that matches the protocol needs.

9. Adverse Event (AE):
   Any compensation and management of AE that sponsor is obligated to provide coverage and what will not be covered by the sponsor, e.g. protocol deviation or negligence.

10. Protected Health Information:
    This section will detail how the subject's health information is protected. Subject identifiers are not to be collected by the sponsor and how the subject's identity is blinded.

11. Confidential information:

    Sponsor will usually define which are the confidential information that the Investigators or Institution should not disclose to the public. How long this confidentiality agreement will last and methods of returning confidential information to the sponsor are also specified here. In addition, the law that governs this section will also be outlined.

12. Trial Data, Biological Samples and Records:

    Ownership of the trial data, medical records, personal information, biological samples and retention of this samples or information will be defined in this section.

13. Inspection and Audits:

    This section defines who will be authorized to perform Inspections and audits for the mentioned clinical trial. In addition, indication of who should be notified if the mentioned trial will be audited by internal or external parties.

14. Inventions:

    What will happen if new inventions or outcomes were generated by the clinical trial.

15. Publications or Publicity:

    Who will have the rights for publications on new findings from the study conduct and also if there is any restriction on using the names for advertising and promotion purposes.

16. Indemnification:

    Sponsor's indemnification, Investigator's indemnification and Institution's indemnification definition will be specified in this section. Exclusions, notification and settlement will be defined according to the applicable laws specified in this section.

17. Terminations:

    Conditions of trial conduct termination are specified in this section. This section also defines who can terminate the study in the specified conditions.

18. Insurance:

    Besides clinical trial insurance by the sponsor, investigator and institution will provide insurance coverage in accordance to local regulations.

19. Debarment, Exclusion, Licensure and Response:

    This is a declaration that the Investigators are not being barred or restricted to conduct clinical trials and have the appropriate license to conduct medical treatment or clinical trials.

20. Clinical Trial Governance:
    a. International Law
        i. Anti-bribery and corruption law
        ii. Personal Data Privacy Act (PDPA)
        iii. Applicable law of the sponsor's country
        iv. Anti-Money Laundering and Countering Financial Terrorism (AMLA) (if applicable)
    b. Country Law
        i. NPRA
        ii. Local or country EC
        iii. MDA
        iv. Cell and genetic engineering
        v. Personal Data Protection Act (PDPA)
    c. Responsible parties/Sponsor company policy
        i. Subject compensation policy
        ii. Compassionate use of IP policy
        iii. Lembaga Hasil Dalam Negeri (LHDN)

21. Governing Law and Dispute Resolution
    a. 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 Government /MOH site setting, the governing Law of the CTA must be Malaysian Law but in certain cases where the parties have limitations in the performance of the study due to their own policy and applicable law, the last resort is to consider contractual silence regarding this issue but cannot negotiate any other terms.

b. Dispute Resolution

This clause is to determine the type of dispute resolution in case there is any dispute encountered by the parties. Ideally, for Malaysia Government MOH Site setting, the parties shall attempt to resolve any dispute through mediation and 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. Eventually, it is up to the parties' preference.

Other sections such as assignment and delegation, equipment provided, duration of the obligations, Force Majeure and contact methods may also be defined in a clinical trial agreement.

6.3 Government/MOH Site/Institution

Government/MOH Site/Institution including full service general hospitals and health clinics where the application will be submitted to the MREC for Ethics Committee review. The CTA shall be submitted to CRM for their review and endorsement. CRM will provide a unique endorsement code number for each CTA that was reviewed and approved by CRM. CRM is authorized by the Institution and Principal Investigator of Government/MOH Site/Institution to manage and administer payments on their behalf and will be the Payee/contracting party (if applicable) of the CTA. According to government policy, the Sponsor/CRO/Collaborator to the CTA involving Government/MOH Site must be a Malaysian locally registered company, as Government MOH Site/Institution and Investigators/Staff are not allowed to sign the agreement directly with a Foreign Entity. When the necessity arises, CRM as a company limited by guarantee wholly owned by the Ministry of Health, Malaysia can sign into an agreement with a Foreign Entity on behalf of the Government Hospitals/Investigators. For more details, please visit their website Clinical Research Malaysia

6.4 University Hospital

For applications submitted to the Research and Ethics Committees of universities or private institutions, the requirement to submit the CTA for review and approval by the said Committees is subject to the specific rules of the university or institution. In most cases, the draft CTA would be one of the documents required to be submitted for approval.

Generally, all University hospitals have their own clinical research center that assist in connecting the interested investigators and sponsors to the correct contacts for legal review. Newly established university hospitals that may not have this special unit to assist in the clinical trial activities may not have a legal review department. Therefore, in such situations, they can utilize CRM to assist in legal review of the CTA for them which CRM's CTA template will be preferred.

6.4.1 University Malaya Medical Centre (UMMC):

Institution has own legal counsel for reviewing contracts including CTA. All CTA must go through legal review before execution. (Template is tripartite agreement)

Below is the brief introduction of the CTA negotiation process.

The process begins upon both parties i.e. Institution and Sponsor/Collaborator have mutually agreed to have a Clinical Trial/Research to be conducted in the said Institution.

Either Institution or Sponsor can be the first party to initiate the drafting process of Clinical Trial Agreement and the team that will be responsible to ensure the terms of the agreement is acceptable for both parties are Legal Officer and also Budget team. The negotiation of the terms of the Agreement will involve legal clauses and budget amount that is suitable for the said study.

The signature part can be either by the standard way i.e. the wet-ink signature or new way i.e. Digital Signature per stated in the procedure in accordance with Malaysia Digital Act 1997.

Upon both parties successfully executing the said Agreement, it is important to have the said copies of the Agreement to be stamped at *Lembaga Hasil Dalam Negeri* (LHDN) in accordance with rules stated in the Malaysia Stamp Act 1949. Please refer to CTA stamping process for more details.

In conclusion, it is important to have a complete agreement between both parties to protect the interest and the right of the parties to the Agreement and most importantly for the Agreement is prepared in accordance with the law so that it is functionable when it is needed.

Contact with the legal department for clinical trial can be found in the link below:
Website: Clinical Investigation Centre
Email Address: cic@ummc.edu.my

6.4.2 UKM Medical Centre (UKMMC)

Contact with the Principal Investigator for CTA and Study Budget review and negotiation process. Website: Clinical Trial Unit (CTU) - Secretariat of Research & Innovation Faculty of Medicine

6.4.3 Hospital Universiti Sains Malaysia (HUSM)

Institution has own legal counsel for reviewing contracts including CTA. All CTA must go through legal review before execution. (Template is tripartite agreement with USAINS named as Payee).
Website: USAINS Group Contract Research

6.4.4 Universiti Teknologi MARA (UiTM)

Contact with the Principal Investigator for CTA and Study Budget review and negotiation process. Website: CenTRE SERVICES

6.4.5 Monash University

Contact with the Principal Investigator for CTA and Study Budget review and negotiation process. Website: Research & Industry - Monash University Malaysia

6.4.6 University Putra Malaysia (UPM)

Contact with the Principal Investigator for CTA and Study Budget review and negotiation process. Website: Research With Agreement | HOSPITAL SULTAN ABDUL AZIZ SHAH (HSAAS) UNIVERSITI PUTRA MALAYSIA

6.5 Private Hospital

Each private hospital settings require some legal review of CTA by their board members. Therefore, each listed private hospitals has own procedures for legal review of any CTA templates that the sponsor may present. Therefore, the legal review timelines for each establishment will differ depending on their resources available.

6.5.1 National Heart Institute (Institut Jantung Negara)

The Institution requires all Clinical Trial Agreements (CTAs) to undergo review by its legal department before execution. The standard CTA template used is a tripartite agreement. All communication with the legal department regarding CTAs must be through the Principal Investigator (PI) at the trial site and facilitated and coordinated by Clinical Research Department.

CTAs can be executed using e-signature, wet-ink signature, or a combination of both, based on the agreement's requirements. Once fully executed, the agreement must be stamped at Lembaga Hasil Dalam Negeri (LHDN).
Website: Institut Jantung Negara - Largest Heart Hospital in Malaysia

6.5.2 Subang Jaya Medical Centre

Clinical Trial Unit coordinates hospital and group legal review of CTA and budget negotiation. Institution does not have specific template for CTA.
Website: SJMC Clinical Research Review Procedure | Subang Jaya Medical Centre

6.5.3 Gleneagles Penang, Loh Guan Lye Specialist Centre, Penang Adventist Hospital, Mount Miriam Cancer Hospital and Pantai Hospital

Having collaborative relationship with SMO Info Kinetics this could be contacted for more details on the website: SMO | INFO KINETICS

6.5.4 Sunway Medical Centre

Institution does not have specific template for CTA. However, their legal counsel must review all CTA before execution. (Template is tripartite agreement).
Website: Sunway Medical Centre Clinical Research Centre

6.5.5 Pantai Hospital Kuala Lumpur

Institution does not have specific template for CTA. However, their legal counsel must review all CTA before execution. (Template is tripartite agreement).
Website: Clinical Research | Pantai Hospital Kuala Lumpur

6.5.6 Beacon Hospital

Institution does not have specific template for CTA. However, their legal counsel must review all CTA before execution. (Template is tripartite agreement).

The CTA and budget draft will be sent to the Clinical Research Department (CRD) by the sponsor/CRO after the site is selected for a clinical trial. CRD will do CTA's first review for a department-level review then will be shared with the legal team for review. The first reviewed copy of the CTA will be shared with the sponsor /CRO for further review and comments. The CTA negotiation process is complete when all the clauses are agreeable by the research site (Beacon Hospital) and the sponsor/CRO. This complete process may take 4-8 weeks.

The study budget with the sponsor/CRO's proposed cost will be shared with CRD for review. CRD is to comment accordingly on the budget spreadsheet if the proposed cost by the sponsor/CRO is agreeable, provide justification if the cost is not agreeable, and propose a new cost. The complete budget negotiation may take 4-8 weeks.

The final clean copy of the CTA with the budget will be shared with the sponsor/CRO, principal investigator, and Institution representative for signatures to fully execute the CTA. Both the wet signatures and digital signatures are acceptable to the research site (Beacon

Hospital). The fully executed CTA will be sent for LHDN stamping if required by the sponsor/CRO.

Contact: clinicalresearch@beaconhospital.com.my
Website: Clinical Research Centre for Cancer Disease - Beacon Hospital

7 Insurance and Indemnity

7.1 Clinical Trial Insurance/Indemnity

According to the Malaysian GCP, section 5.8.1:

> *"If required by the applicable regulatory requirement(s), the sponsor should provide insurance or should indemnify (legal and financial coverage) the investigator/the institution against claims arising from the trial except for claims that arise from malpractice and/or negligence."*

Insurance is a system under individual or business entity or organization, where in exchange for payment (Premium) are guarantee compensation for losses resulting from certain perils under specified condition in a contract or policy.

7.2 Requirements

There are many insurance companies offering a broad range of coverage, each with its own terms and conditions. This can be confusing and a result, the process for acquiring coverage can be time-consuming. Whilst Malaysia has no legal act governing clinical trial activities (including clinical trial indemnification and insurance), the Malaysian GCP guideline states that such indemnification and insurance should be provided if required by applicable regulatory requirement(s).

It is a requirement by IEC/ IRB that all ethics submission for clinical trials must include proof of trial indemnification either by insurance certificate or letter of indemnity. These documents should indicate the protocol title and number, period of coverage and list of coverage for Malaysia sites among others. Insurance certificates that are renewed should be duly submitted to the ethics committee on an on-going basis.

Although NPRA's guidelines for application of clinical trial import license and clinical trial exemption in Malaysia does not mention indemnity/insurance specifically, the declaration document by Investigator (as in Appendix B2 of the guideline) includes a declaration by investigator stating the study has indemnity/insurance which covers for his/her activities in the clinical trial, as required in

Malaysia. This declaration document must be completed and submitted by investigator from all sites for a protocol applying for CTIL/CTX.

Section 4.5.7.2 of the CTIL/CTX Guidelines, 8th Ed. requires proof of insurance for FIH Clinical Studies. The insurance must include compensation policy of any damage suffered by a subject resulting from participation in a FIH clinical trial.

Any institution/center or investigator involved in clinical trial should be indemnified or insured for claims arising from 1) use of investigational medicinal product (IMP), 2) procedures/activities performed for clinical trial and 3) malpractice/negligence. Many sites and investigators normally believe these are provided by sponsor/CRO. However, in actuality, the indemnification/insurance only covers claims arising from use of investigational product and any procedures related to the particular trial. Sponsor and CRO are subject to non-indemnification for claims arising from malpractice and/or negligence by site and investigator.

Having the correct insurance coverage is part of clinical trial and the needs should be addressed as early as possible. At times, running a multi-center clinical trial in Malaysia can be complex due to different administrative or clinical practice culture and therefore, the needs of/for insurance is often misunderstood and warrants a good underwriter with expertise to cover all aspect. Whilst some centers have well documented compulsory insurance requirements outlining specific terms and conditions of the policy which must be in place, others do not.

Sponsor/CRO need to consider the product liability, geographical coverage and cost of clinical trial insurance (among others) when choosing insurance providers for a multi-center trial involving various countries. On the other hand, site and investigators must consider the coverage for all their activities related to clinical trials and negligence when choosing insurance providers.

As much as Sponsor/CRO needing to put in place the necessary Clinical Trial Insurance for their clinical trials, they should also evaluate that the Institutions and/or Investigators have the necessary Professional Indemnities in place for the clinical trials which are undertaken.

7.3 Coverage

The service of providing insurance by insurers (or brokers) in Malaysia is governed by the Financial Service Act 2013. Under this act, the insurers can be a Malaysia company or an international company with license to operate in Malaysia. Some examples are Allianz, , AIG, Chubb, AIA, , and Great Eastern.

The common clinical trial insurance policy coverage is -

1. Agreed Compensation cover – compensation to patients follows the agreed amount under the applicable clinical trial compensation clauses in the policy. It covers all the team members within the same institution or partner (which can be included with extra payment) including error or omission.
2. Legal Liability cover – it covers damages, defense and claimant's costs that are legally liable to paid.

The decision to choose a provider or a policy should be made after considering factors such as how much insurance/ limit of indemnity to provide (per claim/ per patient/ per occurrence; per aggregate/ all claim) with retention/ deductible/ out of pocket for each claim by investigator/ sponsor, and at what cost or premium. Other details that sponsor, institution or investigator should pay attention to are the contract clauses i.e. how long to cover the indemnity after the expiration of the insurance or any exclusion of pre-existing disease that will not be covered.

Another type of clinical trial insurance is "Coverage by Endorsement. Some product liability policy provides clinical trial extension coverage by an endorsement to this policy. If a particular trial is not specified and scheduled on the endorsement, it is not covered. Hence, it is important for investigator to check the policy clause for this rider or extension. This form of insurance premium is usually cheaper. Be careful when you are conducting out of label claim CT/ new indication trial, as this type of policy will be null and void.

Other liability insurance that site/investigators overlook is equipment/ material/ public liability damage coverage. This need to be purchased separately to cover the equipment loaned from sponsor i.e. spoilt by any human or natural disaster, stolen, or not returned by patient. Another scenario is patient who fell and fractured his/her arm due to wet floor, on the day he/she comes for collecting medication only (not registered as patient or seeing investigator that day).

7.4 What information is needed?

The documents needed can vary from provider to provider and depends on the type of coverage is being requested. As part of the insurance application process, applicant must provide an estimate of the number of subjects/ patients taking part in the clinical trial to be covered and insurers use this as basis of premium. As a general guide, the compulsory documents needed are investigator's name and annual practicing certificate (APC) from all sites involved (if applicable and for multi-site), study protocol, institute standard of care for treatment of patient with the primary indication as in the trial), patient consent form, expected approval timeline from regulatory (CTIL/ CTX) and IEC (Approval letter).

For research centers, the premium can be better negotiated if the documentation as listed below can be provided. The annual premium can be competitive and much lower if centers have good track record and usually with no claims for a decade.

a. Annual revenue of the company
b. History of claim(s)
c. Rate of turnover of key personnel
d. Staff competency process
e. SOPs, accredited (ISO system), inspected by regulatory bodies (GCP, GLP etc.)
f. DSMC/DSMB – Data Safety Monitoring Committee or Board report

The policy is normally negotiated for the duration of the trial or on a yearly renewal basis. With this in mind, and it would be good to ensure a guaranteed renewable contract clause is included in the policy and the renewal is promptly made.

7.5 Claim Handling

7.5.1 Potential claims include the following:

a) A subject/patient reports on injuries that is claimed to be caused by participation in clinical trials, for which cost is not covered within the clinical trial budget and with no other means of cost coverage, especially when the claim amount is more than the access or deductible in the policy.

b) A serious side effect or any event that causes bodily injuries during clinical trial. This event will have huge financial impact, i.e. > RM20, 000
c) A technical operational staff realizes that he/she has committed some error or missed some step which would cause adverse event/effect.

7.5.2 Steps to abide when above scenario arise.

a) To inform the following personnel when such a scenario arises as soon as possible. This shall include the CEO of CRC or Institution, PI, Sponsor (depending on SOP of site)
b) The person in-charge or any other person involved should not at any point of time, admit liability or settle any claim or incur any costs or expenses in connection therewith.
c) The personnel as mentioned in 7.5.2a should immediately contact insurance agent within a time limit not exceeding three (3) days. It is advisable to use multiple forms of communications to ensure the agent is informed.

7.6 Challenges and Improvement

The gradual growth and improvement of the clinical trial landscape in the last 20 years has given a good impression to insurers who are now more willing to underwrite a Clinical Trial/ Product Liability/ Errors and Omissions policy. Previously, individual investigators had difficulty in obtaining such insurance coverage but now the process is much easier. The factors causing the change would be a well-designed protocol, use of qualified Study Coordinator (SC), engaging a CRO with an established system and processes in place and a thorough yet easily understood consent form.

Other external factors which are usually considered would be the availability of qualified investigators, medical facilities and equipment at site, patient pool for the said trial, the litigation climate (for multi-country trial), existence of a legal framework that allows a sponsor to adequately defend against a claim, and insurance requirements imposed by regulation (i.e. NPRA), or independent ethics committees (IEC). So far there is no fixed insured amount requested officially by regulation or IEC. The rate is based on fair value for adequate coverage of activities in clinical trial, for example, insurance of RM100,000 for individual investigator to RM500,000 to RM 1,000 000 per occurrence for institution and RM 1,000 000 to RM 5,000 000 per clinical trial or per aggregate.

Clinical trial insurance covers for injuries regardless of fault but as the premium amount increases yearly, sponsor will exclude investigator liability coverage due to negligence. Hence, all investigator and institution/research center are advised to purchase their own professional indemnity or insurance coverage. As a measure of safeguarding the institution and the investigators involved in a clinical trial, the clinical trial agreement should have a clause stating that the sponsor will indemnify the site and the investigator against any claims arising from the use of investigational product, the procedures involved and by being involved in clinical trial provided the site and investigator have followed strictly the protocol with no errors or negligence.

The Swedish Drug Association came up with a strategy for the benefit all parties involved. They made insurance available to investigator and sites through a group facility. The facility allows investigators and sites to pool together and pay for insurance on a group basis, and this reduces the amount of premium each investigator/site pays. This means, payment of future claims will depend on the adequacy of limits available from the facility at the time of a claim. This method is worth exploring as our society is not litigious. Excessive demands by sponsor and CRO for indemnification from site or investigator due to their negligence will cause the site and investigator to shy away from taking up new trials.

8 Summary Process of Clinical Trial Conduct

8.1 Industry-Sponsored Trial (IST)

Clinical trials are classified into two categories: industry-sponsored trials (ISTs) and investigator-initiated trials (IITs), based on their funding sources and sponsors.

According to the Malaysian Guideline for Good Clinical Practice, a sponsor refers to any individual, company, institution, or organization responsible for the initiation, management, and/or financing of a clinical trial.

ISTs are funded by companies (pharmaceutical, biotech, or medical device sectors) and primarily focus on developing new drugs for regulatory approval. In contrast, IITs are initiated by academic researchers or cooperative groups, often driven by unmet clinical needs. Both types of trials play a crucial role in advancing medical innovation and scientific knowledge.

Malaysia has emerged as a significant player in the field of clinical research in Southeast Asia. With its diverse population and growing healthcare infrastructure, the country offers a conducive environment for conducting industry-sponsored clinical trials, particularly in the fields of pharmaceuticals and biotechnology. ISTs in Malaysia cover a wide range of therapeutic areas, reflecting global pharmaceutical trends.

In Malaysia, Phase III clinical trials constitute the largest category of sponsored interventional research, followed closely by Phase II studies. The country is committed to advancing its capabilities in early-phase or First-In-Human (FIH) trials. Launched in 2016, the Phase 1 Realization Project (P1RP) was designed to bolster these capabilities, and the subsequent P1RP 2.0 initiative continues to focus on enhancing Malaysia's expertise in early-phase trials. As of 2024, P1RP has already yielded positive outcomes, exemplified by the selection of Sarawak General Hospital to participate in a global FIH trial.

The landscape of ISTs in Malaysia is constantly evolving. Recent trends include:

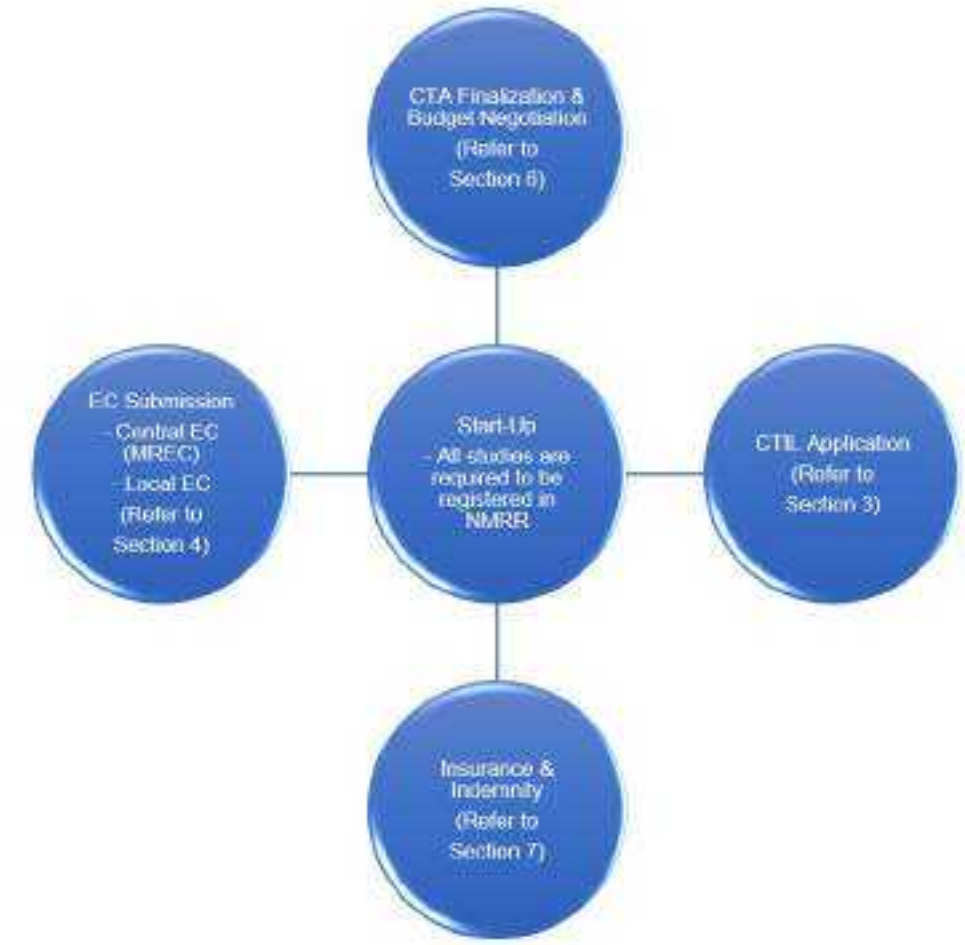
- **Increased Investment in Research**: There has been a noticeable increase in investments from both local and international pharmaceutical companies, driven by Malaysia's strategic position in the region and its supportive regulatory environment.

- **Focus on Biological and Biopharmaceuticals**: There's a growing interest in trials involving biologics and biosimilars, reflecting global industry trends.
- **Digital Transformation**: The adoption of digital tools for patient recruitment, data collection, and monitoring has been accelerating, particularly post-COVID-19.

The COVID-19 pandemic has significantly accelerated the global demand for decentralized clinical trials. Malaysia has not been an exception to this trend; guidance document for decentralized clinical trials version Jul 2023 was released in Malaysia: Malaysia Decentralised Clinical Trial (DCT) Guidance Document. This document offers comprehensive guidance on the implementation of decentralized elements in clinical trial methodologies.

IST in Malaysia are an essential component of the healthcare ecosystem, contributing to the development of new therapies and improving patient care. With a robust regulatory framework, a diverse patient population, and increasing investments, Malaysia is a well-positioned to continue being a preferred destination for conducting clinical research.

The start-up process of an IST in Malaysia is illustrated below:



Other permits or notification that may be required for IST conduct are (Refer to Section 5):

Biological Samples Import/Export Permit	Communication Device Import Permit	Medical Device Importation Notification
Required if the study involves exporting biological samples out of the country or importing biological samples into the country (e.g. tumor biopsy, blood samples, urine samples etc.). Quantity of biological samples importation/ exportation is needed to be listed in the application submission.	Required if the study needs to import communication devices into the country to the study site (e.g. Mifi, Tablet, eDiary).	Required if the study supplies medical device to the study site. (e.g. ECG machine, EEG machine, centrifuge, lab kits)

8.2 Investigator-Initiated Trial (IIT)

Investigator-Initiated Trials (IITs) is an essential component of medical research, especially in addressing localized healthcare needs. Unlike conventional clinical trials, typically sponsored and conducted by biotechnology or pharmaceutical companies, IITs are initiated, managed, and conducted by individual investigators or a team of clinicians and researchers. Under Good Clinical Practice (GCP) guidelines, investigators who also act as sponsor are referred to as sponsor-investigators. These individuals must fulfill both the obligations of a sponsor and an investigator, encompassing a wide range of responsibilities from trial conception to the publication of results. These responsibilities are aligned with the obligations outlined in GCP guidelines, ensuring that trials maintain the highest ethical and scientific standards.

Unlike industry-led trials, which are often aimed at the development and commercialization of new therapies, IITs focus on generating scientific knowledge and addressing specific, often unmet, local healthcare needs. IITs play a pivotal role in expanding content-specific knowledge, especially in settings where healthcare challenges are driven by local patient populations and medical needs. The knowledge generated through IITs has a direct impact on improving clinical practices, influencing policy decisions, and addressing public health issues. The ability of IITs to adapt to local health contexts makes them uniquely positioned to explore areas of unmet medical need, which are often overlooked in industry-sponsored trials.

The COVID-19 pandemic underscored the importance of IITs in responding to rapidly evolving clinical challenges. At the onset of the pandemic, there was a scarcity of data on COVID-19 treatment protocols and prophylactic regimes. IITs emerged as critical avenues for rapid data generation, enabling clinicians to assess the effectiveness of interventions in near real time. The pandemic saw a surge in IITs, as clinicians and researchers sought to generate evidence to guide clinical decisions. These trials, often supported by academic and governmental institutions, provided essential insights that helped shape global and local responses to the pandemic.

While IITs have tremendous potential to impact healthcare, they require meticulous planning and execution to be successful. The process of conducting an IIT can be complex and resource-intensive. Only high-quality IITs with scientific integrity will yield reliable data and robust evidence capable of influencing clinical practice. The protection of the study participants wellbeing, rights and

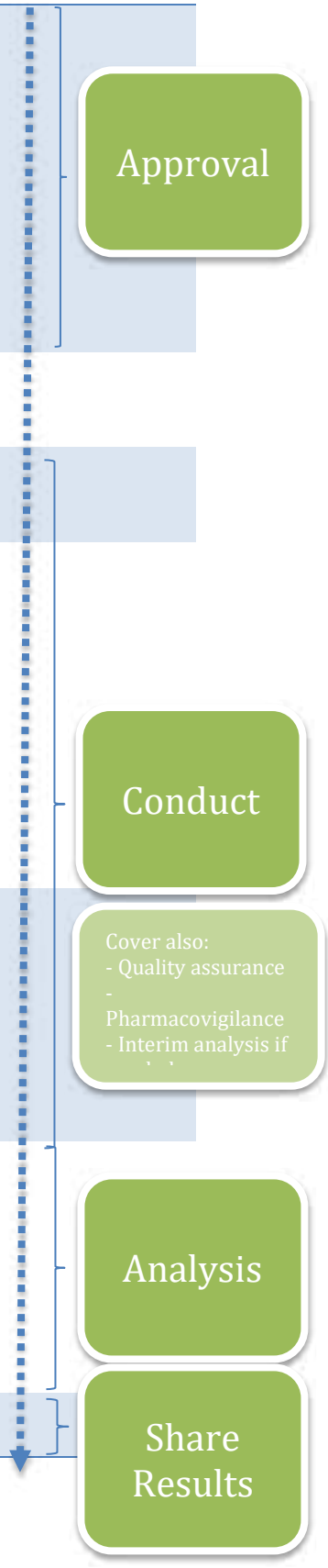
safety are equally important components of an IIT as well. Most often than not, the sponsor-investigator would require a team to ensure a smooth conduct of IIT.

Investigator-Initiated Trials (IITs) are an invaluable tool for advancing medical research, particularly in addressing local healthcare needs. As the landscape of clinical research continues to evolve, IITs will remain a cornerstone of medical innovation and improved patient care.

Below illustrates an overview of the key processes and components of IIT:

Key Component	Description	Process
Study Conception	Research ideas Problem statement	
Literature Review	Identify available information Identify knowledge gap	
Study Proposal / Budget	Project description and rationale Objectives Study Design Measurable variables Sample size Data collection methods Expected timeline Study costing	
Protocol / Methodology	Title of study Investigator(s), trial site(s), collaborator(s) Summary of study Literature review Objective and purpose Study design Assessment of efficacy and safety Primary and secondary endpoints Study site Study population and eligibility criteria Randomization and blinding Study treatment and/or procedures Study duration and timeline Informed consent taking procedures Accountability of investigational product / device Source document/data Data management plan Data collection method Data storage Sample size calculation Statistical analysis plan Stopping rules Unblinding procedures Rescue medication Quality control and quality assurance Ethical issues and considerations Privacy and confidentiality Conflict of interest Publication policy Supplements References	Planning Cover also: - Prepare study documents - Trial insurance and professional indemnity -Setup DMSB (if applicable) -Setup pharmacovigilance team -Setup data management team - Identify collaborators

IRB Review / Regulatory Application	Submit study document to MREC via NMRR or other relevant IRB/IEC CTIL/CTX application is required if the clinical research involves the use of: - an unregistered IP, or - a different form registered IP for unapproved indications, or - a traditional product used for approved therapeutic claim, or - placebo. Export Permit for biospecimen if required
Study Feasibility	Identify potential investigator(s) Assess the suitability of the study sites Site qualification
Study Initiation	Investigator meeting Study training Delegation of authority
Study Conduct	Study participant recruitment Informed consent taking Screening Randomization Intervention Follow up Safety monitoring and reporting (Pharmacovigilance) Subject retention Quality control Study monitoring Risk management
Data Collection	Follow data management plan Data collection using data acquisition tool / questionnaire / interview Data entry Data cleaning Source data verification Data adjudication Database lock
Data Analysis and Interpretation	Follow statistical analysis plan Response rate Demographic data Measurable variables (independent and dependent variables) Appropriate statistical analysis Graphical presentation Data interpretation
Dissemination of Results	Written, poster and oral presentation



8.3 The differences of IST and IIT

	IST	**IIT**
Sponsor	Company (Pharmaceutical, Biotech, Medical Device)	Investigator
Funding	Company	Research grant or self-funding
Study design	Study clinician from the sponsor company	Investigator
Primary Objective	Commercial value	Local context specific knowledge/evidence
Study Management	Sponsor study team	Investigator study team
Intellectual Property	Sponsor will own any patentable inventions developed	Investigator will own any patentable inventions developed

8.4 Compassionate Use Program

According to CDCR 1984, Regulation 15 (6), individuals who wish to import or manufacture products specifically for treating patients with life-threatening illnesses may apply for an exemption from the provisions of Regulation 7 (1). This exemption is granted by the Authority and is subject to specific conditions and restrictions as deemed appropriate.

Due to the ongoing development of investigational products, access for medical treatment is primarily conducted within the framework of clinical trials. Upon the conclusion of a clinical trials, the use of an investigational product may continue under compassionate use program.
Given that the safety and efficacy of the investigational products are still in development, the access to the products for medical treatment should occur in a clinical trial setting. In Malaysia, this program ensure that patients maintain access to investigational products after a trial has ended and before the product is officially registered. Eligibility of this program is limited to participants who were involved in approved clinical trials related to CTIL and CTX and is provided on a named patient basis.

Approval from the Chief Health Director (KPK) or Senior Director of Pharmacy Services (PKPF) is necessary for a named patient application in the following scenarios:

a) **Registered Drug Not Listed**: The drug is registered but not included in the Ministry of Health medication formulary (FUKKM).
b) **Off-Label Use (FUKKM)**: The drug is registered and listed in the FUKKM, but the specific indication for use is not included.
c) **Off-Label Use (PBKD)**: The drug is registered and listed in the FUKKM, but the indication for use is not registered with the Controlling Authority (PBKD).
d) **Unregistered Drug**: The drug is neither registered with PBKD nor listed in the FUKKM.

For further information, applicant can refer to the following link: The Guidelines for Special Approval Medicine (SAM) Applications for MOH Facilities

ADR reporting requirements to NPRA for compassionate use:

Question	**Answer**
What are the ADR reporting requirements to the Authority if the Country of AE occurrence is Malaysia but the medicinal products is not registered in Malaysia.	You may report this ADR to the *Bahagian Perkhidmatan Farmasi* (BPF), of which the contact details are stated in the approval letter for exemption use/compassionate use. A copy of the report is required to be sent to the NPRA.
Who holds the ultimate responsibility of ADR reporting under compassionate use/named patient use?	The prescriber is ultimately responsible for the ADR reporting under compassionate use/named patient use because the approval of use is granted to the prescriber. However, if the ADR has come to the knowledge of the PRH and the ADR has not yet been reported to the Authority, then the PRH holds the responsibility to report to the Authority.
The protocol should encourage the prescriber to report any adverse reactions suspected of being related to use of the medicinal product to the Authority. Can the	The protocol is not exempted for the given situations.

protocol be exempted for “named patient use” requested by one doctor for one patient OR a request that is initiated by hospital on regular and larger quantity basis?	

8.5 Non-Interventional Study (NIS)

“Non-interventional study” is a study where the medicinal product (s) is (are) prescribed in the usual manner in accordance with the terms of the marketing authorization. NIS includes Post-marketing Surveillance studies (PMS), Post Authorization Safety Studies (PASS), cohort studies and case-control studies.

NIS may be either an IST or IIT. The process flow of NIS is similar to IST except that the application of Clinical Trial Import License is not required. Notification of study to NPRA is also not required as the study does not involve administration of medicinal product.

9 Key Contacts for Clinical Trial Conduct

9.1 Regulatory Bodies

Name	**Clinical Research Related Activity**	**Website Link**
National Pharmaceutical Regulatory Agency (NPRA)	Clinical Trial Import License Application	National Pharmaceutical Regulatory Agency (NPRA) - Home
Medical Device Authority (MDA)	Notification of Medical Device Importation for Clinical Trial	Official Portal of Medical Device Authority (MDA) Malaysia
Division of Disease Control Ministry of Health	Biological Import/Export Permit Application	Application process through BLESS: Business Made Simple - BLESS • Business Licensing Malaysia
SIRIM QAS International Sdn. Bhd.	Emitting Device Import Permit Application	i. eComM - Online Certification for Communication and Multimedia products ii. SIRIM QAS Enquiry & Complaint Form iii. Home | Welcome to SIRIM Berhad

9.2 Independent Ethics Committee (IEC)

All IEC that approved drug related trial MUST be registered with DCA. The list of registered IEC may be obtained from NPRA website: Ethics Committee Registered with DCA

Name	Website Link
Medical Research Ethics Committee (MREC)	Application process through NMRR: Version 2: National Medical Research Register Version 1: National Medical Research Register
Medical Research Ethics Committee, University of Malaya Medical Centre (UMMC-MREC)	Welcome to UMMC-MREC
Independent Ethics Committee Subang Jaya Medical Centre (IEC SJMC)	SJMC Clinical Research Application | Subang Jaya Medical Centre
Sunway Medical Centre Independent Research Ethics Committee (SREC)	Sunway Medical Centre Clinical Research Centre
Jawatankuasa Etika Penyelidikan Institut Jantung Negara (IJNREC)	Research Ethics Committee - Institut Jantung Negara
IIUM Research Ethics Committee (IREC)	IIUM Research Ethics Committee
Universiti Teknologi MARA (UiTM) Research Ethics Committee (REC)	Research Ethics Committee UiTM
Jawatankuasa Etika Universiti Untuk Penyelidikan Melibatkan Manusia, Universiti Putra Malaysia (JKEUPM)	JKEUPM (Ethic Committee For Research Involving Human Subject) | Office of the Deputy Vice Chancellor (Research & Innovation)
Human Research Ethics Committee, Universiti Sains Malaysia (JEPeM)	JEPEM USM
Research Ethics Committee, Universiti Kebangsaan Malaysia (RECUKM)	JEPUKM Form - UKM Research Ethics Secretariat
Pantai Hospital Kuala Lumpur Research and Ethics Committee (PHKL REC)	Research Ethics | Pantai Hospital Kuala Lumpur

9.3 Government Support Bodies

Name	Function	Website Link
National Committee for Clinical Research (NCCR)	Steering committee for Clinical Research in Malaysia	Not available
Institute for Clinical Research (ICR)	Promote, support and conduct investigator initiated trial (IIT) by healthcare providers at MOH	Clinical Research Centre | CRC Malaysia
Clinical Research Malaysia (CRM)	To establish Malaysia as a preferred destination for Industry Sponsored Research (ISR)	Clinical Research Malaysia

9.4 Society

Name	Function	Website Link
Society of Clinical Research Professionals Malaysia (SCRPM)	Promote Clinical Research in Malaysia through education and networking.	SCRPM - Home page

9.5 Local CRO

Name	Website Link
Info-Kinetics Sdn Bhd	INFO KINETICS
Klinsel Sdn Bhd	Klinsel – Leading CRO in Malaysia
Questra Clinical Research Sdn. Bhd.	Questra – Clinical Research
Veras Research Sdn. Bhd.	Veras Research
MyXMO	Think clinical research, think MyXMO!
ClinData Consult Sdn Bhd	ClinData Solutions - Home
Innosignum	Innosignum | Contract Research Organization & Regulatory Services | Malaysia
M&B Healthcare Sdn Bhd	Home - M&B Health Care
USMARI	Usmari – Ungku Shahrin Medical Aesthetic Research & Innovation Centre

9.6 International CRO That Are Based in Malaysia

- IQVIA Solutions Malaysia Sdn Bhd.
- PAREXEL International (Malaysia) Sdn. Bhd.
- Syneos Health
- ICON plc
- Pharmaceutical Product Development (M) Sdn. Bhd. (PPD)
- Novotech Clinical Research (M) Sdn. Bhd.
- George Clinical
- Fortrea
- Tigermed
- CSI Medical Research

List above is not exhaustive.

9.7 Pharmaceutical Company

Refer to Pharmaceutical Association of Malaysia (PhAMA) membership directory: Pharmaceutical Association of Malaysia (PhAMA) - PhAMA Member Directory

If you have any enquiries regarding the key contacts for clinical trial conduct in Malaysia, you may refer to SCRPM or write to us at **scrpmalaysia@gmail.com**

10 Glossary

10.1 Adverse Drug Reaction (ADR)

In the preapproval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase “responses to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. Regarding marketed medicinal products: A response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

10.2 Approved Training in Good Clinical Practice

Training which is approved by the National Committee for Clinical Research (NCCR). The content of the training must incorporate the curriculum as stipulated by the committee.

10.3 Audit

A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor’s Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

10.4 Case Report Form (CRF)

A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

10.5 Clinical Trial Exemption (CTX)

Any person who wishes to manufacture any products solely for the purpose of producing samples for clinical trials, for registration or issuance of notification note under these Regulations may on application be exempted by the Director of Pharmaceutical Services from the provisions of regulation 7(1) or regulation 18A of the Control of Drugs and Cosmetics Regulations 1984.

A CTX is an approval authorizing the applicant to manufacture any local product for the purpose of clinical trial.

10.6 Clinical Trial Import Licence (CTIL)

A CTIL is a licence in Form 4 in the Schedule of the Control of Drugs and Cosmetics Regulations 1984, and issued by Director of Pharmaceutical Services under regulation 12(1)(c) of the same Regulations. With the Clinical Trial Import Licence the sponsor is authorized to import any product for purposes of clinical trials, notwithstanding that the product is not a registered product.This regulation provides a mechanism for clinical trial subjects to gain limited access to unregistered product (investigational products) during the clinical trial.

10.7 Clinical Trial Study Report

A written description of a trial/study of any therapeutic, prophylactic, diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report (see the ICH Guideline for Structure and Content of Clinical Study Reports).

10.8 Contract

A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

10.9 Contract Research Organization (CRO)

A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

10.10 Coordinating Investigator

An investigator assigned the responsibility for the coordination of investigators at different centers participating in a multicenter trial.

10.11 Drug Control Authority (DCA)

An authority set up under the Control of Drugs and Cosmetics Regulations 1984 and as such its responsibility, role and mandate are defined by law.

10.12 Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

10.13 Independent Ethics Committee (IEC)

An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guideline.

10.14 Independent Review Board (IRB)

An independent body constituted of medical, scientific, and non-scientific members whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

10.15 Informed Consent

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

10.16 Inspection

The act by a regulatory authority (ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority (ies) to be related to the clinical trial that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority (ies).

10.17 Interim Clinical Trial/Study Report

A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

10.18 Investigational Product

A pharmaceutical form of an active ingredient including plant/ animal-derived medicinal products or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way

different from the approved form, or when used for an unapproved indication (off-label use), or when used to gain further information about an approved use.

10.19 Investigator

A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

10.20 Investigator's Brochure (IB)

A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

10.21 National Committee for Clinical Research (NCCR)

A committee established for the purpose of coordinating and promoting clinical research in Malaysia, chaired by the Director General of Health, Ministry of Health Malaysia.

10.22 National Institutes of Health (NIH)

National Institutes of Health (NIH) is a network of Ministry of Health (MOH) research institutes. NIH was approved in the 7th Malaysian Plan (7MP), and officially launched by Hon. Minister of Health Malaysia on 11 August 2003. NIH is consisting of 6 institutes which are:

- Institute for Medical Research (IMR)
- Institute of Public Health (IPH)
- Institute for Clinical Research (ICR)
- Institute for Health Systems Research (IHSR)
- Institute for Health Management (IHM)
- Institute for Health Behavioural Research (IHBR)

NIH aims to create seamless continuum from identification of research priorities, conduct of research to utilization of research findings.

The National Institutes of Health is under the preview and headed by the Deputy Director General of Research & Technical Support [DDG(R&TS)].

10.23 National Medical Research Register (NMRR)

NMRR is a web-based service initiated by the National Institutes of Health (NIH) of the Ministry of Health (MOH). It is a web based tool designed to support the implementation of the National Institute of Health (NIH) Guideline on the conduct of research in the Ministry of Health Malaysia (MOH).

Current MOH policy on research, as specified in the guideline, requires:

- Registration of all research that involves MOH personnel OR that is to be conducted in MOH facility OR to be funded by MOH research grant
- Review & approval of the research by a designated entity to whom authority has been delegated for the purpose
- In addition, research involving human subjects requires prior review and approval by the MOH Research and Ethics Committee (MREC)
- Approval of all research publications, whether in the form of research report, journal article or conference proceeding, by the NIH initially and thereafter by the Director General of MOH

The NMRR is thus specifically designed to enable:

1. Online registration of research. This brings us in line with international practice which requires medical research, especially clinical trial, to be registered in publicly accessible research registers. This is to ensure transparency and to increase public trust in the conduct of medical research; as well as to inform physicians and prospective volunteers about ongoing research in which they may wish to enroll.
2. Online submission to an appropriate authority for approval, as well as online review of the submitted research by relevant appointed reviewers. The online system ought to reduce the research review time as well as to enable investigators to track the status of their research online.
3. Online submission of research publication to the NIH for approval.

4. Finally, the NMRR also enable MOH management to document the level of research activity in the MOH, and also to track the progress of the research it has approved and/or provided support such as funding.

10.24 Poison

Any substance specified by name in the first column of the Poisons List and includes any preparation, solution, compound, mixture or natural substance containing such substance, other than an exempted preparation or an article or preparation included for the time being in the Second Schedule.

10.25 Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments.

10.26 Regulatory Authority

Bodies having the power to regulate. In the Malaysian Guideline for Good Clinical Practice the expression Regulatory Authorities includes the authorities that review submitted clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities.

10.27 Serious Adverse Event (SAE)

Any untoward medical occurrence that at any dose:
- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

10.28 Sponsor

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

11 Acronyms

ADR	Adverse Drug Reactions
AE	Adverse Event
APC	Annual Practising Certificate
ARC	Annual Retention Certificate
BE	Bioequivalence
CIOMS	Council for International Organizations of Medical Sciences
CMA	Compliance Monitoring Authorities
CRC	Clinical Research Centre
CRM	Clinical Research Malaysia
CRO	Contract Research Organization
CTA	Clinical Trial Agreement
CTIL	Clinical Trial Import Licence
CTX	Clinical Trial Exemption
CV	Curriculum Vitae
DCA	Drug Control Authority
DG	Director General
DSMC/DSMB	Data Safety Monitoring Committee or Board
EC	Ethics Committee

EPP	Entry Point Project
ETP	Economic Transformation Programme
FIH	First-In-Human
GCP	Good Clinical Practice
GDP	Gross Domestic Product
GGE	General Government Expenditure
GGHE	General Government Health Expenditure
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GNI	Gross National Income
GST	Goods and Services Tax
ICF	Informed Consent Form
ICH-GCP	International Council on Harmonisation - Good Clinical Practice
ICR	Institute for Clinical Research
IEC	Independent Ethics Committee
IIT	Investigator-Initiated Trial
IA-HOD-IA	Investigator Agreement, Head of Department and Institutional Approval
IRB	Institutional Review Board
IST	Industry-Sponsored Trial
JEPeM	Human Research Ethics Committee, Universiti Sains Malaysia

MAD	Mutual Acceptance of Data
MADRAC	Malaysian Adverse Drug Reactions Advisory Committee
MCMC	Malaysian Communications and Multimedia Commission
MDA	Medical Device Authority
MOH	Ministry of Health
MOPI	Malaysian Organisation of Pharmaceutical Industries
MPS	Malaysian Pharmaceutical Society
MREC	Medical Research and Ethics Committee
NCCR	National Committee for Clinical Research
NIH	National Institutes of Health
NKEA	National Key Economic Area
NPRA	National Pharmaceutical Regulatory Agency
OECD	Organization of Economic Cooperation and Development
PASS	Post Authorization Safety Studies
PD	Protocol Deviation
PDPA	Personal Data Protection Act
PhAMA	Pharmaceutical Association of Malaysia
PI	Principal Investigator
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PIS	Patient Information Sheet

PMS	Post-Marketing Surveillance Studies
RA	Regulatory Authority
REC	Research Ethics Committee
RECUKM	Research Ethics Committee, Universiti Kebangsaan Malaysia
SAE	Serious Adverse Event
SC	Study Coordinator
SCRPM	Society of Clinical Research Professionals Malaysia
SOP	Standard Operating Procedure
SREC	Sunway Medical Centre Independent Research Ethics Committee
SSO	Single Sign On
SUSAR	Suspected Unexpected Serious Adverse Reaction
TVF	Trial Validation Form
UiTM	Universiti Teknologi Mara
UKMMC	Universiti Kebangsaan Malaysia Medical Centre
UMMC	University of Malaya Medical Centre
USM	Universiti Sains Malaysia
VAT	Value Added Tax
WHO	World Health Organization

A Guide to Conducting Clinical Trials in Malaysia Second Edition

e ISBN 978-967-14323-1-0

Published and distributed by
Society of Clinical Research Professionals Malaysia
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