catalyst

ACCELERATING **RESEARCH**

A NEWSLETTER FOR THE RESEARCH COMMUNITY IN SINGAPORE

AUG/SEP 2011
MICA (P) 166/04/2011

National Healthcare Group
Adding years of healthy life

BENCH *to* BEDSIDE

UPCOMING EVENTS

SOCIETY OF CLINICAL RESEARCH ASSOCIATES (SoCRA)

CLINICAL RESEARCH

BRINGING COLOURS BACK TO LIFE

RESEARCH EDUCATION

NHG RESEARCH ONLINE ADMINISTRATION & MANAGEMENT

contents

from the editor-in-chief

Dear Readers,

First of all, the editorial team would like to express their appreciation for your continual support for Catalyst.

In this issue, it is our pleasure to highlight the importance of clinical research as the cornerstone of healthcare improvement. It is the bridge in bringing the beneficial findings from the bench to the actualization of better healthcare at the bedside of patients.

We are pleased to feature 2 outstanding preliminary clinical research studies in Singapore. We are glad to have Dr Jimmy Lee, one of our Small Innovative Grant (SIG) Awardee, and Dr Steven Thng from the National Skin Centre to share with us the experiences and outcomes of their studies on Psychosis and Vitiligo respectively. I hope that their sharing will inspire clinical professionals to persevere in their research and in their strive to provide better care for patients.

To boost the professional standards of clinical research, NHG Research and Development Office (RDO) is proud to host the Society of Clinical Research Associates (SoCRA) to provide their Certification Programme for Clinical Research Professionals in March 2012, in conjunction with the 2nd Asia Pacific Research Ethics Conference (APREC). This Certification Programme will recognize clinical research professionals who have attained a high standard of knowledge in this field.

In this issue, we have also included practical information and resources for clinical research professionals. This includes an article on obtaining informed consent in clinical studies, a book review on "Becoming a Successful Clinical Research Investigator", as well as educational platforms available such as the Singapore Health & Biomedical Congress (SHBC) 2011.

I hope you will enjoy this resource-packed issue and I look forward to receiving your feedback.

Enjoy reading.

Yours Sincerely,

Kin Poo

Your Newsletter Your Comments

Do you have... Research articles to share? Research topics that you want covered? Comments/Feedbacks on published contents of this newsletter? Comic strips/Cartoon Illustrations that is science /research-related that can bring smiles to your colleagues?

If you have answered "YES" to any of the above, we invite you to write in and share with us your thoughts, feedback on published articles or cartoon clips *(original materials, jpeg format please)*. And if your contribution is accepted for print, we will send you a token of appreciation, with compliments from the Editorial team!

Do remember to add in your contact details, where applicable, for our future communications with you.

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National Healthcare Group
Adding years of healthy life

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Small Innovative Grant I (SIG I) Awardee

Dr Jimmy Lee
Associate Consultant
Institute of Mental Health/Woodbridge Hospital

"Psychosis is a serious mental illness that affects approximately 3% of the population. Till today, it is only diagnosed after careful assessment and close observation of behavior, and there is no laboratory measure to aid clinicians in diagnosis or monitoring of treatment effectiveness. Researchers have traditionally viewed psychosis as a purely brain disorder, but we know now from recent findings that psychosis has associated peripheral manifestations."

The first pilot study into this area conducted by our group involved exploration of a suitable peripheral target to examine changes associated with the disease. We also decided to focus on peripheral lipid changes, reviving a decades-old hypothesis that psychosis could be a cellular membrane disorder. We profiled cell membrane lipids via a mass spectrometry approach and discovered significant changes in blood-based lipids between patients and controls. This spurred more questions rather than answers. Armed with the encouraging pilot data, we embarked on another study to examine some of these lipid changes in a group of drug naïve patients suffering from their first psychotic episode. Funding from the Small Innovative Grant (SIG) was important in realizing this study to answer some of the research questions.

In this prospective study, we recruited never treated before patients suffering from their first psychotic episode, and followed them up for 3 months. We collected clinical data and blood samples from them at different time points over the 3 months. We also recruited age and gender matched controls to serve as comparison. There were 2 main objectives of this research. Firstly, we compared blood-based lipids between patients before treatment and healthy controls to identify dysregulated lipids. Then, we monitored these lipid changes prospectively in relation to the effects of treatment and clinical outcomes.

From this longitudinal study, we identified lipids that were deranged in patients with psychosis that were not affected by psychotropic treatments. This could represent a peripheral lipid signature in patients and would support the notion of peripheral manifestations associated with psychosis. Following on these preliminary findings, our group was awarded the National Medical Research Council (NMRC) New Investigator Grant (NIG) to attempt to validate some of these findings in a larger study population. This study is still ongoing and the findings will help shed new light on role of lipids in psychosis and examine their clinical utility as potential biomarkers.

Dr Jimmy Lee *(right)* with Associate Professor Chong Siow Ann *(left)*, Vice Chairman Medical Board (Research), Institute of Mental Health

A Tribute to Allied Health Professionals

Elaine Seah
Clinical Research Coordinator
National University Health System

Ms Elaine Seah *(left in photo)* is currently supporting research work at the Department of Haematology-Oncology, National University Health System. The department is active in Phases One to Three clinical researches in both solid tumors and blood malignancies.

We all have our dream job – a pretty fit to our passion. Intrigued by the American medical drama 'ER', I've wanted to be involved in healthcare since I was a teenager. Then, I only knew about being a doctor, a nurse or a social worker. After graduating with a BSc, I waited 10 desperate months, hoping for the chance to work in the healthcare industry. The opportunity to be a Clinical Research Coordinator (CRC) was truly serendipity. I was recommended for an interview for this job by suggestion of a friend who was working in the department. Back then, my idea of clinical research was vague – it was some experimenting involving humans.

During my interview with the manager of the clinical research team in the Haematology-Oncology Department of National University Hospital, I was cautioned that this would be a steep learning curve for me: having to learn about working in a hospital setting with patients and balancing all that with the requirements of clinical research. The introduction to the job appealed to me. Having been involved in bench research in the area of cancer during my undergraduate years, I was happy to apply my skills of inquisition. It was a natural progression to me – having spent time doing scientific research in vitro and in vivo, I was keen to learn how work in the laboratory translates to potential benefit to patients. Indeed, upon my entry, the learning curve was so steep that it felt like I was propelled to almost a vertical ascension!

During the initial months of very hard work in a supportive department, I spent hours trying to familiarize myself with the workflow of the hospital, and sleepless nights cramming the protocol and the medical history of the patients into my brain. Among the many responsibilities of a CRC, I was taught how to digest a protocol. I had to consider many factors – logistic and financial constraints, scientific precision, data management, administrative requirements, pharmaceutical companies' requirements etc with my Principal Investigator and my other colleagues before a study can be up and running. I learnt to preempt any possible pitfalls as best as I could by painting a few possible scenarios in my head before implementation.

A few years ago, I was the CRC for a first-in-man Phase 1 trial. The drug yielded encouraging results in the laboratory and our department was approached to recruit patients for clinical testing. Through the duration of the study, I was able to observe how investigators and the pharmaceutical company had vigourous discussions on toxicities, patient safety, pharmacology of the drug, efficacy and future development. It was an eye-opener to see how my day-to-day coordinating of appointments, recording of adverse events and managing of the data contribute to credible clinical information for future drug development.

While the beginning was tough, my passion for patients kept me going. The best part of the job to me is the opportunity to work with my colleagues for our patients. When I was new, it felt like I was there for the work, stressing myself with getting things done right. Over the years, I have now learnt to enjoy the time I spend with my colleagues and our patients. It has been my privilege to share in the journey of our cancer patients. As coordinators, time is spent coordinating and changing multiple appointments for our patients and being involved in their care. There is trust built over the participation on trial, as patients share with us their medical, social and emotional concerns.

My department has been gracious in giving me opportunities to keep improving, by giving me the chance to do trials involving various malignancies in the various clinical trial phases. I have also helped Principal Investigators in collating of data for publication and getting accreditation with Society of Clinical Research Associates (SoCRA). The tight demands of excellent implementation of the trials have been made easier by the dedication of a team of my colleagues at National University Health Systems, who have been willing to accommodate the sometimes non-routine practices required by the research protocols.

Clinical research should be motivated by the desire to improve medical options for ourselves. Cost of medical care will be perennial concern and hopefully with the advent of new drugs, governments and pharmaceutical companies will continue to work on keeping the costs of drugs affordable to the general population. I am glad to be able to contribute to the knowledge of drug development and to the future of healthcare.

Bringing Colours Back to Life

Dr Steven Thng & Dr Goh Boon Kee
Associate Consultant Dermatologist
Consultant Dermatologist
National Skin Centre

Vitiligo is a common acquired or inherited disease with loss of normal color pigments and functioning melanocytes from otherwise healthy looking skin. Although once considered as a "cosmetic problem", vitiligo has been recognized as an important disfiguring skin disease having major impact on quality of life of patients, many of whom feel distressed and stigmatized by their condition, with some even suicidal.

In the National Skin Centre (NSC), about 300 new cases of vitiligo are seen every year. Although treatments are available, they are usually either not very effective, like the use of topical creams, which have a success rate of about 20%; or very inconvenient, like the use of light-therapy which requires patients to come to NSC 2-3 times per week for more than 6 months. In addition, medical treatments are usually ineffective for the subset of patients with segmental vitiligo, thus condemning them to go through life with their disfigurement.

Recognizing this need to better understand vitiligo, NSC established a melanocyte culture lab in 2005, with funding support from NHG, to conduct basic research into melanocyte biology. Concurrently, a sub-specialized pigment clinic was initiated to standardize treatment processes as well as exploring novel treatment methods so as to improve treatment outcomes for these patients. Over the last 5 years, much progress has been made through the numerous research projects undertaken by the pigment clinic. Significant projects include:

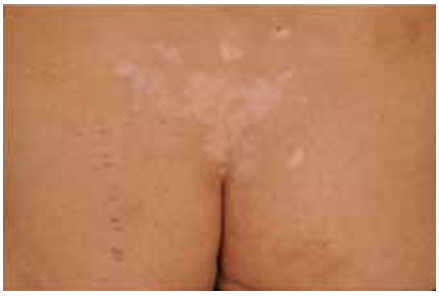
1. Understanding Vitiligo Pathogenesis

Currently, we are collaborating with researchers from A*STAR and from Taiwan to map out susceptibility genes for vitligo. Through this project, we hope to isolate specific genes that are associated with the various types of vitiligo, so that we can better understand the disease pathogenesis and devise new ways to treat the condition.

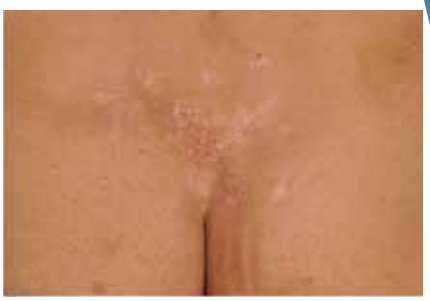
2. Developing New Therapeutic Modalities

While light therapy is the mainstay of treatment for vitiligo, with a success rate of close to 70%, light therapy, however, has considerable consequences for the patient because it needs to be carried out in NSC. The treatment itself only takes a few minutes, but to receive the treatment, patient needs to travel to NSC during working hours 2-3 times a week and wait for the treatment. As this is rather time consuming, many patients default treatment or is not consistent with treatment regime, resulting in treatment failure. For patients who are compliant, the time taken to come for the treatment, cost of transport as well as time taken off work/school is considerable. Recognizing this, we initiated a study looking at the use of handheld phototherapy devices to treat patients with limited vitiligo, with funding support from the National Medical Research Council (NMRC).

The aim of this study is to see if treatment with these handheld devices is as effective as institution based phototherapy, but with reduced cost and inconvenience to patients. Currently, we have recruited about 20 patients in the treatment arm using handheld devices and so far, the results have been encouraging with up to 60% of patients reporting more than 75% repigmentation with the use of these handheld devices. This is almost similar to institution based phototherapy but with better compliance as it offers the patient the convenience of doing the treatment at home, at a time of their choice.



Before Handheld Phototherapy



1 Month After Handheld Phototherapy

3. Improving Treatment Outcomes

Pioneering the work on cellular grafts in Singapore with funding from NHG, Dr Goh Boon Kee has, in recent years, modified and optimized the cellular grafts techniques for transplant of harvested melanocytes into depigmented skin of vitiligo patients. Currently, we have successfully translated research into clinical service and are able to successfully repigment more than 90% of patients with vitiligo who do not respond to conventional therapies with surgical options.

Grafting — Before & After

Looking back, significant progress has been made in the field of vitiligo management through research. Going forwards, the pigment team in NSC will continue to press ahead to unravel the mysteries surrounding vitiligo through research so as to develop more effective and cost-efficient ways to treat our patients.

Institution Feature: National Skin Centre (NSC)

Dr Mark Tang,
Director of Research
(1st row, second from left)
with his Research team at NSC.

Significant achievements to date

The establishment of autologous non-cultured epidermal cell grafting for vitiligo, leukoderma and chronic recalcitrant wounds; identification of gene mutations in Singapore Chinese patients with atopic dermatitis and psoriasis; a molecular database of basal cell carcinomas to identify molecular differences between Asian and Caucasian skin cancers; large ongoing cohorts of patients with Asian skin disease such as cutaneous lymphomas, eczema and immunobullous diseases

Find out more about National Skin Centre (NSC) at their website **www.nsc.gov.sg.**

This is an extract from the NHG Biennial Research Report (BRR) 2008-2009 – now available on NHG's research website **www.research.nhg.com.sg.**

Grab a copy now to learn more about NHG institutions and their research capabilities!

A subsidiary of the National Healthcare Group, the National Skin Centre (NSC) is a major outpatient specialist dermatological referral centre and the national tertiary academic centre for dermatological diseases in Singapore.

NSC is committed to high quality and clinically relevant research to advance dermatological knowledge in Asian skin diseases and enhance clinical care for patients. This is supported by the active engagement and fostering of multi-disciplinary research collaborations with local and overseas institutions including A*STAR and the National Technological University (NTU). Noteworthy research initiatives include:

- Focusing on high burden, high morbidity skin diseases such as atopic dermatitis, psoriasis, acne vulgaris, pigmentary disorders, as well as niche areas such as sexually transmitted infections and immunobullous diseases.
- The establishment of research work teams in various subspecialty clinics, such as the Eczema, Paediatric Dermatology, Acne, Cutaneous Lymphoma and Psoriasis Clinics.
- The NSC Cell Culture, Genetics and PCR Laboratory to advance research in basic science and boost translational research.
- Active collaboration with key local and overseas institutions such as the Institute of Molecular Biology, A*STAR, NTU and NUS.
- Active collaboration with the pharmaceutical industry to be the center of choice for clinical trials and research studies in Asian skin diseases.

Key research areas - Atopic Dermatitis, Psoriasis, Pigmentary Disorders, Cutaneous Oncology, Acne Vulgaris, Sexually Transmitted Infections and Asian skin diseases

"As the national tertiary academic centre for dermatological diseases in Singapore, we remain committed to conducting high quality, clinically relevant research that will not only advance dermatological knowledge but impact our clinical services and distinguish NSC as a reputable, leading opinion leader for skin diseases."

Useful Resources for CRCs and PIs – Local Institutional Review Boards (IRBs)

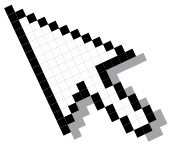
1. **Nanyang Technological University IRB**
   http://research.ntu.edu.sg/GuidelinesnForms/Pages/default.aspx

2. **NHG DSRB (Domain Specific Review Board)**
   www.research.nhg.com.sg

3. **National University of Singapore IRB**
   www.nus.edu.sg/irb

4. **Singapore Management University IRB**
   http://www.smu.edu.sg/research/IRB.asp

5. **SingHealth CIRB (Centralised Institutional Review Board)**
   http://research.singhealth.com.sg/Ethics/CIRB/Pages/Default.aspx



About Responsible Conduct of Research (RCR)

In the course of conducting research, researchers may face challenges that place them in moral dilemmas. In such situations, researchers usually rely on their personal principles or moral compass to do the "right things".

Being a responsible researcher means not engaging in dishonest acts, not allowing personal bias to influence scientific findings, reporting results accurately, and ensuring that funds are appropriately used. It also means stepping forward to report an act of research misconduct, or imbling the professional values of good and responsible research to the next generation of researchers.

The RCR division in the Office of Human Research Protection Programme (OHRPP) intends to develop a set of research best practices to address tricky issues, such as in areas of Research Misconduct, Protection of Human Subjects, Conflicts of Interest, Data Management Practices, Mentor and Trainee Responsibilities, Collaborative Research, Authorship and Publication, and Peer Review.

Stay tuned for more information on RCR in the next issue of Catalyst.

Becoming a Successful Clinical Research Investigator

David Ginsberg

Reviewed by Doreen Lim
Research Quality Management Executive
NHG Research & Development Office

This book serves as an introduction and guide to aspiring or new investigators in the clinical research or pharmaceutical industry. It is a good educational resource for potential investigators seeking to understand the realities of clinical research and the preparation needed to be successful. Readers may also determine whether clinical research is right for them as Chapter 1 of the book starts with 'Is Clinical Research for me?' It explores the opportunities for learning as well as the effects of research on patient safety, medical practice and potential legal liabilities.

The subsequent chapters provide the practical aspects and knowledge on the drug development process, business development and the hiring and retention of Clinical Research Coordinators. Those who are newly involved in the management and set-up of clinical research units and those in departments conducting research in healthcare institutions may find this book helpful as it provides insight into the basic infrastructure, including space planning, standard operating procedures and financing.

Although it is mostly written in the setting and context of United States with references to the Code of Federation Regulations (CFR) of the US, there are still useful insights and knowledge to be learnt. Investigators or research institutions are also exposed to the responsibilities and ethical considerations for the conduct of clinical trial/research.

Other topics in this book include:

- Hiring and training
- Interacting with IRBs
- Preparing for a study
- Working with study subjects
- Study Closure
- Adverse Events & Safety Monitoring
- Audits

This book is available for purchase at Amazon.com at USD59.00

PCR Teasers

NHG's Proper Conduct of Research (PCR) courses are designed to provide Investigators and Clinical Research Coordinators with foundational knowledge of good research practices and to familiarize them with the regulatory requirements and good clinical practice guidelines among others. There are 3 levels to the PCR courses - Basic, Intermediate and Advanced.

Here are a few questions taken from the PCR Basic Courses. Try them!

Question 1: An application of the Belmont Report's principle of 'Respect for Persons' can best be seen in:

(a) Equitable selection of participants
(b) Risk benefit analysis
(c) Informed consent process
(d) Screening process

Question 2: Ms France is planning to conduct a survey to find the attitudes and perceptions of the patients who attend the weight loss clinic at Alexandra Hospital. The survey will not contain identifiers. The Domain Specific Review Board (DSRB) will review this by:

(a) Exempt
(b) Expedited
(c) Full Board Review
(d) Does not require review

Question 3: **Aim:** To test the efficacy of acupuncture in the management of chronic backpain.

Problem: A subject with a history of ischemic heart disease and chronic back pain developed a cardiac arrest and died during an acupuncture session.

Safety Monitoring: The autopsy revealed that the patient died from acute myocardial infarction. The investigator concluded that the subject's death was unrelated to participation in the research.

How should the Principal Investigator classify this event?

(a) Adverse Event
(b) Serious Adverse Event
(c) Unanticipated Problem Involving Risks to Subjects or Others
(d) Important Medical Event

Did you get them right?

Answers:
1. (c) 2. (a) 3. (b)

Proper Conduct of Research

(For New Investigators, Clinical Research Coordinators or Study Team Members)

Essential Regulatory Documents Prior to Starting a Trial

Are you familiar with the essential regulatory documents that the Principal Investigator (PI)/ Investigator and study team should obtain before the initiation of a clinical trial/research?

Regulatory documents including the Domain Specific Review Board's (DSRB) approval letter and the Clinical Trial Certificate (CTC) issued by the Health Sciences Authority (for clinical trial type of research) should be part of your Investigator File before you start enrolling subjects or any study procedure. Apart from that, the signed Clinical Trial Agreement (CTA) or grant approval letter (if it is an agency funded trial) ought to be available prior to the commencement of a trial.

In order to avoid frustrations, delayed timelines and penalties from violating local regulations and ethical guidelines, both Investigators and Clinical Research Coordinators (CRCs) should work together with the institution's research office, Clinical Research Unit and Sponsor's Representative (the Clinical Research Associate), if it's an industry sponsored trial, to ensure that all the documents required to start a clinical trial or research study are ready.

Tips

1. The PI or CRC should start filing essential documents in the Investigator File prior to the start of the study.

2. Apart from all the essential documents, the PI and CRC should also make sure that essential supplies are at the site (e.g. drugs and clinical trial supplies) prior to the study initiation.

The Clinical Research Coordinator (CRC) Role

The Clinical Research Coordinator's (CRC) plays a significant supporting role in maintaining the Investigator File binder. Learn more about essential documents from experienced research coordinators/managers in supporting the PI and Investigators under NHG's Proper Conduct of Research (PCR) Online – Basic I (PC101) course.
The NHG's PCR training courses are designed to equip Clinical Research Team Members with the understanding of the key principles of PCR Standard Operating Procedures SOPs and apply their knowledge in their work.

For more information or to register for the PCR Online course, go to www.research.nhg.com.sg *(Training and Education › Search for a Course › PCR Online)*

Reference:
NHG PCR Standard Operating Procedures 501-B03

Waiver of Informed Consent

The NHG Domain Specific Review Board (DSRB) may waive some or all of the requirements for informed consent in a research study, should the study meet the criteria for waiver of consent.

Nevertheless, investigators need to understand the criticality of obtaining informed consent from research subjects prior to the start of any research. With the questionable practices of past human experiments in mind, it is with little wonder as to why the Belmont Report included "Respect for Persons" as the first of the three fundamental ethical principles underlying all research involving humans. This principle demands that subjects voluntarily enter the research with adequate information, provided through the process of informed consent.

In practice, the DSRB may waive the requirement to obtain informed consent completely, provided that all 5 criteria of waiver of consent are met.

We refer to **Section P** of the current Online DSRB Application Form (**Section Q** in the new Research Online Administration & Management). Investigators are expected to provide the following information to the DSRB for consideration:

a. **The research involves no more than minimal risk to the subjects.**

The investigators must provide:

- verification that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life;
- affirmation that the information collected is not sensitive in nature; and
- assurance that the data has been collected and are derived from standard clinically indicated procedures.

b. **The waiver or alteration will not adversely affect the rights and welfare of the subjects.**

The investigators must provide assurance that regardless of being part of the research or not, the information will still be collected as part of patients' clinically indicated procedures or as part of the normal running of business operations. None of the information collected would affect the clinical decisions about the individual's care, and patients are not being deprived of clinical care to which they would normally be entitled to.

c. **The research cannot practicably be carried out without the waiver or alteration of informed consent.**

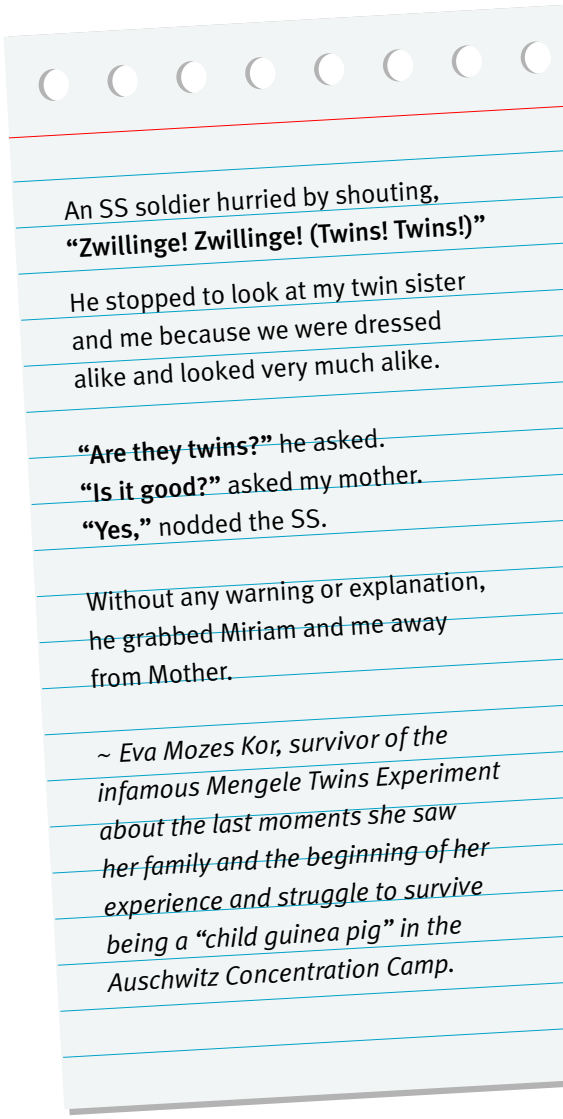
Investigators must assure the DSRB that identifying and contacting thousands of patients/subjects, although not impossible, would not be feasible for a collection of information that would not change the care they would already have received. In some cases, investigators must assure the DSRB that it may not be feasible to contact the patients as they are no longer on follow-up, lost to follow up or deceased.

d. **Whenever appropriate, the subjects will be provided with additional pertinent information after participation.**

Investigators must provide assurance that the subjects will be informed of vital information if there is a means of identifying the subject. Otherwise, investigators must justify why it is not appropriate to provide the information to the subject. For example there is no identifiers collected that would enable the investigator to identify the subject , or information cannot be verified due to the experimental nature of the protocol and would be of the patients' best interest not to receive the information.

e. **Waiver of informed consent does not apply for studies that are under the regulations of the US Food and Drug Administration (FDA).**

The DSRB may request for supporting documentations or alternatives to waiver of informed consent in its effort to protect the subject's rights, safety, and well-being.



NHG Research Online Administration & Management (ROAM)

How to complete Section B of the NHG Domain Specific Review Board (DSRB) Online Application Form in ROAM

Section B *(Study Team & Submission Domain)* of the NHG Domain Specific Review Board (DSRB) Online Application Form tells the DSRB who are involved in the Study, their respective study roles and the locations where the Study will be conducted. This section is important because it affects the DSRB's approval for the locations where the study can be conducted, and who is responsible for the conduct of the Study.

Overall Principal Investigator (PI), Site PIs and Study Sites

Each Study Site which is under the purview of the DSRB must have one Site PI.

For Studies which have only one Study Site, the Site PI is also the Overall PI *(Fig. 1)*.

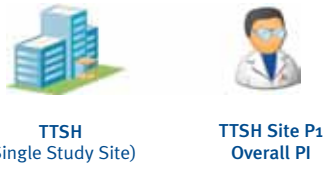


Fig. 1

For a Study with multiple Study Sites *(which are under the purview of the DSRB)*, the Overall PI must be chosen from among the Site PI's. The following example shows a Study with 3 Study Sites – TTSH, NUHS and KTPH *(Fig. 2)*. Each Study Site must have one Site PI from that Institution. Here, the TTSH Site PI is also appointed as the Overall PI.

The Overall PI has the responsibility of communicating with the DSRB for the overall conduct of the Study in all the Sites. The Overall PI is also the only person who can submit any form to the DSRB.

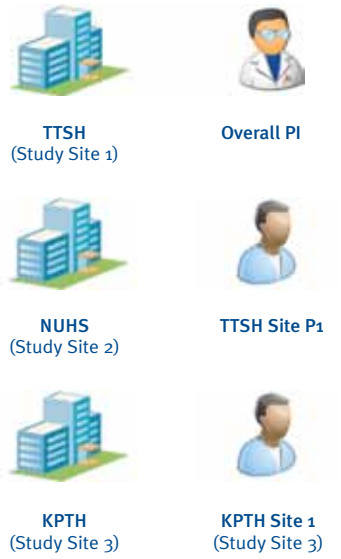


Fig. 2

Changing the name of the Overall PI in the DSRB Application Form

When a user creates a new draft DSRB Application Form, the ROAM system will default them as the Overall Principal Investigator and include the user's Institution as the default Study Site.

By default, the system has made Kian Wah Yeo the Overall PI *(question B1(i))*, as well as being the Site PI for the Study Site - NHG HQ *(question B1(ii))*.

Important Points

While any member of the Study Team or Study Administrator can initiate and edit a draft Application Form, only the Overall PI can submit the Form to the DSRB.

This act is equivalent to the Overall PI signing on a physical form.

Access to any Study is based on the name-list found in Section A *(Study Administrators)* and Section B *(Study Team Members)*.

If any person has left the Study, we strongly encourage the Overall PI to update these sections of Application Form through a Study Amendment Form.

Fig. 3

In this example, Kian Wah Yeo, from NHG HQ, is the person who has created a new draft DSRB Application Form *(Fig. 3)*.

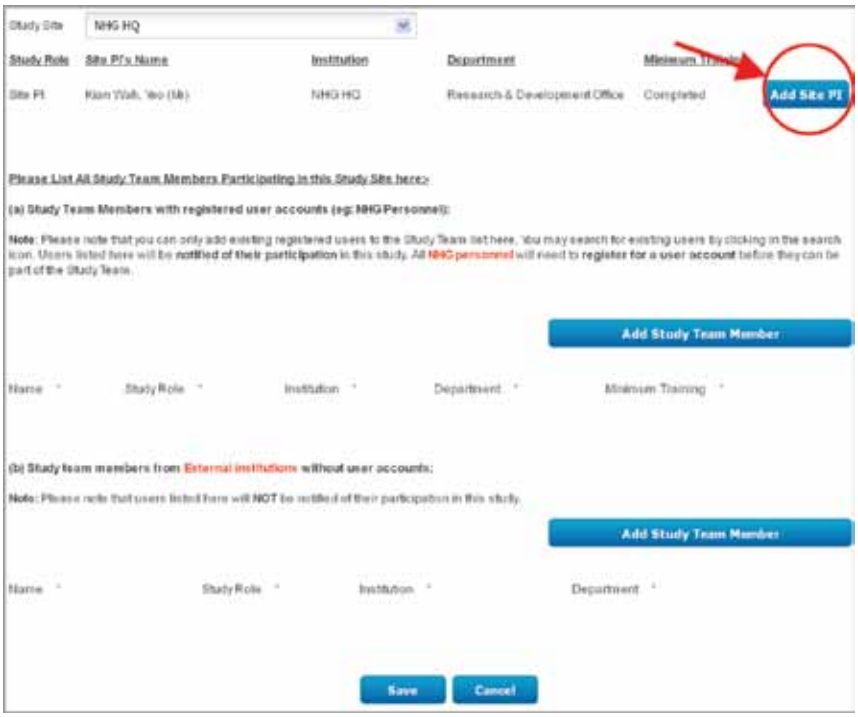


Fig. 4

To change the name of the Site PI, click on the 'man' icon found at the end of the table. This will open a new panel as shown in Figure 4.

Click on 'Add Site PI' *(Fig. 4)*.

Fig. 5

This will bring up a search panel so you can search for the name of the actual person who is to be the Site PI *(Fig. 5)*.

Once you have found the person you are looking for, click on 'Select'. The panel will automatically change back to the previous window and update its information *(Fig. 5)*.

In our example, we are making Kee Peck Tan the new Site PI.

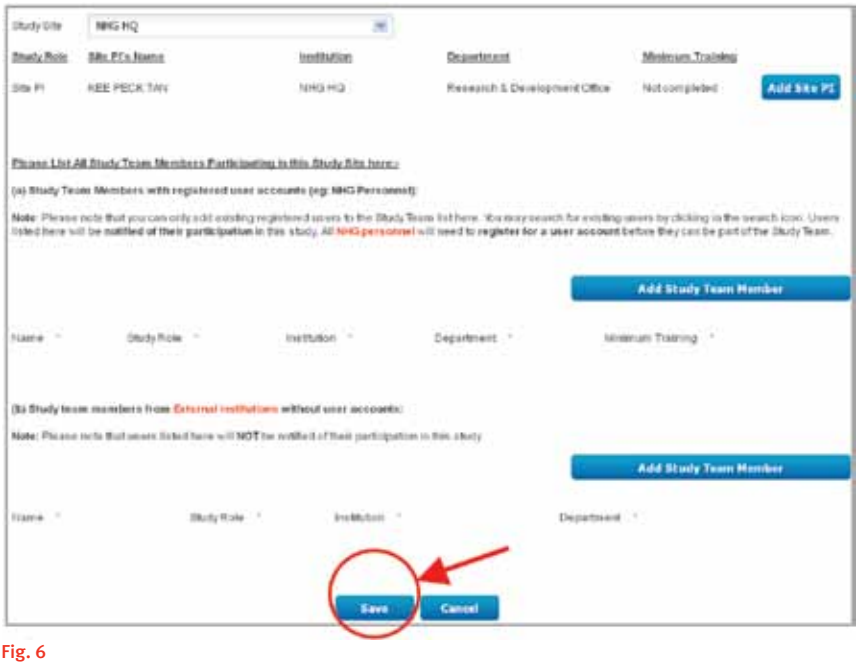


Fig. 6

Now, the new Site PI for NHG HQ is Kee Peck Tan *(Fig. 6)*.

Click on 'Save' when you are done. The panel will close and the new information updated to the Application Form.

Important: If you are to be a Study Administrator or to be part of the Study Team, remember to add yourself in either Section A or Section B.

If you forget to do so, you will not be able to access the draft Application Form once you have logged out. Otherwise, you will need to contact the new Site PI to add you back to the Application Form.

Fig. 7

The table in Section B1(ii) is now updated *(Fig. 7)*.

Kee Peck Tan is now the Site PI for NHG HQ, as well as being the Overall PI for the Study.

Adding a New Study Site

To add a new Study Site, click on the 'Add Study Site' button *(Fig. 7)*. A window as shown in Figure 8 will appear.

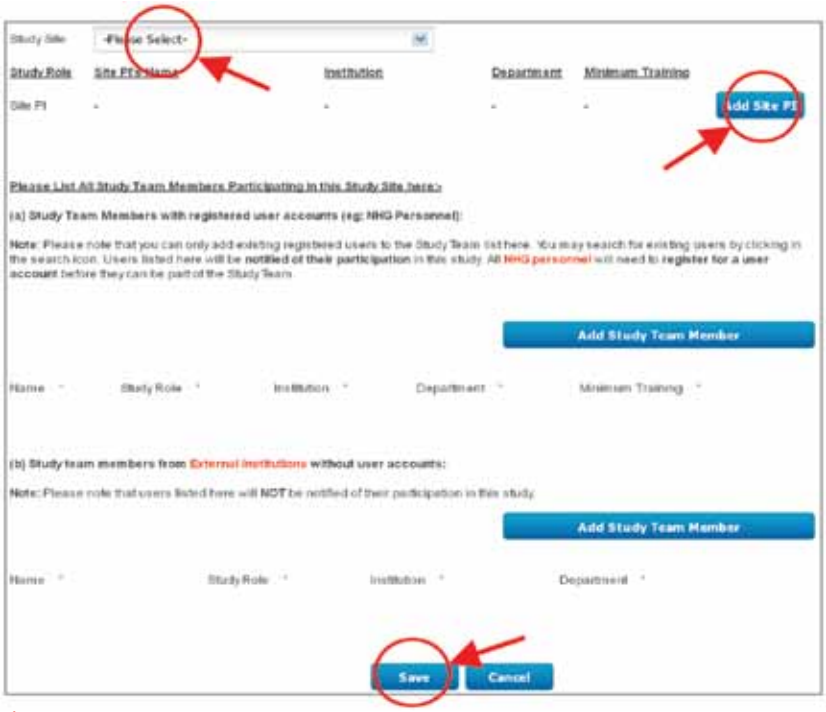


Fig. 8

First, you must select the Study Site that you wish to add from the dropdown list *(Fig. 8)*.

Next, click on the 'Add Site PI' button to add the Site PI.

Finally, add any other Study Team members for the Study Site using the 'Add Study Team Member' button.

Once the information is correct, click on the 'Save' button. This panel will close and return to the Application Form.

Fig. 9

We have thus added 'Tan Tock Seng Hospital' as the other Study Site *(Fig. 9)*.

This is now a two-center Study, with Kee Peck Tan and Felicia as the respective Site PIs.

In addition, Kee Peck Tan is the Overall PI for the Study.

Fig. 10

Changing the Overall PI

To change the Overall PI, use the radio button under the 'Main Site' column to indicate who the Overall PI will be. *(Fig. 10)*

Toggling the radio button will instantly update B1(i), where the name of the Overall PI is shown.

In this example, we have changed the Overall PI from Kee Peck Tan to Felicia PI1 NUH.

Society of Clinical Research Associates (SoCRA)

Background

The Society of Clinical Research Associates (SoCRA) is a non-profit, professional organization which was developed with the purpose of providing educational programmes, certification and a forum for research professionals to exchange information.

SoCRA was originally established to benefit researchers at the site, but its membership has grown to include monitors, data managers, quality assurance, and regulatory representatives from industry, academia, research centres, and regulatory agencies. SoCRA currently boasts over 13,200 members worldwide and has certified 8,290 Clinical Research Professionals.

About SoCRA Certification Programme for Clinical Research Professional

SoCRA established the Certification Programme for Clinical Research Professionals, in order to create an internationally accepted standard of knowledge, education, and experience by which clinical research professionals will be recognized by the medical research community. The certification examination was developed by SoCRA's Certification Committee and designated members who have demonstrated expertise in the development, management and administration of clinical trials.

In order to be considered for SoCRA certification, applicants must fall under one of the following categories:

- **Category 1:** Candidates with minimum 2 years of full-time employment during the past 5 years as a clinical research professional
- **Category 2:** Candidates holding a degree in "Clinical Research" and having completed a minimum of 1 year of full-time experience
- **Category 3:** Candidates holding an Undergraduate or Graduate certificate in "Clinical Research" and holding a Bachelor's Degree in science or related field and having completed a minimum of 1 year full-time experience.

Individuals who pass the certification programme successfully will be designated the title "Certified Clinical Research Professional" or "C.C.R.P. (SoCRA)".

Taking the Certification Programme in Singapore

The National Healthcare Group Research & Development Office (RDO) first hosted the Certification Programme in 2009. Of the 26 candidates who took part in this programme, >75% were successfully certified as a Research Professional.

This year, RDO is pleased to invite SoCRA to SIngapore once again to proctor the Certification Programme.

Ms.Susan Devine, a SoCRA procter, will be in Singapore from 7-8 March 2012 to conduct the SoCRA CCRP Preparation & Review Course and oversee the CCRP Examination. This exam will be held in conjunction with the Asia Pacific Research Ethics Conference (APREC) 2012 and held at the Grand Copthorne Waterfront Hotel, Singapore.

The rates are as below.

S/N	Category	Fees
		With APREC Conference Pass ($)
1	NHG Institutions	1070.00
2	Non-NHG Public Institutions	2380.00
3	Private Institutions	2990.00

To register for the Certification Programme or to make enquiries, please email to researchcoord@nhg.com.sg.
For more information on SoCRA, visit www.socra.org.

Upcoming Grant Calls in Singapore

1. National Medical Research Council (NMRC) Grants

The National Medical Research Council (NMRC) aims to establish a comprehensive and transparent set of grant schemes that support Principal Investigators (PIs) in targeted program areas. The Individual Research Grant (IRG), Exploratory Development Grant (EDG) and New Investigator Grant (NIG) are grants designed specially for PIs with different levels of research expertise.

Grant calls are open for all 3 grants on the first working day of May and November each year. Visit NMRC's website at www.nmrc.gov.sg for more information.

2. BEP Grant Call 2011

The Biomedical Engineering Program (BEP) is a competitive, multi-disciplinary grant program aimed at engaging the local clinical community with engineers and scientists to develop cost-effective innovations through a needs-driven approach that will improve patient care.

The BEP Grant Call is funded by the Science and Engineering Research Council (SERC) and seeks to foster Clinician-Engineer collaborations to develop medical devices and solutions to improve patient care and cost-efficiency of the healthcare system. The BEP Grant Call will open in November 2011. More information is available on A*STAR's website at **www.a-star.edu.sg.**

NHG Research Training Calendar

for September - December 2011

Date	Time	Training Programme	Course Category	Module	Venue	Seats
Ongoing	00:00-23:59	Proper Conduct of Research Online – Basic I-III	Proper Conduct of Research	PC101-103	www.elearning.nhg.edu.sg	120
30 Sept	08:30 – 17:30	Grant Preparatory Seminar	Research Methodology	RM105E	National University Hospital, Kent Ridge Wing Level 2, ASTC, STLab	30
2 Dec	08:30 – 17:30	Proper Conduct of Research Advanced II	Proper Conduct of Research	PC302	TBC	30

NHG Institutions Training Calendar

for September - December 2011

NHG COLLEGE

Date	Training Programme	Venue
3 Nov	Root Cause Analysis (RCA)	NHG College
14 Oct & 9 Dec	Quality Improvement (QI) Toolkit Workshop	NHG College
15 - 18 Nov	Clinical Practice Improvement (CPI) Programme	External
Medical		
9 - 11 Nov	Becoming an all rounded Consultant Course	TBC
29 & 30 Nov	Communication Skills Courses by the Cognitive Institute	NHG College
23 Nov	End of Life Conversations	NHG College
17 & 24 Sep	Evidence-Based Medicine (Basic)	NHG College
22 Oct	How to Read CT Head Scans	NHG College
29 Oct	X-Ray Reading	NHG College
Nursing		
3 - 31 Oct	Clinical Instructor Course for Registered Nurses	NHG College
11 Oct	Coaching Skills for Senior Enrolled Nurses	NHG College
10 Oct & 11 Nov	Patient Teaching Course	NHG College
24 & 25 Nov	Risk Management and Patient Safety Course for AN/SAN	NHG College
14 - 16 Nov	Risk Management and Patient Safety Course for Nurse Leaders	NHG College
14 & 15 Sep, 1 & 2 Nov 9 & 10 Nov, 5 & 6 Dec	Risk Management and Patient Safety Course for Registered Nurse	NHG College
IILTC (Institute of Intermediate & Longterm Care)		
7 Oct, 4 Nov & 8 Dec	Coaching	NHG College
16 Sep & 22 Nov	Legal and Ethical Framework	External
23 Aug, 6 Sep (half day) & 4 Oct (half day)	Quality Improvement Basic Toolkit Workshop	External
12 & 13 Oct	Risk Management & Patient Safety Workshop	External
1 & 2 Nov	Workplace Safety in Nursing Home	External

For more information and registration, please visit www.nhg.com.sg/college/institute-iiltc.html

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ISSUE 2011/09

THE PRINCIPAL INVESTIGATOR'S ROLES & RESPONSIBILITIES (Part 4/5 series)

No.7: Ensure that the Investigational Product is Properly Administered and Stored

No.8: Direct all Relevant Site Operations

CONTINUATION OF PARTICIPATION IN CLINICAL TRIALS AT STEP-DOWN CARE FACILITIES

Step-down care facilities, in particular, cater for patients who require inpatient convalescent and rehabilitative care, those who do not have families or caregivers to look after them at home, or where the caregiver is unable to provide the nursing care required.

THE PRINCIPAL INVESTIGATOR'S ROLES & RESPONSIBILITIES

The Principal Investigator (PI) is responsible for the Investigational Product (IP) accountability at the trial site. This includes ensuring proper usage and storage of the IP. The investigator can familiarise himself or herself with the use of the IP through reading the product information leaflet or the Investigator's Brochure.

No.7: Ensure that the Investigational Product is Properly Administered and Stored

Investigational Product (IP) Management Responsibilities

Responsibilities of IP management include, but are not limited to, maintaining proper records for receiving and dispensing the IP, counselling the study participant on the usage of the IP, ensuring that the IP is stored according to the manufacturer's or protocol's requirements.

The PI may choose to delegate some or all the responsibilities of managing the IP to a pharmacist and/or Clinical Research Coordinator. When doing so, the PI needs to ensure that the duties are appropriately delegated. The PI still retains the responsibility of providing supervision and oversight to the proper management and accountability of the IP.

Documentation and Accountability

It is necessary for the PI to maintain records of the IP's delivery to the trial site, the inventory at the site, the amount used by each subject, the return to the sponsor and the destruction of unused products, if applicable.

These records should include dates, quantities, batch/serial numbers, expiration dates *(if applicable)*, and the unique code numbers assigned to the IP and trial subjects.

The PI ought to also provide adequate documentation in the drug accountability/dispensing log and the subjects' medical records that the subjects were provided the doses specified in the protocol. All IP, whether used or unused, should be reconciled.

Storage, Usage and Administration

The PI is responsible for ensuring proper storage and usage of the IP at the site, as specified by the sponsor or as stated in the Institutional Review Board (IRB) approved protocol. Most IP's are required to be stored within a specific range of temperature.

The PI will have to arrange for or purchase appropriate storage equipment if freezing or refrigeration is required. The IP should be stored in a secured location with access limited to authorised personnel only *(e.g. pharmacist or Clinical Research Coordinator)*.

When dispensing the IP to the subject, the PI or delegated personnel need to explain the correct method of usage and check at appropriate intervals that subjects are following the instructions given.

References:

- *Singapore Guideline for Good Clinical Practice (SG-GCP)*
- *NHG PCR SOP 501-A02 Responsibiities of the Research Team*
- *NHG PCR SOP 501-B06 Investigational Product Accountability*

No.8: Direct all Relevant Site Operations

Proper Delegation of Responsibilities

Prior to the initiation of any study, the Principal Investigator (PI) has to ensure that the study team members are familiar with the protocol and possess the appropriate training and qualifications for the duties they are delegated.

The study team will be required to be trained on the protocol and attend all study-related training and start-up meetings before initiation of the study.

In addition, the PI has to ensure appropriate delegation of duties in the study. An example is: a study coordinator who has qualifications in phlebotomy being delegated for the blood specimen collection procedure in the study.

Another example of appropriate delegation would be the PI or Co-Investigator (Co-I) being delegated the task of obtaining informed consent from potential participants.

This will ensure that medical opinions and advice will be available to all subjects before they agree to participate in the study.

Meanwhile, a list of qualified persons and their corresponding research-related delegated duties in the study responsibility log should be maintained. This list has to be updated accordingly whenever there are changes to manpower or delegation of duties in the study.

Assuring Continuing Protocol Compliance

During the study, the PI is accountable for continuing protocol compliance and dissemination of information to the participants and relevant authorities.

Participants have to be informed of any new information that may affect their willingness to continue participation. This may be done through, but not limited to, the following means:

- Information Letter
- Addendum to previously signed consent form – to be signed by subject
- Revised consent form – to be signed by subject

The PI also ought to be familiar with reporting requirements to the relevant authorities, and ensure prompt reporting on issues, such as unanticipated problems involving risks to subjects or others (UPIRTSO), and protocol deviations.

Reporting requirements to the NHG Domain Specific Review Board (DSRB) will include the following issues:

- UPIRTSO
- Protocol Deviation and Noncompliance
- Continuing Review Reports
- Protocol Amendments

Monitoring and Auditing

During the study, there may be instances of monitoring and audits by the Sponsor, NHG Research Quality Management and Regulatory Authorities. The PI should see to the availability of all necessary documents during monitoring and audits and that study team members are available for queries.

The PI may also consider providing oversight of protocol compliance and progress by meeting the study team regularly to discuss and identify issues relating to the study, and ensuring that necessary actions are taken.

References:

- *NHG PCR SOP 501-A02 Responsibiities of the Research Team*
- *NHG PCR SOP 501-C01 Informed Consent Document and Process*
- *NHG DSRB SOP 201-C05 Continuing Review*

CONTINUATION OF PARTICIPATION IN CLINICAL TRIALS AT STEP-DOWN CARE FACILITIES

Step-down care facilities play an important role in Singapore's healthcare system, and consist of community and chronic sick hospitals, nursing, psychiatric rehabilitation and sheltered homes, inpatient hospice institutions, day rehabilitation, dementia day care and psychiatric day care centres. Step-down care facilities, in particular, cater to patients who require inpatient convalescent and rehabilitative care, those who do not have families or caregivers to look after them at home, or where the caregiver is unable to provide the nursing care required.

For clinical trials approved by the DSRB, subjects by and large are recruited and consented at acute care hospitals. Currently, there are no clear guidelines defining obligations of investigators who wish to have their clinical trial protocols continued uninterrupted at step-down care facilities. However, as a responsible researcher and physician, the investigator must ensure that trial-related information is properly communicated to members of the staff at the step-down care facility. Communication plans are essential to maintaining compliance to the trial protocol, ensuring continuity of the clinical trial, and more importantly, providing the assurance to subjects and their caregivers that their safety and welfare are not being overlooked. The investigator is encouraged to communicate the following items to members of the staff at the step-down care facility:

- Contact number and person for trial-related issues;
- Trial procedures to be followed, especially when it relates to the administration of Investigational Product(s) (IP);
- The foreseeable adverse events;
- Arrangements in the event of trial-related injury;
- Circumstances under which the subject's participation in the trial may be terminated;
- Communication of non-compliance and adverse events to investigators.

"Therefore, before conducting a clinical trial or research study, the investigator should anticipate and plan ahead. If there is a likelihood that the study subjects may be transferred from the acute care hospitals to step-down care facilities, appropriate communication plans should be put in place."

The Singapore Guideline for Good Clinical Practice (SG-GCP) Section 4.2.4 states that the investigator is responsible for ensuring that all persons assisting with the trial are adequately informed about the protocol, the IP and their trial-related duties and functions. Negligence of the investigator to ensure proper communication of the research to the staff at the step-down care facility, or failure of the investigator to protect the safety and welfare of the subjects may be considered as non-compliance.

References:
- *Singapore Guideline for Good Clinical Practice (SG-GCP)*

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