



## TAKING THE EXTRA MILE BEST PRACTICES IN ENSURING QUALITY & REGULATORY COMPLIANCE

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### INTRODUCTION TO THE HAEMATOLOGY-ONCOLOGY RESEARCH GROUP (NUHS)

The Haematology-Oncology Research Group (HORG) comprises of a team of leading haematologists, oncologists, clinical research coordinators, data managers, genetic consultants, internal auditors and administrators. HORG seeks to succeed as one of the top cancer research groups in Asia. The research team works together in synergy, from screening to monitoring to the final closing out of the study, to ensure that protocols are followed, and adhere to the Singapore Guideline for Good Clinical Practice. In this article, HORG shares their best practices with our readers.

#### Best Practice 1 - Ensuring Proper Handover of Duties Prior to Leave of Absence

To ensure the continuity of patient care at all times, it is HORG's practice that every research coordinator conduct a proper handover of their studies to a backup coordinator before taking any leave of absence. Thus, advance planning of annual leave is highly encouraged. In addition, Principal Investigators (PIs) have pre-assigned co-investigators to take over their responsibilities whenever they go on leave.

#### Best Practice 2 - Specialisation of Roles in the Research Team

To lessen the administrative burden imposed on research coordinators, department administrators are assigned the task of assisting the PIs in the submission of protocol and consent form amendments to Domain Specific Review Board (DSRB) and Health Sciences Authority (HSA).

The research coordinator is in charge of reminding the respective Principal Investigators to obtain the necessary DSRB and HSA approvals or renewals. The Principal Investigator then with the assistance of the administrators, completes the application to the applicable regulatory body. This allows research coordinators to focus on screening, enrolling, monitoring and following-up with study participants in accordance with study protocols, maintaining proper documentation and safety reporting in a timely manner.

#### Best Practice 3 - Utilising a Tracker to Monitor Expiry of Ethics/Regulatory Approvals for all Studies

To help ensure quality and regulatory compliance, HORG also instituted a departmental DSRB/HSA tracker for its research studies. This DSRB/HSA tracker is used to assist in monitoring ethics approvals, Clinical Trial Certificate (CTC) approvals and highlight expiry dates, for

both in-house and pharma-sponsored studies. Information kept within the tracker includes:

#### 1. DSRB approval

- 1.1. Protocol version and date
- 1.2. Informed Consent Form (ICF) version and date
- 1.3. DSRB expiry date

#### 2. HSA approval

- 2.1. Protocol version and date
- 2.2. ICF version and date
- 2.3. CTC expiry date

#### 3. Renewal status

Pending or completed

#### Best Practice 4 - Conduct of In-House Audits

HORG regularly conducts in-house audits for all ongoing studies. The audits include a review of the investigator's file, case notes, case record forms, adverse event submissions, ethics and regulatory submissions, pharmacy and accountability logs.

Through these regular in-house audits, HORG aims to ensure the protection of subjects enrolled in the clinical trials, confirm the validity of data collected and verify compliance with all regulatory and ethical guidelines. The results of these in-house audits are presented and discussed at research team meetings every month. This also serves as a great learning experience for team members.

#### Best Practice 5 - Conduct of Regular Research Team Meetings

The entire research team including investigators, research coordinators and pharmacists gather every month to discuss all ongoing studies, monitor patient accruals, discuss all deviations and monitor toxicities and/or adverse events. Solutions are proposed to address challenges raised

during the meeting. To support research coordinators and ensure that they are given adequate support for their work, a monthly research coordinator's meeting is also held. During these meetings, useful lectures are given on relevant topics such as consent taking, eligibility, hand washing, *Methicillin-Resistant Staphylococcus Aureus* (MRSA) precautions, chemotherapy, targeted therapy, common side-effects, etc.

**Best Practice 6 - Training to Equip and Empower the Research Team**

Adequate and proper training is imperative to each and every personnel involved in the research team. Aside from the usual Collaborative Institutional Training Initiative (CITI) and Singapore Guideline for Good Clinical Practice (SGGCP) training, research coordinators also attend extra training for self-development such as Proactive Time and Stress Management

and 7 Habits of Highly Effective People. Senior research coordinators may also apply for the International Certification offered by the Society of Clinical Research Associates (SoCRA).



PROTOCOL NON-COMPLIANCE

**CONTINUOUS OVER-RECRUITMENT OF RESEARCH SUBJECTS**

**Background**

A multicenter clinical trial had exceeded the approved maximum recruitment target due to an oversight by the Principal Investigator (PI) and his study team. The PI reported the over recruitment to the DSRB in a non-compliance report and informed that additional effort would be made to check on the recruitment status before enrolling new subjects in future.

However, the PI continued to over-recruit subjects. This over-recruitment was detected by the DSRB during the study's annual continuing review submission.

**Findings & Implications**

Because the PI had continued with an over recruitment of research subjects despite the initial reporting, DSRB deems this as a case of continuous non-compliance. As a result, a DSRB warning letter was issued to the PI. A temporary renewal was also issued under the condition that no

subjects should be enrolled until the PI could provide a satisfactory response on the situation. Subjects who were recruited above the target number should also be re-consented.

**Tips and Recommendations**

- a. If the Principal Investigator anticipates subject recruitment beyond the approved target, he/she should submit an amendment to the target number and must ensure that recruitment does not exceed the approved target until an approval is received from the DSRB.
- b. It is the responsibility of the PI to ensure that communication is kept tight within the study team and that the study team is updated on the study status promptly. Team communications should include the recruitment strategy, recruitment timelines and plans to manage the study.

**References from Singapore Guideline for Good Clinical Practice (SG GCP) and NHG – Proper Conduct of Research SOPs (PCR-SOPs):**

[SGGCP 4.5.2] The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s)).

[PCR 501-B03 - Study Initiation] 9. Principal Investigator and the study team should discuss the recruitment strategy and recruitment timelines and plan to manage the study accordingly.

**The NHG Proper Conduct of Research Standard Operating Procedures may be referenced at the following portal:**

<http://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops>

GCP TOPIC  
**INFORMED CONSENT**



**Informed consent is the process by which a subject voluntarily confirms his or her willingness to participate in a particular research project after being informed of all aspects of the research study that are relevant to the subject's decision to participate.**

Informed consent needs to be documented by means of a written, signed, and dated informed consent document. This process is necessary to ensure that subjects are fully informed before deciding to volunteer as research subjects in research projects

of any type. It is a good practice and responsible conduct of the researcher to apply the "reasonable man" criterion. The term "reasonable man" criterion includes the following:

- Sufficient time for a person at the appropriate literacy level to read and digest the consent,
- Sufficient time for the individual to ask the study staff questions and consult with a relative or friend,

- Sufficient time, if requested, to review and research some of the provisions in the informed consent form (i.e. alternative therapies), or
- Sufficient time to reflect on the decision.

As a general rule of thumb, if the proposed study, protocol, consent form and decision making process are complicated, a reasonable person would require additional time to think through the decision. For older adults, children, and cognitively impaired