

Network Coordinating Centre:

Site Development Road Map

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Introduction and Purpose

All members of the South East Asia Influenza Clinical Research Network (SEA ICRN) are committed to the conduct of clinical research at the highest scientific, ethical and clinical practice standards currently followed in the international medical research community. The SEA ICRN seeks to provide training, mentoring and assistance to all research sites to facilitate their acquisition of the necessary knowledge and skills that will enable them to conduct clinical research at these internationally accepted standards, become widely recognized for research excellence, enhance their opportunities for receiving outside research funding, and publish their data in peer-reviewed academic journals.

Each site that joins the Network brings its own history and experience in conducting clinical research. They enter with varying levels of practice and knowledge of current international standards of research ethics, The International Conference on Harmonization Good Clinical Practice Guidelines (ICH GCP), quality assurance, prior trials conduct, data management and laboratory standards and the many other characteristics that make a site completely self-reliant in their ability to comply with widely accepted guidelines. Through participation in the Network, sites will embrace and use international benchmarks enabling harmonization of practices across the sites and ensure compliance through internal and external monitoring. This harmonization along with the concomitant cooperation and sharing between Network members are principal contributors to the real ‘power’ of the Network, bringing efficiency in answering questions no one partner can and affords results applicable generally for global health benefit. Those benefits, however, bring responsibilities that all sites meet international norms, are properly staffed and managed and maintain internal quality controls to assure that results are comparable between countries and sites.

Regardless of their entry experience level, all sites require assistance with the process of learning and applying the international research standards adhered to by the Network. The Network has established the **Network Coordinating Center (NCC)** to assist sites in setting operational standards of research, training sites and staff in understanding and applying these standards, and supporting the sites to achieve the highest levels of excellence that they and the Network desire.

The successful conduct of a clinical trial requires a number of systems, policies, practices, and procedures to be in place. Participation in the SEA ICRN training and mentoring activities enables investigators to build research portfolios in accordance with current international expectations of ICH GCP practices and comply with the requirements of the European Medicines Agency (EMA), the US Food and Drug Administration (US FDA), and other regulatory agencies. By meeting these expectations and standards, they contribute data to internationally funded, multicenter studies and research, leading to greater international recognition, improved publication opportunities, and participation in trials of pharmaceutical drugs and devices that benefit member countries and their global partners.

The SEA ICRN has adopted the following ethical codes and standards, in addition to the specific requirements of each member country's own regulations:

- The Declaration of Helsinki (<http://www.wma.net/e/policy/b3.htm>)
- The International Conference on Harmonization / Good Clinical Practices (<http://www.fda.gov/cder/guidance/959fnl.pdf>)
- International Organisation for Standardisations's Technical Committee 212 (ISO/TC 212):Laboratory quality standards of ISO/IEC 15189

Research staff who are directly involved with patients enrolled in SEA ICRN studies are required to receive training in:

- Protection of Human Subjects (also known as Research Ethics)
- ICH Good Clinical Practices

Building on this general training, site research staff participate in systematic and customized site training in human subjects protection, research ethics, data management, research pharmacy systems, project management, clinical procedures, participant safety monitoring and laboratory practices and procedures.

To facilitate the sites achieving these standards the **Clinical Trials Support Specialist (CTSS)** is available to assist and guide the sites through this learning process. The CTSS is the direct link between research sites and the Network at the operational level of implementing the research protocol and building enhanced capacity for conducting research.

This document describes the process by which the NCC together with the CTSS work with each research site to assess its state of readiness for managing clinical research, map out a plan for enhancing site research skills, and assist the site in achieving its capacity goals. The process outlined here is the Road Map.

Responsibilities of the Research Site

The Site Principal Investigator (PI) is ultimately responsible for the implementation of the study protocol at his/her site. The PI cannot do this job alone. A well-trained and dedicated team of staff, empowered to handle the day-to-day details of conducting the study, is necessary to get the job done. The PI oversees the activities, expects frequent reports from the staff, and ensures the safety of study participants (volunteers) and that they are properly managed medically. The PI is responsible for the development and implementation of a Quality

Management Plan (QMP) that addresses all aspects of proper study management, and overseeing the staff who implement it.

Before a study begins at a site the PI will work with the Network operations staff and the CTSS to evaluate the site readiness for conducting a Network protocol. After the study is initiated at the site, the CTSS will continue to assist the study site as it works toward achieving full understanding and application of the Network procedures. Over time the site will continue to increase their skills in conducting research to international standards.

Research Study Team

The research study team is composed of the site staff who implement the study protocol under the direction of the site PI. For each study protocol there are specified study roles that must be fulfilled. For a large study with many participants, the site may choose to have one or more staff members for each role. For smaller studies, or studies that are slow in recruitment, a single person may handle more than one role on the team. In many sites one staff member may serve a role on more than one research study team.

The site PI will choose how to assign the different responsibilities to its research team. Each of the following roles will be assigned to named persons on the team prior to the beginning of screening and enrollment. The team assignments are recorded on a Delegation of Duties Log. This Log lists the research team role, the named staff who are performing that role, and other information relevant to the protocol. Staff team assignments may change over time, and when this happens the site will update its Delegation of Duties Log.

Team Roles

The study team works together closely to effectively implement the research protocol. Each member has one or more assigned roles to perform. The size of the team depends on the nature of the study being conducted.

- **Principal Investigator (PI)** has primary responsibility for the conduct of the study at the site and represents the study to the hospital, health services and regulatory agencies. The PI is responsible for clinical conduct and assessments of the clinical trial and provides treatment and care to all patients that meet study eligibility criteria and are enrolled in the clinical trial. The PI may be actively involved in clinical care of participants, or may delegate much of that work to the sub-investigator(s). The PI bears the ultimate responsibility for the conduct of the clinical trials team, and the care of the study participants.
- **Study Coordinator (SC)** is essential to the successful management of the study protocol. He/she is empowered by the PI to direct the operational details of the study, and is the person who keeps track of the progress of the study and communicates with the sponsor to provide required information on study progress. Both the PI and the sponsor rely on the SC to provide accurate and timely information, ensure proper data collection and to be ever vigilant regarding patient safety.

The SC interacts with both the research team onsite and with the external Network staff. He/she manages the internal workings of a site and as well as external communications to the Network. He/she is responsible for the day to day coordination of all study activities at the site, ensuring the procedures are in place and followed. The study coordinator is key to assisting the PI in managing all the recordkeeping required of the clinical trial. He/she tracks study enrollment, may oversee the consenting process, ensures the quality of all the site operations and procedures, including staff training requirements been met, Case Report Forms (CRF) are completed each day, drug accountability is tracked, Standard Operating Procedures (SOP) are being followed, etc. The study coordinator will serve on Network committees and communicate with staff from other sites and the NCC.

- **Sub-Investigator(s) / Study Clinician(s)** are medical doctors who oversee the day-to-day study operations of the research study and implement the study protocol under the guidance of the PI. They conduct study procedures, evaluate adverse events, may complete CRFs, contact pharmacists for study drugs and evaluate new patients. The sub-investigators may administer the informed consent process to potential study participants. These staff must have strong clinical care skills and also understand the principles of clinical trials research and practice. The sub-investigators make clinical care decisions for study participants.
- **Study Nurse** is responsible for recruiting, evaluating and consenting study participants. The Study Nurse is responsible for providing nursing expertise in the care of participants enrolled in the study. He/she maintains patient records and ensures all items on the CRFs are complete. He/she follows research subjects throughout the duration of the study. In collaboration with the Study Coordinator will manage and assist the research team in the coordination of all activities of the study as required for the successful implementation of the study protocol and the safety of the study participants.
- **Research Pharmacist** is responsible for ensuring that systems and procedures are developed and implemented to control study drugs used in clinical research.
- **Research Lab Technician** is responsible for ensuring that systems and procedures are developed and implemented to control all study lab procedures used in clinical research.
- **Administrative Assistant** will provide the study team with assistance in administrative tasks such as answering telephones, faxing, typing and printing documents, copying documents, filing, scheduling meetings, and taking meeting notes.
- **IT Support person** will provide technical assistance to the core study team and the study support team to support the proper function of all research computer and technical equipment including hardware, software and internet connections.
- **Study Accounting Manager** is responsible for managing the accounting and financial records for all functions of the approved research study budget. He/she is responsible for approving and maintaining records of purchase acquisitions for study equipment and facilities, study staff payroll, and other associate study costs. He/she monitors and reviews financial activity and provides regular reports to study sponsor.
- **Quality Control Manager** will develop and assist with the implementation and filing of all site SOPs. He/she will provide oversight of quality assurance strategy and function for adherence to all SOPs and ethical and GCP standards. Assists the PI to improve the QMP and apply any needed corrective action plans.

- **Site Data Manager** will ensure the CRFs are properly completed, file them according to the filing procedures, and ensures the CRFs are managed in accordance with the data management plan.

Expectations for Site Performance: The Road Map

Successful management of a clinical research site is challenging especially when the regulations and procedures are not familiar. Each research site in the Network has agreed to conduct research according to ICH GCP guidelines and the policies and procedures of the Network, as well as specified rules and regulations of the US government and their local government agencies.

The Network is dedicated to assisting its research sites achieve successful study implementation according to all these standards. The goal of the Network is to help the sites build their own research skills to the point of becoming independent from external assistance from the NCC. This skill building is a process that involves engaged participation from the site PI, his/her site research staff, and the NCC.

- Sites will be evaluated according to a set of accepted international standards outlined by the NCC, and its level of readiness and competency in the various standards rated
- The site PI will work closely with his/her study coordinator, the NCC Country Office (CO) and the Clinical Trials Support Specialist (CTSS) to develop a Site Qualification Plan to achieve higher levels of competency in each of the site responsibilities
- The study coordinator and CTSS will work together to provide any necessary training and develop appropriate systems to achieve higher competencies
- When a site can fully accomplish a designated responsibility on its own, the CTSS will update the Plan to certify the site has completed the training on that task
- As the site gains experience it will advance through the Plan and achieve greater independence

Sites will be recognized at the Network level for completing the Site Qualification Plan.

Site Responsibilities and Competencies

Sites will be evaluated for the following competencies against development standard and performance indicators noted in Table 1.

Assessing Baseline Site Capacity Levels

Sites will be evaluated according to established development and performance criteria at the initial site assessment or at a later date if site is already a Network member. Assessment dates will be mutually agreed upon between PI, NCC and responsible CTSS. The evaluation team will be composed of a member of the NCC, the responsible CTSS and the SC. The team will out-brief with the PI and study team at the completion of the review and together wherever possible immediately develop plan for establishing necessary skills and competencies. There will be a periodic re-assessment every six (6) months to follow-up on areas requiring attention as well as

a general review to ensure maintenance of key skills and systems that already meet site self-reliance standards.

Creating the Site Self-reliance Plan and Process for Reaching Site Goals [PI, SC, CTSS, NC CO collaborate]

At the time of the initial evaluation, the evaluating team will meet with the PI and selected members of the study team, forming a working group. Site status in the various competencies will be reviewed with the team in detail and consensus reached regarding the missing elements. Missing elements might include staff additions, specific training or certification, equipment or facilities improvements. An action plan will be developed with the PI, appropriate team members, NCC staff and CTSS. The plan will include a timeline, milestones and indicators for success. If there are unanticipated expenditures associated with plan, a budget will be submitted to the NCC for funding approval. The PI, SC, CTSS and NCC will work together toward meeting the milestones outlined in the qualification plan. There will be semi-annual evaluations but the working group will monitor developments at the site more regularly and seek to solve problems, remove obstacles to the achievement of the desired objective on schedule.