Global Alliances: Steps to Self-Sustainability for the Good of Public Health

by

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9 April 2007

A Master's paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the School of Public Health, Public Health Leadership Program.

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Abstract

Creating global alliances to fight disease and build infrastructure in developing and middle income countries has become a popular topic in the last several years. The global burden of disease and disparities in the level of health and healthcare make it difficult for any one group or funding source to make significant improvements in these areas, and in many areas of the world, the infrastructure simply does not exist. Global alliances have been instrumental in helping to build this infrastructure and research capacity, thereby reducing the impact of HIV/AIDS, TB, malaria, and many other diseases. The ultimate goal of building sustainable capacity and infrastructure is to facilitate the transfer of knowledge gained through research into clinical practice and policy but it is a complex, resource-intensive process with many challenges. In 2005, the threat of an influenza pandemic led the National Institutes of Health and the Wellcome Trust to form the Southeast Asia Influenza Clinical Trial Network, supported by Oxford University and Family Health International. Although much progress has been made in a short time, challenges persist and the long term benefits have yet to be established.
Introduction

Creating global alliances to build infrastructure and fight disease in developing and middle income countries\(^1\) has become a relatively common endeavor in the last ten to twenty years. A growing awareness of the shared burden of disease and the consequences of disparities in health and healthcare for global citizens has cast increased attention on the need for synergistic alliances that combine the strength, resources, and expertise of different sectors to help alleviate this unequal distribution (Widdus, 2001). As noted recently in *Epidemiology*, “Networks, by virtue of their greater scope, resources, population size, and opportunities for interdisciplinary collaboration, can address complex scientific questions that a single team alone cannot” (Seminara et al., 2007). Global networks have been formed and used successfully in the field of genome sequencing (Camargo & Simpson, 2003) and to reduce the impact of diseases such as HIV/AIDS, tuberculosis, malaria, polio, and river blindness by intervening at multiple points: community and household level, health-service delivery level, and at the policy and strategic management level (Bill and Melinda Gates Foundation, 2002; Travis et al., 2004). By working on health problems at multiple levels, the complex interplay of factors affecting population health can be addressed (Travis, et al., 2004).

The broader picture encompassing this is the need to develop sustainable research capacity in developing and middle income countries. There is a growing recognition that a strong link exists between health and development (Ijsselmuiden & Matlin, 2006; Lansang & Dennis, 2004; Pang, Sadana, Hanney, Bhutta, Hyder, & Simon, 2003). Investing in human, physical, and

\(^1\) The World Bank defines low income countries as those with a yearly per capita income of ≤ $875 USD; middle income countries are defined as those with a yearly per capita income between $1,025-$6,055 USD. (http://web.worldbank.org; accessed 3/27/2007)
intellectual capital works to improve global health by stimulating economic development and improving the health of both individuals and populations (Distlerath & Macdonald, 2004; Pang et al.). In essence, a positive feedback loop is created. Improved population health increases the capacity for economic development; in turn, economic development spurs better health outcomes.

This paper will examine how networks can be used to build sustainable research capacity, some of the challenges of building them and some of the practicalities involved. Finally, this paper will discuss the formation and considerations of the Southeast Asia Influenza Clinical Research Network, a two-year old alliance, as it seeks to develop centers of clinical research excellence that can respond to influenza and other emerging infectious diseases in participating countries.

**Building Sustainable Research Capacity**

By strengthening health research capacity, global networks have been cited as one way to alleviate a funding disparity termed the “10/90 gap.” The “10/90 gap” refers to the fact that only 5-10% of all global research funding is targeted towards health problems that are responsible for 90% of the world’s health problems (Global Forum for Health Research, 2006; Harris, 2004; McCoy, Sanders, Baum, Narayan, & Legge, 2004). In order to close the “10/90 gap,” it is important to develop research capacity that is sustainable over the long term and research systems that can “define and prioritize problems systematically, develop and scientifically evaluate appropriate solutions, and share and apply the knowledge generated” (Lansang & Dennis, 2004, p. 765). Both long and short-term strategies must be formulated and directed at individual, institutional, and national levels in order to create sustainable systems of health
research. To promote sustainability, research must focus on the social, economic, and political determinants of health, especially as they relate to clinical and biological research. Lastly, there must be a mechanism for the successful transfer of knowledge from research into policy and practice (McCoy et al., 2004).

The ultimate goal is to create a health research system that encompasses all types of research “including biomedical, clinical, epidemiological, health systems and policies research, socioeconomic and behavioural research...it also includes research not usually considered to be health related—for example, engineering studies to improve car or road safety or economic research leading to policy changes that affect poverty” (Pang et al., 2003, p. 816). Recognition that capacity building within a country or region takes place within a larger environment of socioeconomic and political circumstances is crucial. For efforts to be sustainable, they must take into account the local politics, economics, and institutions; to be effective, they must be “country-owned” rather than “donor-driven” (Dayrit, Morin, & Matlin, 2006). The Global Forum for Health Research recommends that developing countries devote 2% of their national health expenditures to build research capacity and that donor organizations allocate 5% of their budgets to this function to help ensure sustainability over the long term (Usselmuiden & Matlin, 2006).

Private, for-profit, non-governmental/non-profit organizations, and foundations have combined in various ways to create alliances, recognizing that the health problems in developing and middle income countries are too complex to be remedied by the actions of any single person, organization, or sector. These partnerships “involve a diversity of arrangements, varying with regard to participants, legal status, governance, management, policy-setting prerogatives, participants, contributions, and operational roles” (Widdus, 2001, p. 717). Although some such
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alliances have been primarily focused on research and development, the majority have been partnerships of donation and distribution whereby medications for disease control are distributed among those in need while efforts are made to see that the product is used effectively. Although there are welcome short term benefits to this type of arrangement, in the absence of other sector services the drugs themselves do not usually address the health problems of highest priority. To be truly successful and sustainable over the long term, partnerships must strengthen healthcare service infrastructure, delivery, and outcomes while addressing the issues that are pertinent to the local area served (Widdus, 2001).

To this end, the early stages of network development may include logistical steps, such as helping scientists “gain access to education, training, funding, information, equipment and supplies” (Harris, 2004, p. 7). Although some middle income countries have advanced avenues for scientific development such as graduate, doctorate and post-graduate programs, low-income countries may not. In many low-income countries, research is not considered to be a priority or a “profession” and therefore is seen as an activity to be done “on the side” with many researchers holding multiple jobs in order to earn an adequate income or leaving their countries to pursue more lucrative opportunities. Funding that allows for researchers to be fully dedicated to research can help alleviate this problem.

Equipment and Training Considerations

Strengthening capacity and infrastructure in middle income and developing countries may require expenditures for equipment and facilities in order to conduct research. For example, laboratories may not have the equipment to perform certain tests, so the network may have to invest in facility renovation and then provide the equipment, associated systems, and reagents (Pang et al. 2003). Once the new equipment is purchased and installed, the training of lab staff
on its operation can begin, but to encourage sustainability, this training should not be strictly process oriented (i.e., how to run the newly purchased lab equipment). Network collaborators should incorporate a broader based training. For example, teaching epidemiological surveillance methods alongside laboratory technique helps regional scientists understand local disease patterns and gives them an opportunity to provide input on the design of appropriate interventions. Laboratory staff can also be trained on international standards of laboratory practice, which, when incorporated over time, can improve the practices of local laboratories. By training research scientists on proposal development, grant-writing, and manuscript writing skills, additional steps are taken to foster sustainability (Harris, 2004).

Other individuals new to research may require training as well. Initially, training should follow a careful needs assessment in order to be responsive to the requests of local staff, should encourage group participation, including examples and situations that are applicable to the local environment, and be as hands-on as is possible. Whenever feasible, local and regional experts should serve as instructors. As more individuals receive training and become proficient in the subject matter, they can become local and regional trainers. Training conducted by instructors who work under similar conditions and constraints as the trainees helps build trust and empowerment (Harris, 2004).

*Goal setting*

In developing and increasing capacity at the local and national levels, network collaborators should create short and long term goals. Short term goals may be task-oriented, such as purchasing equipment, up-fitting facilities, and hiring staff. A long-term goal of the network alliance, however, must be to engender an environment that is conducive to research and a career ladder that will entice and retain talented individuals. "This includes good research
management, availability of funding for research, opportunities to present and openly discuss research data, and...rapid access to current research information” (Pang et al., 2003, p. 817). Additionally, the alliance should develop leadership and management competencies among local researchers. Skills that need to be advanced include “strategic planning; research priority setting; knowledge management; advocacy and demand creation; consensus building and negotiation; resource generation and allocation; partnership building across many stakeholders; communications, including virtual forms of networking; financial management; and systems performance assessment” (Lansang & Dennis, 2004, p. 767). Attempts should be made to have training sessions on a regular basis to ensure that new researchers and other team members are kept up to date on new and current research and practice.

To reap the benefits of a collaborative effort, the network should have a well defined, compelling overall goal and scope (Bill and Melinda Gates Foundation, 2002). Seminara et al. state that “Elements deemed essential for launching a network are a strong scientific rationale, the agreement of all teams to work together and combine data on overarching research questions, and the ability to support initial communication, coordination, identification, and recruitment of partners” (Seminara et al., 2007, p. 2). Beyond this, managers and donors must have an understanding of what value is obtained from working within an alliance and what is needed to attain that value; determine an appropriate structure for the alliance; determine what metrics will be used to measure success, how milestones will be met, and contributions of other partners; and create models for governance that allow for effective and efficient decision-making while allowing for input from network members (Bill And Melinda Gates Foundation, 2002).
Benefits of Working Within an Alliance

There are many benefits of working within an alliance, including: avoiding duplication of investments and effort; gaining economies of scale, sharing or reducing risks to allow new initiatives to take place that individual partners or donors might not have been able or willing to take on alone; sharing knowledge, resources, and best practices to improve effectiveness; and accelerating momentum and attracting funding by building a common “brand” that gains legitimacy and monetary support (Bill And Melinda Gates Foundation, 2002). Other valuable, but less tangible, benefits of collaboration include “new and better ways of thinking about health issues” (Lasker, Weiss, & Miller, 2001, p. 184). This can include creative thinking, comprehensive thinking, practical thinking, and transformative thinking.

Creative thinking occurs when partners come together, more voices are heard, and differences are explored, which in turn welcomes new ideas and innovations. When working alone, individuals or organizations may only see one facet of a problem or issue. When working in collaborations, however, they may experience comprehensive thinking in that they can “construct a more holistic view—one that enhances the quality of solutions by identifying where multiple issues intersect and by promoting broader analyses of problems and opportunities” (Lasker et al., 2001, p. 184). Practical thinking is an outcome of collaboration because academics and health professionals come together with those who are most affected by a health problem, and therefore, there is the possibility of solutions that bridge science to local experience, culture, and capability. Finally, collaborating with partners who have different assumptions, expectations, and ways of working may bring about change in the mindset of individuals and organizations involved in the process and allows for innovative thinking and ideas to be brought to the forefront (Lasker et al., 2001).
**Drawbacks of Working Within an Alliance**

For all the advantages of working within a collaborative network, there are costs and frustrations as well. First, development of a network is time consuming and resource intensive as relationships are established, goals are set, and work is initiated. Collaborations involve multiple groups that are each used to working in their own ways and within their own form of governance, and weaker partners within an alliance may not see an immediate return on their investment of time and resources. Diversity among partners and cultures can create conflict and tension if differing needs and assumptions are not addressed. Individuals may have to ignore or abandon other priorities and obligations, leading to conflict between network activities and other job-related responsibilities. Governance issues can lead to frustration, particularly in the areas of communication and decision making if partners do not have a defined communications plan and a voice in the decision making process. Partners within the alliance may not feel that their contributions are adequately recognized and appreciated (Bill And Melinda Gates Foundation, 2002; Lasker, Weiss, & Miller, 2001). Working within the extra layers of bureaucracy and differing regulatory requirements in member countries can also create delays as documents make their way back and forth through multiple agencies.

Although it is crucial to have organizational partners feel they are all working on the same team, differences in language, culture, and even working across multiple time zones can make team-building difficult. In the absence of daily face to face contact, conflicts can intensify as they are not easily managed from afar. Successful collaboration hinges upon creating an atmosphere of trust, and trust can be the one of the most important, but most difficult, areas to achieve. Creating clear goals and expectations and conveying them to all parties, allowing for face to face meetings when possible, providing frequent feedback, giving credit for tasks that
have been accomplished, fostering cultural understanding, and making the work visible and transparent are steps that can be taken to build trust (Ross, 2006).

When alliances are able to implement sustainable programs that provide important research, it may afford a country or region a greater opportunity to address broader determinants of health by bridging scientific knowledge to local culture. With this information, local researchers and policy-makers can better analyze the burden of disease in a particular area, set priorities, hasten the implementation of research findings to confront health problems, and create new tools to fight the disparities and inequities of current policy (Sitthi-amorn & Somrongthong, 2000). As stated by Pang, et al., “Knowledge produced by health research, if disseminated widely, is a global public good. Knowledge contributes to the policies, activities, and performance of health systems” (Pang, 2003).

**Background on infectious diseases**

Emerging infections, those that appear for the first time or those that were known to exist but that increase in incidence or geographic range, have been documented for thousands of years. Biblical plagues, bubonic plague, smallpox and measles are just a few examples of emerging infections that decimated large populations. Today, infectious diseases--particularly those found in tropical and subtropical regions--kill upwards of 15 million people a year, and over 90% of those deaths are in developing countries. Infants and children are particularly hard-hit with over 3 million deaths annually from malarial and diarrheal diseases. Many of these infections are thought to result from microbial evolution, development of microbial resistance, zoonotic encounters, and environmental encroachment. Cyclical re-emergence of disease may also be climate-related, as in the re-appearance of cholera and malaria (Morens, Folkers, & Fauci, 2004; World Health Organization, 2004).
Influenza

Documented influenza pandemics occurred in 1888, 1918, 1957, and 1968. The pandemic of 1918-1919 killed an estimated 50 million people worldwide and led to major social and economic disruption. Although the timing of the next pandemic cannot be predicted, scientists feel that one will occur at some point in the future (United States Department Of Health And Human Services, 2007). As described by Morens, Folkers, & Fauci, although much remains speculative about how influenza viruses emerge and spread, it seems clear that the process is driven by prolific and complex viral evolution (genetic reassortment and mutational ‘drift’), interspecies mixing and adaptation, and ecological factors that bring humans into contact with animals and each other. By whatever means new influenza virus pandemic strains emerge, they eventually reach a critical threshold of human transmission beyond which epidemic and pandemic spread follows mathematically predictable patterns (Morens et al., 2004, p. 247).

In 1997, the emergence of avian influenza (H5N1) infections in humans fueled fears across the globe of a new pandemic. Since then, the H5N1 strain has been found in wild and domestic birds and poultry throughout Asia, Europe, Africa and the United Kingdom (World Health Organization, 2007). Transmission to humans has occurred through direct and indirect contact with infected birds and there have been over 288 confirmed cases of H5N1 in humans since 2003. The current mortality rate is about 60% among those who have been infected (World Health Organization, 2007). Avian influenza is difficult to transmit from human to human, but there have been at least two suspected cases of human to human transfer and multiple outbreaks in family clusters in Indonesia and Vietnam. The H5N1 virus is more pathogenic than other influenza strains and, according to a statement by Anthony Fauci, MD, the Director of the
National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health, H5N1

is evolving in ways that increasingly favor the start of a pandemic, including becoming more stable in the environment...Given the poor condition of public health systems in many underdeveloped regions and the speed of modern air travel, the consequences of such an event, should it result in an influenza pandemic, would be severe (United States Department Of Health And Human Services, 2005, p. 2).

**NIAID support of influenza research**

NIAID has been supporting influenza research for many years, and has been involved with many projects aimed at increasing understanding of how influenza viruses replicate, interact with their host organisms, stimulate immune responses, and evolve into new strains. Fueled by growing fears of a pandemic, funding for influenza research by NIAID has grown rapidly since 2001. In fiscal year 2001, $20.6 million was spent on influenza research; by fiscal year 2005, the estimated amount was $119 million. Since 2004, NIAID has been involved with an influenza genome sequencing project with the Centers for Disease Control and Prevention (CDC) and several other organizations to determine the complete genetic sequences of thousands of influenza viruses and to provide this data to scientists. They are also involved with a surveillance program based in Hong Kong to detect the emergence of influenza viruses in animals that have pandemic potential. Surveillance activities also occur in Vietnam, Thailand, and Indonesia as a part of this program (United States Department of Health And Human Services, 2005).

Part of NIAID's activities since 2001 have included vaccine development and studying the use of four different antiviral medications for prophylaxis and treatment of influenza. Research
has shown that H5N1 strains currently being isolated in Southeast Asia and Africa are resistant to two of the antivirals, rimantadine and amantadine. However, two other antivirals, oseltamivir and zanamavir, both of which are neuroaminidase inhibitors, are effective against most of the isolates found in these regions. In response to these findings, the NIH, and NIAID particularly, have collaborated with the World Health Organization (WHO), the Wellcome Trust, and other institutions in Indonesia, Thailand, Vietnam, and the United Kingdom to develop the South East Asia (SEA) Influenza Clinical Trial Network (SEA Network), which is developing in-country research capacity in a region directly infected by the H5N1 influenza outbreak and conducting studies of antivirals in people affected with the H5N1 virus (United States Department Of Health And Human Services, 2007).

**Formation of the Southeast Asia (SEA) Influenza Clinical Trial Network**

Discussions regarding the concept of the SEA Network began as a dialogue between NIAID and the WHO in 2004 about what efforts might be useful in helping researchers in Southeast Asia learn more about the influenza viruses being isolated there. Representatives from the WHO identified that there was a gap in clinical research capabilities in the region. Due to the pressing nature of the problem and limited resources, researchers in SEA felt that a network approach would be the best way to study the pandemic threat of H5N1. With input from these researchers, NIAID and the WHO developed a short list of what was needed and wanted by potential partner participants: to support clinical research that works for countries where avian and human influenza is occurring, to build infrastructure and research capacity, and to share information. Interest among institutions within the countries affected by H5N1 grew from there. After these discussions, NIAID approached Oxford University and the Wellcome Trust and the
SEA Network was formed in 2005 (Elizabeth Higgs, MD, NIAD, personal communication February 21, 2007). The network has now grown to include 20 partners in six countries:

**Indonesia:**
- Eijkman Institute, Jakarta
- Persahabatan Hospital, Jakarta
- Sulianti Saroso Hospital, Jakarta
- National Institute for Health Research and Development, Jakarta
- U.S. Naval Medical Research Unit No. 2 (NAMRU 2), Jakarta

**Thailand:**
- Queen Sirikit National Institute of Child Health, Bangkok
- Siriraj Hospital, Mahidol University, Bangkok
- Chest Disease Institute, Nonthaburi
- Bamrasnaradura Infectious Disease Hospital, Nonthaburi
- Faculty of Tropical Medicine, Mahidol University, Bangkok

**Vietnam:**
- National Institute for Infectious and Tropical Diseases, Hanoi
- National Hospital of Pediatrics, Hanoi
- Hospital for Tropical Diseases, Ho Chi Minh City
- Children’s Hospital # 1, Ho Chi Minh City
- Children’s Hospital # 2, Ho Chi Minh City

**United Kingdom/Europe:**
- Oxford University, UK
• Wellcome Trust, UK
• World Health Organization, Geneva, Switzerland

United States:
• National Institute of Allergy and Infectious Diseases (NIAID), Bethesda, MD
• Center for International Research and Support (CIRAS), a group within Family Health International, Durham, NC

Funding for the SEA Network comes primarily through NIAID and the Wellcome Trust (Southeast Asia Influenza Clinical Research Network [SEA ICRN], 2006).

Network structure.

The structure of the Network currently includes a Network Steering Committee (NSC), Trials Operation Committee (TOC), Network Coordination Center, Center for International Research and Support (CIRAS), and an independent Data Safety and Monitoring Board (DSMB). A Network organizational chart and a chart depicting the protocol development process are attached as Appendix A. The Network Steering Committee provides overall leadership to the Network, including the Network’s mission and objectives; membership; prioritization and timing of clinical trials; oversight of the TOC and DSMB; policies for publication and presentation; administrative issues for the Network; external relations including interactions with national and/or international media; and expansion of Network-related training capacities. Membership on the NSC is comprised of one voting representative from each of the participating country and international institutional partners. Members serve for 2-4 year terms and they may serve no more than twice, although their terms do not have to be consecutive. Each country is responsible for choosing its own representative. Each protocol has its own
Protocol Committee with representation from several sub-committees that deal with specific areas essential to the conduct of clinical trials including Data Management, Clinical Operations, Pharmacy, Regulatory, and Site Management. Members on these committees represent the various partner institutions.

NIAID has contracted with SAIC-Frederick, an operations and technical support contractor for the Department of Health and Human Services based in Frederick, MD to hold sub-contracts with CIRAS, a group within Family Health International (FHI), a public health research organization based in Durham, NC and Pharmaceutical Product Development, Inc. (PPD), a contract research organization based in Wilmington, NC. CIRAS provides administrative support, technical and operational training to the sites, support to the DSMB, and helps with the activities of the NSC, TOC, and other Network committees. (SEA ICRN, 2006) CIRAS is officially based in the Durham, NC offices of FHI, but there are CIRAS team members, called Clinical Trial Support Specialists (CTSS), in FHI offices in each of the member countries of the Network. The role of the CTSS’s, who are native language speakers, is to work closely with the study sites, providing technical assistance and guidance to them, as well as on-site study management support if needed. PPD has been hired to fulfill contractual duties of monitoring the conduct of the clinical trials done by the network; however, due to the nature of their contract with SAIC, their role in the study is not discussed in this paper.

Objectives of the Network

As stated on the Network website, the Network objectives are:

(1) build a multilateral, collaborative network based on shared principles of respect and commitment to improve patient management through quality clinical research; (2) conduct protocol-based, multi-institutional studies in human influenza in accord with
international standards; (3) enhancing international capacities for the conduct of clinical research; (4) promptly disseminating information and sharing samples based on approval of the relevant national ministries of health and other relevant national authorities with the aim of improving human health. Protocols may be aimed at the diagnosis, pathogenesis, treatment, and prevention of human influenza, with the goal of producing data and evidence that will be used to help guide health policy and clinical practice in SE Asia (SEA ICRN, 2006).

One of the missions of the Network is to enhance the clinical research capacity of individuals and institutions within the Network. This will be accomplished through scientific training, and instruction in leadership, management, conduct, administration, and oversight of studies. Eventually, this will include “training of staff in conducting studies according to international guidelines, developing laboratory and diagnostic expertise, enhancing institutional support structures for conducting and overseeing studies, and fostering education...A long-term goal...is to develop centers of clinical research excellence that could respond to other emerging infectious diseases in participating countries” (SEA ICRN, 2006).

Training efforts

Training member institutions and their study staff are integral to the success of the Network and theses activities have been ongoing since early 2006. In March 2006, a Network Kickoff Meeting was held in Hanoi, Vietnam to bring together representatives from the partnering institutions for training. Sessions were held to acquaint participants with the Network and other member institutions and to provide instruction on influenza, Good Clinical Practice, protocol training on the first clinical trial to be conducted in the Network, regulatory topics, and
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data management, among others. In August and September 2006, 3-day sessions were held in each of the member countries (Vietnam, Thailand, and Indonesia) on Good Clinical Practice and Research Ethics. Research Ethics training is required for anyone working on projects funded by NIH.

Protocol Specific Training

Training of pharmacists and data managers.

The first clinical trial to be conducted within the network is a standard-versus high-dose trial of oseltamivir in patients ≥ 1 year old with severe and/or avian influenza. Each clinical site that has been chosen has many ancillary staff that will be working on the study; many are new to research so they have required more intensive training than is normally done in U. S. clinical research centers. In July, data managers from each member country traveled to North Carolina for a week-long data management training session. A five-day pharmacy training took place in August 2006 in Bangkok, Thailand for the lead pharmacists in each country.

Training of trainers (TOT).

In September, Clinical Trial Support Staff (CTSS) from CIRAS Asia were brought to Bangkok for a one-week “Training of Trainers” session. Staff from CIRAS North Carolina, NIAID, and Oxford University led training sessions on various aspects of the operational management of the first clinical trial to be conducted, including protocol training, regulatory aspects of clinical trials, and methods of adult learning. As much as possible, these training sessions were participatory in order to create a comfort level among the CTSS’s because the CTSS’s then returned to their respective member countries to lead week-long protocol-specific training there.
Study-initiation training.

Study staff from all participating clinical sites were brought to one city in each country for training on the topics that had been covered at the TOT in Bangkok. Because English is not the primary language of most of the trainees, trainings in the member countries were conducted in local language. Staff from CIRAS North Carolina and NIAID went with the CTSS’s and received simultaneous English back-translation of the sessions to ensure that the CTSS’s were sharing correct information. While site staff training was ongoing, other staff from CIRAS North Carolina, CIRAS Asia, NIAID, and Oxford University conducted abbreviated training sessions for study investigators and sub-investigators in English.

Site-specific training.

After the country-level trainings were completed, the CTSS’s traveled to each of the clinical sites within their country to conduct two-day on-site training on how to operationalize the study at their respective institutions. During this training, site staff worked through seven influenza clinical case studies developed by CIRAS NC that were designed to make them think through study-related processes and then determine how and where study-related procedures would be carried out at their site. In addition, they worked on drafting site-specific standard operating procedures to be used during the study.

Additional trainings.

In November 2006, data managers from CIRAS-NC traveled to Asia to do more in-depth data management training with sites and regional data management centers. In early 2007, staff from Oxford University’s Vietnam laboratories conducted training at each site on computer software that will be used to track virology and pharmacokinetic specimens that will be obtained as part of the study. Due to regulatory and logistical delays in starting up the initial study,
CIRAS NC and the CTSS's led in-country refresher training sessions on various aspects of the study in January-April, 2007. As a result of all of these training sessions, over 250 study staff have received instruction (Southeast Asia Influenza Clinical Research Network, 2006). The first participant is expected to be enrolled in this trial in early-mid April 2007.

*Yearly Network meetings.*

Yearly Network meetings are planned to bring investigators and study staff together for refresher training as well as protocol updates and training in new content areas. In order to perpetuate a sustainable research network, it is felt that this training must be held regularly to keep current researchers up to date on best practices and standards and to equip those moving into the field of research. Training sessions will be geared towards not only physicians, but also nurses, research managers, laboratory technicians, data managers, pharmacists, and other study support staff. The next yearly Network meeting is planned for May 16-18, 2007. A proposed agenda for this meeting is attached in Appendix 2. Although much of the focus will be on influenza and the Network studies, other training sessions will cover broader research topics such as considerations for clinical trial design, mathematical modeling, and protocol development. The Network also plans to identify and support junior researchers who would be “sponsored” and mentored by a senior member of the Network.

The extensive trainings that have been done to launch the first study may or may not be adapted and utilized with other studies done by the Network. However, the Network is clear in its Mission Statement that training in research is crucial to guaranteeing its sustainability. The benefit of research training lies in building the capacity of individuals and institutions “to conduct clinical research that meets international academic standards, regulatory requirements and ensure patient safety and the highest standards of clinical care” (SEA ICRN Training Plan,
This in turn should help institutions in the future as they work individually or with other partners to reduce the disease burden in their respective countries by transferring the knowledge learned through research to clinical practice and by informing government policies.

**Logistical Challenges to the Development of the SEA Network**

*Communication*

Although much has been accomplished in the last two years to establish the SEA Network, there have been logistical challenges to initiating the first planned study. In effect, the Network has functioned much like a virtual team, since partners are spread across the globe. A relatively simple task, such as planning a teleconference becomes more difficult because there are two or three different time zones to consider. International teleconferences are set up with a toll-free dial-in number; participants from Indonesia and Thailand can call in, but participants from Vietnam cannot dial a 1-800 service and therefore have to be dialed in by an international operator. Connectivity and voice quality are often poor. The eleven or twelve hour time difference between the US and Asia means that office hours do not overlap leading to lags in communication.

Language differences also must be considered. English is not the local language in any of the countries where the Network is conducting its clinical trials, and proficiency in speaking and understanding it varies widely among the study staff in each country. This has necessitated the translation of study manuals and informed consents into local languages. Having the materials translated and then back translated into English in order to verify the accuracy of the translation adds another layer of time and complexity into the process of study start-up.
Cultural Differences

Cultural differences and holidays in the member countries have led to the re-working of work and training schedules. In Vietnam and Indonesia, it is considered rude if former students are put into positions of teaching their former professors, so some of the CIRAS-Asia staff who had trained under the study investigators could not lead training sessions in which their former teachers were going to be the trainees. Indonesia is a predominantly Muslim country, so schedules for study initiation training sessions in October 2006 had to be rearranged due to Ramadan. During the yearly celebration of Tet in Vietnam, offices are closed for up to two weeks and work virtually comes to a halt.

Trust Building

Building trust among participating institutions has been a slow process. A lack of clear contracts, communications plans, and clear communication regarding which group is charged with completing specific tasks, and inconsistent decision making has made the development of trust more difficult, although some advances have been made in the last several months. Network partners have become more comfortable with each other and have developed more harmonious working relationships as individuals from partnering institutions have had more chance to interact during trainings and regional meetings.

Communications within the Network

Teleconferences

Teleconferences for the committees and teams within the Network have been an essential part of the communications process and have helped foster the development of trust between Network members. Most of the Network committees and subcommittees have set up monthly
calls and CIRAS, Oxford, and NIAID staff conduct weekly project tracker calls to monitor the progress of study and Network activities. CIRAS NC and CIRAS Asia also have weekly teleconferences to get updates from the CTSS assigned to each country; this information is shared with Oxford and NIAID during the weekly tracker calls. These teleconferences are also used to discuss internal issues and create action items for the NC and Asia teams to address. Minutes drafted from the committee and tracker calls are posted on an internet-based portal, Sharepoint, which is maintained by CIRAS, for review and comment prior to finalization. These minutes can be accessed and edited by anyone who has been granted privileges to use the portal.

**Sharepoint**

The internet based portal, Sharepoint, is a restricted-access repository for internal study documents and can be accessed by CIRAS NC, CIRAS Asia, certain staff at NIAID, and their sub-contracted company SAIC-Frederick. There have been problems with slow internet access due to low bandwidth, particularly in Indonesia, that have made it difficult for the CTSS’s there to log on and use Sharepoint. The application is also not entirely intuitive and training people to use it correctly has been challenging.

**SEA Network Website**

As already noted, the SEA Network has developed a web site which is also maintained by CIRAS. Network information, information about partnering organizations and institutions, protocols, protocol specific documents such as training manuals and training presentations, and other resources are posted on the site. This website has been an invaluable tool for spreading information about the Network, and provides a central source for study sites that have internet access to retrieve protocol related materials.

**Logistical Challenges of Operationalizing a Study**
Equipment and Facilities

There have been logistical issues that have required attention to bring the individual clinical sites up to generally acceptable standards for conducting international clinical trials. These are conditions that are generally taken for granted in the United States, but are not always standard in developing countries and which add delays to getting a study started. At some of the clinical sites, air conditioning is not available in all areas of the hospital or is only available during certain hours of the day and not on weekends. The study drug for the initial trial, oseltamivir, must be stored below 25° Celcius, so air conditioning had to be installed in some of the pharmacies. Locked storage cabinets for investigational products are not widely available, so these had to be ordered and installed. Uninterruptable power sources are not available at all centers, so back-up generators for power supply have been purchased for sites that needed them. Laboratory equipment has been purchased so that the local labs will have the equipment that they need to conduct the testing required by the protocol(s). During laboratory inspections conducted to determine which hospitals would be clinical sites for the first trial, it was not uncommon to find reagents several years out of date, so the Network has provided each site with all the kits, reagents, and probes that will be needed for the analysis of protocol-required specimens. Some of the virology and genetic phenotyping studies to be done as part of the initial protocol can only be done at one of the labs in Vietnam and there have been multiple issues around shipping hazardous specimens across international borders. Study offices and one of the data management centers required renovations to provide internet access which is required for the study.

Regulatory Approval Process
The regulatory approval process has posed additional challenges to study start-up. Protocols generated by the NIH, such as the protocol for the initial study, have to go through an approval process by the NIH Institutional Review Board, as required by the Food and Drug Administration. Once that step is completed, the protocol and other documents are released to the individual countries, where the documents are translated into local language and then back translated into English for verification of accuracy. Then the approval process starts over with each country’s Ministry of Health (MOH) and local Ethics Committees (EC). If the country MOH or local EC requests any changes to the protocol or informed consent or if there is a protocol amendment, the whole process has to be repeated.

**What Does the Success of the Network Look Like?**

The Network has only been in existence for about two years and although there have been significant accomplishments, the process has not moved as smoothly as was initially hoped. A single-center pharmacokinetic study is currently underway in Thailand, and the study that was supposed to be the first study for the Network has not yet enrolled its first participant. Several more clinical studies are in the proposal stage or have been approved for development by the Network Steering Committee, but have not advanced beyond that point. Long-term markers of success may be more difficult to define and assess in a way that is evidence-based. According to Elizabeth Higgs of NIAID, success will be a self-sustaining Network that goes on when the funding from the National Institutes of Health ends. Researchers within the Network will be publishing their data in peer-reviewed journals and will be competing successfully for international grants. Once the Network is fully established and running smoothly, it is hoped that the research done by network participants will be used to inform health policy and clinical practice in the member countries. Although the presence of avian influenza in SE Asia was the
impetus for the formation of the Network, Dr. Higgs would like to see the scope of the Network broaden as new diseases emerge. Finally, she would like to see trust and relationships deepened and richened by years of collaboration (Elizabeth Higgs, MD, NIAD, personal communication February 21, 2007).

Conclusion

Developing a research network is a time-consuming process with many challenges, some of which are anticipated and some are not. Some are easily dealt with, but others are more difficult. For the SEA Network, the intentions for success are there as are the building blocks, but the political environments in which the Network functions do not guarantee achievement. Short term solutions will be easier to bring about than long-term ones. Improvements in healthcare and decreased mortality from influenza may be easier to accomplish than creating deep-seated change and transferring research into practice and policy. Travis et al. makes the argument that focusing on a specific disease is short-sighted because concentrating resources in specific programs can lead to under-resourcing of other areas. This results in only limited gains because efforts do not address issues such as an inadequate health workforce, limited drug supply, financing, and information systems (Travis, et al., 2004). If the results of research generated by the Network are to be used to improve the health of people in Southeast Asia, support from the highest levels of government in the member countries is critical. Greater investment in research can lead to better health outcomes but the member countries have to begin to take more and more of this responsibility on themselves and rely less on international funders. At this point in time, it is too early to assess whether the SEA Influenza Clinical Trial Network will be successful in helping its institution and country members achieve these goals.
References


United States Department Of Health And Human Services. (2005). The role of NIH biomedical research in pandemic influenza preparedness: Statement by Anthony S. Fauci, MD, before the Committee on Government Reform, United States House of Representatives.


Appendix 1. Network Structure and Protocol Development Process

SEA ICRN
Network Steering Committee
WHO, US NIAID, Wellcome Trust, Oxford University, Representatives of Vietnam, Thailand and Indonesia

Network Coordinating Center
OUCRU CIRAS

Trial Operations Committee
Protocol Teams

US NIH Clinical Center
Oxford University Administrative Support
Thailand Country Coordinating Group

Bamrasnaradura Infectious Disease Hospital
Chest Hospital
Mahidol University Faculty of Tropical Medicine
Queen Sirikit Children’s Hospital
Siriraj Hospital

Eijkman Institute
National Institute for Health Research and Development
Persahabatan Hospital
Prof Dr Sulianti Soeroso Hospital

Indonesia Country Coordinating Group

National Institute for Infectious and Tropical Disease
National Pediatric Hospital
Children’s Hospital #1 HCMC
Children’s Hospital #2 HCMC
Hospital for Tropical Diseases HCMC

Independent Monitors

Vietnam Country Coordinating Group
Appendix 2. Draft Annual Meeting Agenda

SEA Influenza Clinical Research Network 2nd Annual Meeting

16 – 18 May, 2007

Bangkok Marriott Resort and Spa

Bangkok, Thailand

Purpose:
1. To provide an update on the current status of present and future Network research projects.
2. To provide a technical update on Avian and pandemic influenza;
3. To review the structure of the Network and responsibilities of the Network Committees and the Network Coordinating Center (NCC).
4. To allow Network committees to meet and address specific committee training needs.

Learning Objectives:

At the end of this conference, the attendees will have:
- an awareness of the current status of ongoing Network projects.
- an increased knowledge base of AI and pandemic influenza.
- their outstanding questions and management issues for current activities answered.
- their selected new research ideas targeted for expanded proposal development.
- continued consolidation and strengthening of institutional, national and regional teams and Networks.
- a draft work plan for Network based protocol development and implementation.
- an understanding of the launching of Network training activities.

Meeting Rooms:

General Sessions will take place in the Chao Pray Ballroom.
Concurrent Sessions and Committee Meetings will be assigned to either the Charoen Nakorn Room or the Thonburi Room.
# Meeting Agenda

**Tuesday, 15 May**

<table>
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<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>18.00 – 18.45</td>
<td><strong>Cocktails – Chao Praya Ballroom</strong></td>
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<td>18.45 – 19.30</td>
<td><strong>Welcoming Remarks</strong></td>
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<tr>
<td></td>
<td>- Professor Tawee Chotpitayasunondh</td>
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<td>- Dr. Libby Higgs</td>
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<td></td>
<td>- Dr. Jeremy Farrar</td>
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<tr>
<td>19.30 – 21.00</td>
<td><strong>Dinner – Chao Praya Ballroom</strong></td>
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# Meeting Agenda

**Wednesday, 16 May**

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<tr>
<th>Time</th>
<th>Session</th>
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| **7.30 - 8.30** | **BREAKFAST MEETINGS**  
1. **Country Lead Investigators**  

Lead Investigators from Thailand, Vietnam and Indonesia meet to discuss country updates with Dr. Farrar, Dr. Higgs and Dr. Whitworth.  

2. **Meet the Experts**  

Opportunity for junior investigators to meet with invited speakers and well known authorities in the field of influenza and infectious disease research. Open to all attendees. |
| **8.30 - 8.45** | **WELCOME**  
Professor Jimmy Whitworth, Chair of the Network Steering Committee |
| **8.45 - 9.30** | **COUNTRY UPDATES ON INFLUENZA EPIDEMIOLOGY**  
A representative from each country will present what the current epidemiologic status of influenza is their country and what their progress is on study initiation for study SEA-001.  

10 minutes presentation + 5 minutes Q&A / per country.  
- Prof. Tawee Chotpitayasunondh, Thailand  
- Prof. Nguyen Duc Hien, Vietnam  
- Prof. Santoso Soeroso, Indonesia |
| **9.30 - 9:50** | **NETWORK STRUCTURE**  
Review of the Network structure and roles of Network committees.  
Over view of the country team concept.  
- Dr. Jeremy Farrar |
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<tr>
<td>9.50 – 10.15</td>
<td><strong>COFFEE BREAK</strong></td>
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| 10.15 – 10.45 | **NCC UPDATE**<br>Update on the role of the Network Coordinating Center (NCC) and upcoming training opportunities within the Network. Where we have been and where we are now.  
- Dr. Jeremy Farrar  
- Dr. Libby Higgs |
| 10.45 – 11.15 | **QUESTION & ANSWERS REGARDING THE NETWORK STRUCTURE AND NCC**<br>Members from the audience will have the opportunity to ask questions about the Network structure and the NCC. Audience is welcome to stand and ask a question or write a question on the cards provided. Translators will be available for questions written in local languages.  
- Elaine Stockwell, Moderator |
| 11.15 – 12.15 | **UPDATE ON SEA NETWORK STUDIES**<br>An update will be provided on the progress of SEA studies 001, 002 and 003. Protocol concept for SEA studies 004 and 005 will also be presented. 10 minutes presentation + 5 minutes Q&A / per presentation.  
- Dr. John Beigel—SEA-001  
- Dr. Nick Day—SEA-002  
- Prof. Sasithon—SEA-003  
- TBD—SEA 004 and 005 |
<p>| 12.15 – 13.30 | <strong>LUNCH</strong>                                                                                       |</p>
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| 13.30 – 14.00 | **REPORT FROM THE 2ND WHO CONSULTATION ON CLINICAL ASPECTS OF HUMAN INFECTIONS WITH H5N1 VIRUS**  
A review of the highlights and recommendations from the report.  
- Dr. Menno de Jong |
| 14.00 – 14.45 | **INTENSIVE TREATMENT UNIT MANAGEMENT**  
A description of genetic susceptibility to pneumonia and Acute Respiratory Distress Syndrome (ARDS). A review of the data demonstrating reduced mortality with lung protective ventilation and increased mortality with steroids in (ARDS)/sepsis. An evaluation of Sequential Organ Failure Assessment (SOFA) score for prediction of mortality in intensive care unit (ICU) patients.  
- Dr. Jean Daniel |
| 14.45 – 15.15 | **COFFEE BREAK** |
| 15.15 – 16.00 | **AI CASE MANAGEMENT**  
A clinical case study presentation of a recent case of Avian Influenza, including patient assessment, clinical course, treatment and lab values.  
- Dr. Tjandra Yoga Aditama  
- Dr. Sorasak – Pediatric Management |
| 16.00 – 17.00 | **COMMITTEE MEETINGS AND COMMITTEE SPECIFIC TRAINING:**  
**SITE MANAGEMENT**  
Committee chairs and lead CTSS to discuss purpose and role of the committee in the Network; review leadership structure, and review... |
SMC training with study coordinators and site CTSS for the following day.

- Christian Yoder
- Elaine Blackwell
- Pongphaya Choosakulchart
- Sujitra Sundarasardula
- Peggy Coyle
- Hasan Basri

**Clinical**

*Case study presentation and hands-on exercises for potential AE/SAE for SEA-001 study. Review of Toxicity table.*

- Joseph Chiu and Bob Taylor, Moderators
- All study Investigators
- Study sub-Investigators
- Study Coordinators

**Pharmacy**

*Discuss lessons learned implementing the study drug shipping and pharmacy specific procedures, and how we can enhance the procedures for the Oseltamivir Study and for future studies.*

- Antonia Kwiecien and Watcharee Lemankul, Moderators
- All study Pharmacists

**Data Management**

*To discuss current and future status of data management for the Network.*

- Patrick Murphy and Barbara Avery, Moderators
- All members of the RDMC
- All Data Managers
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<th>¼ of Chao Praya Ballroom</th>
<th><strong>REGULATORY</strong></th>
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<tr>
<td></td>
<td><em>To discuss role of the regulatory committee in the Network.</em></td>
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<td></td>
<td>• John Tierney, Moderator</td>
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<td>• All members of the Regulatory Committee</td>
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<td></td>
<td><em>To discuss current and future status of the laboratory committee for the Network.</em></td>
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<tr>
<td></td>
<td>• Menno de Jong and Heiman Wertheim, Moderators</td>
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<td>• All study lab staff</td>
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# Meeting Agenda

**THURSDAY, 17 MAY**

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<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Details</th>
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<tbody>
<tr>
<td>07.30 - 08.30</td>
<td><strong>Optional Breakfast Meeting – Meet the Experts</strong></td>
<td>Opportunity for junior investigators to meet with invited speakers and well known authorities in the field of influenza and infectious disease research. Open to all attendees.</td>
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<tr>
<td>08.30 - 09.30</td>
<td><strong>Animal Models and Preclinical Testing of Novel Therapeutic Agent</strong></td>
<td>Overview of novel mathematical method to study variation of influenza virus strains as they emerge. In addition, a reverse genetics system and new molecular systems have been established, which will be useful for the rapid production of influenza vaccines. 45 minutes presentation + 15 minutes Q&amp;A. Prof. Albert Osterhaus, Professor of Virology, Medical Faculty, Erasmus MC, Rotterdam</td>
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<td>09.30 - 10.15</td>
<td><strong>Overview of DSMB</strong></td>
<td>Presentation of the role and purpose of a Data Safety Monitoring Board (DSMB). Discussion of why DSMBs are desired and how they operate. Introduction of the Network DSMB, the members and their responsibilities. 30 minutes presentation + 15 minutes Q&amp;A. Dr. Mario Chen</td>
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<td>10.15 - 10.30</td>
<td><strong>Break</strong></td>
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<td>Time</td>
<td>Concurrent Session A</td>
<td>Concurrent Session B</td>
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<tr>
<td>10.30 - 11.30</td>
<td><strong>AE/SAE REPORTING AND EMERGENCY UNBLINDING</strong></td>
<td><strong>LABORATORY QUALITY AND ISO 15189 CERTIFICATION</strong></td>
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<td>To provide a clear understanding of the roles and responsibilities surrounding AE/SAE reporting within the Network.</td>
<td>A short review on criteria of clinical laboratory assurance ISO 15189</td>
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<td>• Janet Robinson</td>
<td>• Janet Robinson</td>
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<td>• Kelly Cahill</td>
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<td>• Cynthia Kleppinger</td>
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<td>• Dr. Bob Taylor</td>
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<tr>
<td>11.30 - 12.15</td>
<td><strong>INFORMED CONSENT PANEL</strong></td>
<td><strong>ASSAYING ANTI-INFLUENZA DRUGS</strong></td>
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<td><em>A panel discussion on the cultural challenges and solutions for meeting the requirements of informed consent when consenting minors into clinical studies.</em></td>
<td>Overview of susceptibilities of influenza viruses and their drug-resistant variants to neuraminidase inhibitors in the NA inhibition assay.</td>
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<td>• Susan Vogel</td>
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<td>• Peggy Coyle</td>
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<td>• Pongphaya Choosakulchart</td>
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<td>Time</td>
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<tr>
<td>12.15 - 12.30</td>
<td><strong>CLINICAL MONITORING EXPECTATIONS</strong></td>
<td>Hasan Basri, Niklas Lindegard</td>
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<td><em>Brief overview what will be included in a monitoring visit. What monitors will ask and what they will review. What will be included in the monitoring reports? How to prepare for a monitoring visit, maintenance of regulatory binder and essential documents.</em></td>
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<td><em>Responsibilities of clinical staff during a monitoring visit.</em></td>
<td>Susan Vogel</td>
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<tr>
<td>12.30 - 13.30</td>
<td><strong>LUNCH</strong></td>
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<tr>
<td>13.30 - 14.00</td>
<td><strong>VIRAL DRUG RESISTANCE</strong></td>
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<td><em>Oseltamivir resistance can have much graver consequences in H5N1 cases than in ordinary flu. In the latter, drug resistance has not been associated with treatment failure or a severe outcome, but &quot;with H5N1 this may be a very different outcome.&quot; A review of sequence analysis of the H5N1 virus's neuraminidase gene to look for resistance, signaled by the substitution of tyrosine for histidine at amino acid position 274.</em></td>
<td>Dr. Menno de Jong</td>
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<tr>
<td>14.00 - 15.00</td>
<td><strong>PRACTICAL LESSONS TO BE LEARNED FROM MATHEMATICAL MODELS OF INFLUENZA</strong></td>
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<td><em>How mathematical models are used to predict the likelihood of emerging novel human influenza virus subtypes and help prepare for</em></td>
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possible pandemics. How mathematical models are used to derive estimates for the levels of drug stockpiles needed to buy time, how and when to modify vaccines, whom to target with vaccines and drugs, and when to enforce quarantine measures. 45 minutes presentation + 15 minutes Q&A.

- Prof. Derek J. Smith

<p>| 15.00 – 15.30 | BREAK |
| 15.30 – 17.00 | COMMITTEE MEETINGS/REPORTS AND COMMITTEE SPECIFIC TRAINING: |
| Thonburi Room | SITE MANAGEMENT |
| | Present the role and purpose of the SMC to all the study Coordinators. |
| | Discuss the role and responsibilities of the study coordinator in Network studies. Review of data discrepancy forms. |
| | • All Study Coordinators |
| | • All CTSS |
| Charoen Nakorn Room | CLINICAL |
| | WHAT IS THE 1572 AND HOW DOES IT AFFECT YOU? |
| | An overview of the 1572 forms and PI responsibilities as stated in the document. Relationships and obligations PIs have to the IRB. |
| | Common mistakes made during clinical trials. |
| | AUDITS AND FDA WARNINGS? |
| | What is an audit? What is an FDA warning? What to do if you get |</p>
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<tr>
<td>¼ of Chao Praya Ballroom</td>
<td><strong>PHARMACY</strong></td>
<td>Review pharmacy forms completion.</td>
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<td>· Antonia Kwiecien and Watcharee Lemankul, Moderators</td>
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<td>· All study Pharmacists</td>
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<tr>
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<td><strong>DATA MANAGEMENT</strong></td>
<td>Continue discussion on current and future status of data management for the Network.</td>
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## Meeting Agenda

**FRIDAY, 18 MAY**

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<th>Session</th>
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<td>07.30 - 08.30</td>
<td><strong>OPTIONAL BREAKFAST MEETING – MEET THE EXPERTS</strong></td>
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<td>Opportunity for junior investigators to meet with invited speakers and well known authorities in the field of influenza and infectious disease research. Open to all attendees.</td>
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<tr>
<td>08.30 - 09.00</td>
<td><strong>PROTOCOL TEAM OVERVIEW</strong></td>
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<td>Presentation of who should be on a protocol team. What are the responsibilities of a protocol team: protocol design implementation, amendments, reports, publications, and responsibilities to the DSMB.</td>
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<td>- Dr. Joseph Chiu</td>
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<td>09.00 - 09.30</td>
<td><strong>PROTOCOL DEVELOPMENT PROCESS IN THE NETWORK</strong></td>
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<td>Considerations for protocol development; what needs to be included from the perspective of Code of Federal Regulations and ICH guidelines. Steps from inception to publishing.</td>
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<td>- Dr. Bob Taylor</td>
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<td>09.30 - 10.00</td>
<td><strong>IND REGULATIONS</strong></td>
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<td>What is an IND study? Broad overview of process from concept development, validation, preclinical testing, IND application process, Phase I-III studies, up to NDA application.</td>
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<td>- John Tierney</td>
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<tr>
<td>10.00 – 10.15</td>
<td>COFFEE BREAK</td>
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**CLINICAL TRIAL DESIGN – WHAT TO CONSIDER WHEN DESIGNING A STUDY**

Review of reasoning behind randomization; analytical hazards imposed by not doing a randomized clinical trial. A discussion about the ethics of clinical research requirement of equipoise as a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial.

- Kevin Baird
- Libby Higgs

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**PRESENTATION OF INVESTIGATOR’S CONCEPTS FOR RESEARCH**

Investigators will present ideas for future research.

- Dr. Joseph Chiu, Moderator

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**FUTURE OF THE NETWORK**

Panel discussion and Q & A of the vision for the Network. Save the date for next year’s meeting in Indonesia.

- Dr. Jeremy Farrar
- Dr. Tawee Chotpitayasunondh
- Dr. Sangkot Marzuki
- Prof. Nguyen Duc Hien

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<th>12.15 – 12.30</th>
<th>WRAP UP AND CLOSING</th>
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- Dr. Jeremy Farrar
- Dr. Tawee Chotpitayasunondh
- Dr. Libby Higgs

| 12.30 – 13.30 | LUNCH – ADJOURN |