For discussion
on 27 September/4 October 2004 **SARS MC 12/04**

Strategic Direction of Research on Infectious Diseases

Purpose

The purpose of this paper is to introduce to members the strategic direction of research on infectious diseases in Hong Kong.

Background

2. In this modern era, infectious diseases are once again posing a major global threat: to health, prosperity, social stability, and security. The SARS epidemic worldwide last year demonstrated vividly the devastating effects that a single, previously unknown virus could cause. Its impact was felt not only by the affected individuals and their families but also the general public and the global community.

3. After the SARS epidemic, infectious diseases remained high on the agenda of health officials and news media in Hong Kong. The topics discussed were diverse and included:-

- possible resurgence of SARS
- pandemic potential of avian flu
- cholera in fish tanks
- local cases of dengue fever and Japanese encephalitis
- hospital acquired infections
- multi-drug resistant tuberculosis

In addition, there is a persistent threat of international bioterrorism.

Research on Infectious Diseases

4. The public health challenge posed by infectious diseases is therefore immense and formidable. Tackling the agenda requires evidence-based knowledge, amongst other things, for the effective functioning of the surveillance system (to provide early warning), efficient development of rapid diagnostic techniques (for early detection) and formulation of vaccine strategies and treatment regimens (for prompt and effective control).

5. Hence, research and development is a critical factor in making progress in combating infectious diseases. In Hong Kong, research on infectious diseases has been accorded high priority by the Government. A research fund for the control of infectious diseases (RFCID) with a capital commitment of HK$450mn has been established to encourage, facilitate and support research on the prevention, treatment and control of infectious diseases. A Research Council has also been formed to provide the leadership and strategic direction of research on infectious diseases. The Council is chaired by the Secretary for Health, Welfare and Food.

Strategic Direction of Research

6. The policy goal of research on infectious diseases is to generate new knowledge that is evidence-based that will contribute to the overall framework of prevention and control. The strategic direction of research centres on the following:-

i) establishing thematic priorities
ii) fostering collaborative partnerships
iii) enhancing capacity building
iv) pursuing excellence and innovation

Establishing thematic priorities

7. Infectious diseases are caused by a diverse spectrum of pathogens some of which remain unknown. The field of research is vast, ranging from molecular research to vaccine development and treatment evaluation, to public health surveillance and population studies. The Research Council considers it important to have a clear, focused research agenda through the development of

thematic priorities. In this way, research efforts will be better coordinated, and resources better targeted, to address the priorities of local relevance and importance.

8. For the purpose of establishing the thematic priorities for research, infectious diseases have been grouped into categories and assessed for the following:-

- burden of disease and potential for health gain
- outbreak potential, risk the scale and magnitude
- preventability and methods of prevention
- level of public concern

9. Against this background, thematic priorities for research on infectious diseases have initially been established as described below. Commencing from next year, the Centre for Health Protection (CHP) will develop and establish thematic priorities, and report to the Research Council on an annual basis.

(a) *Infectious respiratory diseases*

With great potential to cause major outbreaks, research studies needed for this category include:-

- epidemiological characteristics of the common type of infectious respiratory diseases
- role of rapid diagnostic tests in early detection
- cost benefit of different control strategies including vaccine deployment
- improving the surveillance and diagnosis of respiratory viral infections and community acquired pneumonias

(b) *Food-borne enteric diseases*

Eating is a popular pursuit of the Hong Kong people. Ensuring that food is microbiologically safe is an essential element of public health. Research on food-borne enteric diseases includes:-

- studies to identify risk profiles of foods and/or food processes, and linking of the level of risks with the level of consumer protection gained
- quantitative research on microbial hazards in food production systems
- development of feedback models to enhance outbreak detection
- studies on enteric disease transmission and prevention

(c) *Hospital-acquired infections and antibiotic resistance*

Hospital-acquired infections and antibiotic resistance are a growing concern, both locally and internationally. Research on this category include:-

- levels of antibiotic resistance in the community/primary care facilities
- links with agricultural use of antibiotics
- rapid diagnostic tests for effectiveness in reducing antibiotic use and cost benefit
- evaluation of existing infection control programmes
- assessment of best practice guidelines

(d) *Environment and infectious disease*

The SARS epidemic in Amoy Gardens revealed the key contributory role of the environment to the outbreak. Studies on this category include:-

- building design and infection risk
- relationship between environmental factors and mode of transmission of pathogens

(e) *Zoonoses*

Zoonoses are diseases caused by organisms that primarily infect an animal host (wild or domestic) but may be transmitted to and infect humans, e.g. verotoxin-producing *E. coli* (VTEC) and avian flu. Research in this category includes:-

- epidemiological characteristics of certain zoonoses including their transmission routes
- appropriate methods of animal handling by high-risk occupational groups
- evaluation of vaccination of animal herds
- assessment of the ability to respond rapidly to outbreaks

Fostering collaborative partnerships

10. Research on infectious diseases, by its nature, has to be multifaceted and intersectoral. There are many organisations, institutions and agencies that can bring valuable expertise, commitment, enthusiasm and resources to potential research initiatives. Hence, the second strategic direction of research on infectious disease is to develop and foster collaborative partnership. This is done at two levels:-

(a) amongst funding bodies

At the level of the funding bodies, RFCID has strengthened its link with other funders such as the Research Grants Council of the University Grants Committee, and the Innovation and Technology Fund. A mechanism has been established for mutual exchange of information at regular intervals. A stated purpose is to ensure there are no overlaps in the approved projects, avoiding potential double funding and ensuring best use of resources.

(b) amongst research institutions

At the level of the research institutions, appropriate skillmix in undertaking the research is crucial to its success. Where expertise is not available in one institution, it is a requirement that the investigators seek appropriate expert input from another institution. Additionally, a stated preference of the RFCID grant application is collaborative research involving different disciplines and across institutions.

Enhancing capacity building

11. For research on infectious diseases to flourish, the third strategic direction is to enhance capacity building. Two interconnected components are

recognised: the need to recruit young talent into the research system and the need to support the work of established investigators. It is usually the latter group who are the 'engine' of research growth, and act as a magnet for young researchers to enter the system.

Pursuing excellence and innovation

12. To bring about vibrant research on infectious diseases, the fourth strategic direction is to pursue excellence and innovation. Both qualities are essential for our researchers to extend the frontiers of science and gain international repute and recognition. The pursuit of excellence and innovation can be nurtured and facilitated through an open, competitive research environment.

Framework for Action

13. Striving towards the strategic direction of research relies upon two complementary approaches:-

- Investigator-initiated research
- Commissioned research

Investigator-initiated research

14. Investigator-initiated research supports the strategic direction of research on infectious disease by fostering collaboration, enhancing capacity building and encouraging the pursuit of innovation and excellence. Research proposals are submitted by individual research teams in response to open calls for applications issued twice per year. During the first three open calls for RFCID applications, proposals were not limited by adherence to established thematic priorities, as it was important to test the level of support of the new fund in the scientific community. Commencing with the next open call, thematic priorities will be advertised, and fundable proposals falling within the thematic priorities will be given precedence over other fundable projects.

Commissioned research

15. Portfolios of research studies have been commissioned from universities and public agencies to address specific areas of infectious disease research. Commissioned research studies tend to be of broader scope, greater depth and longer duration than investigator-initiated projects, therefore allowing a more thorough analysis of the research questions posed. Commissioned research addresses all the elements of the strategic direction of infectious disease research including thematic priorities, collaborative partnership, capacity building and pursuit of excellence and innovation.

Progress to Date

16. Since the RFCID was established in July 2003, considerable progress has been made in strategic research on infectious diseases.

Investigator-initiated research

17. The RFCID has issued three calls for investigator-initiated research applications. The first open call closed in November 2003. The second open call closed in February 2004. Of the research proposals submitted during the first and second open calls, a total of 38 projects were approved with a combined total value of $27.7 million. The third open call closes in September 2004.

18. Capacity building in investigator-initiated projects takes several different forms. At one level, it is fulfilled by the recruitment of a new cohort of junior research staff (approximately 2 new research assistants or other staff are recruited for each funded project). At another, it includes the provision of new equipment so that the facilities available to researchers are equivalent with those in other developed societies ensuring that they can compete effectively in the rapidly changing research arena.

19. Excellence and innovation are ensured due to rigorous two-tier peer review by a panel of international external reviewers in addition to a Grant Review Board comprising over 40 local experts in a wide spectrum of clinical, basic and applied scientific research. The overall success rate in approving funding for investigator-initiated projects is about 25%. Applications are therefore extremely competitive in nature.

20. Approved projects to date address a diverse array of research specialties, including:-

- genetics, molecular biology and immunogenicity of the SARS coronavirus (SARS-CoV);
- seroepidemiological analysis of SARS-CoV antibody prevalence in Amoy Gardens;
- genetic characterisation of novel H5N1 avian influenza variants;
- cost-effectiveness studies of influenza vaccination in the institutionalised elderly;
- novel therapeutic interventions for control of infectious disease;
- epidemiology and control of food-borne pathogens;
- evaluation of risk-reduction behavior programmes, among many others.

Commissioned research

21. To date, the Research Council has approved funding for three commissioned research studies. Two commissioned studies are underway while the third is awaiting finalisation of the contract. The total value of the three commissioned studies is $63.6 million.

University of Hong Kong

22. On 15 May 2004, the RFCID provided $30 million to the University of Hong Kong (HKU) over the course of 5 years to enhance its research infrastructure and to support a portfolio of studies on basic laboratory, public health and epidemiology research. All of the elements of the strategic plan have been addressed in considering the nature of the research funded.

Thematic priorities

23. $22 million was provided for at least 27 different studies on the microbiological and epidemiological aspects of infectious disease, specifically those that addressed gaps in scientific knowledge and public health needs or threats. These studies addressed many of the thematic priorities identified earlier, including:-

– infectious respiratory diseases using SARS-CoV and H5N1 influenza as archetypes, specifically the ability to identify influenza viruses with pandemic potential and to determine the mechanism of transmission of SARS-CoV to prevent a recurrence;
– hospital-acquired infections and antibiotic resistance, e.g. surveillance of multiple multidrug resistant pathogens, risk communication strategies, research on rapid diagnostics;
– environment and infectious disease, e.g. understand the influence of environment on the transmission characteristics of SARS-CoV and other infectious diseases;
– zoonoses, e.g. enhance the response and control of SARS-CoV, H5N1 influenza, dengue fever, and other novel or re-emerging infectious diseases.

Capacity building

24. $8 million was used to complete a Biosafety Level 3 laboratory for animal studies greatly enhancing the capacity of the university to conduct relevant studies on emerging and re-emerging infectious diseases in a safe and controlled environment. In addition, several new staff were recruited to enhance the research and training capacity of the project team. These new staff include professorial level clinical and non-clinical researchers and post-doctoral senior research staff, among others.

Enhancing collaboration

25. The commissioned study enhances inter-disciplinary collaboration between the different departments of the HKU Faculty of Medicine, specifically the School of Public Health and the Department of Microbiology. HKU will also leverage its links with other partners e.g. Department of Health, Hospital Authority and HWFB to provide a seamless continuum of nosocomial and community surveillance, informatics management, data analysis and modelling. Overseas partners of HKU who will periodically contribute their expertise include Department of Infectious Disease Epidemiology (Imperial College, London, UK) and Department of Epidemiology, Harvard School of Public Health (USA).

Pursuit of excellence

26. HKU has an enviable reputation throughout Asia as one of the premier seats of learning. As such it is able to recruit and retain considerable expertise across a wide range of disciplines and to independently raise considerable sums of private finance to accomplish its long-term research goals. Support of HKU through the RFCID will further enhance these capabilities increasing the likelihood that the commissioned research will not only be successful but will lead to further novel research avenues to be explored.

Chinese University of Hong Kong

27. On 15 June 2004, the RFCID provided $25 million to the Chinese University of Hong Kong (CUHK) over the course of 5 years to support a portfolio of at least 30 different research projects on clinical trial and public health research. Again the aims of the commissioned research are to satisfy the elements of the strategic plan outlined earlier.

Thematic priorities

28. The commissioned research studies conducted by CUHK complement those of HKU.

- infectious respiratory diseases including development of rapid diagnostics, development of novel treatment therapies, epidemiology of upper respiratory tract infection in children;
- food-borne enteric diseases including surveillance of diarrhoea in children, evaluation of efficacy of rotavirus vaccines;
- environment and infectious disease including super-spreading events in hospital settings, minimising transmission of infectious diseases by use of personal protective equipment, and a comparative study of stigma associated with infectious diseases;
- zoonoses including molecular (genetic, proteomic and immunological) characterisation of SARS-CoV.

Capacity building

29. The commissioned studies will build capacity by training a pool of highly skilled researchers in the field of emerging infectious disease. To assist

this aim, additional high-ranking staff will be recruited including an infectious disease clinician (professor), a field epidemiologist (senior lecturer), a scientific officer and two post-doctoral researchers.

Enhance collaboration

30. The project team at CUHK comprises an interdisciplinary team with expertise in epidemiology, microbiology, clinical medicine, and health economics to strengthen infectious disease preparedness. They have established a Centre for Emerging Infectious Diseases (CEID) to enhance the control of emerging infectious diseases locally and globally by training healthcare professionals and researchers; conducting epidemiological, basic science and clinical management studies; promoting infectious disease preparedness in hospitals; and providing consultancy services to health agencies. Expertise is also available from other partners e.g. CDC China, CDC (USA), Johns Hopkins University, UC Berkeley, London School of Hygiene and Tropical Medicine, and WHO.

Pursuit of excellence

31. CUHK commands considerable respect in Hong Kong and beyond for its scientific and clinical excellence. With the funding provided by RFCID it can build on this reputation and leverage its considerable international network of contacts to ensure that its 5-year plan of research will be successful. The new CEID will focus attention on the regional importance of emerging infectious diseases and show CUHK's long-term commitment to extending its influence in this important area of research.

Hospital Authority Consortium

32. Funding has been approved for 9 research projects conducted by the Hospital Authority and its collaborators, including the Hong Kong Polytechnic University (HKPU) and the Hong Kong University of Science and Technology (HKUST). The total value of the funding is approximately $8.6 million. The studies will last two years and address research on nosocomial infection and long-term follow-up of SARS patients.

Thematic priorities

33. Under the thematic priorities outlines earlier, HA will focus on nosocomial infection and long-term sequelae of SARS. Specific research projects address the incidence of avascular necrosis in SARS patients; determining the significance of various means and routes of dispersal of infectious aerosols and droplets in a variety of clinical settings and under various typical invasive procedures; studying the factors affecting ventilation effectiveness in the new SARS wards and to improve existing designs; studying novel local exhaust devices in a clinical environment; evaluating different nursing practices in the management of SARS patients.

Capacity building

34. The commissioned study by the HA will build capacity by enhancing the knowledge of the HA clinical staff through collaboration with a diverse range of disciplines, e.g. by exposing its clinicians to research techniques in non-clinical settings such as mechanical engineering (HKU), sustainable development (HKUST) and safety and environmental protection (HKUST), thus extending their knowledge and appreciation of the non-clinical sphere. In addition, capacity can be increased by optimising the use of resources by evaluating the effects of contamination posed by infectious patients, the effectiveness of personal protective equipment used by healthcare workers and the efficiency of various models of ventilation to cope with the potential infectious load, and by modifying clinical practice according to the research findings. Capacity will also be increased indirectly through the hiring and training of research assistants at the collaborating institutions. Importantly, the HA proprietary SARS database will be extensively enhanced allowing detailed clinical data to be readily available and analysed, facilitating collaborative research and enhancing output for peer reviewed publications, etc.

Enhance collaboration

35. HA is in a unique position in that it can have access to and foster connections with high-level government based clinicians and researchers around the world. This will make it an enviable partner for collaborative research projects of a diverse nature.

36. Regarding the specific collaborations in place, Prof. Ming Fang and his team at the Institute for Sustainable Development at HKUST will engage in a project on profiling hazardous bioaerosols in a hospital environment. Likewise, Prof. Joseph Kwan and his team at the Safety and Environmental Protection Office (also at HKUST) will study source isolation systems for the protection of healthcare workers. Both projects are likely to directly impact the health of healthcare workers in contact with potentially infectious patients. Research conducted in collaboration with HKPU concerns the correct use of personal protective equipment and the effectiveness of different approaches to nurse performance in infectious disease wards. Again, the results of both studies will likely influence HA practice. Other studies conducted in collaboration with Dr. Yuguo Li at the Department of Mechanical Engineering at HKU will focus on the dispersion of droplets and the effectiveness of different ventilation systems in a clinical setting.

Pursuit of excellence

37. HA continues to recruit high-calibre clinicians into its ranks. This enhances the contribution the agency makes to public health. Exposure of these staff to non clinical setting through collaborations such as that funded by the RFCID will allow the HA to continue to play a vital role in the control of infectious diseases.

Advice Sought

38. Members are respectfully requested to note and provide comments on the contents of this paper.

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