

The state of research: Fueling up to lead the world

As the economic mantle of power shifts from the West to the East, more and more pharmaceutical companies are focusing their attention on Asia. Malaysia, being gifted with a smorgasbord of races from around the region, is a good choice for pharmaceutical companies seeking to get a bigger bang for their buck. Logically, our country, being populated by ethnic Chinese, Indians and Malays, allows a broad range of data to be collected on a drug's interaction and efficacy among different races. *Medical Tribune* interviewed two key persons involved in research in the region and in Malaysia to get their thoughts on how things are coming along. (Reports on pages 20 and 21.)

Pank Jit Sin speaks to Dr. Gilberto Lopes, assistant director for clinical research at Johns Hopkins University School of Medicine in Singapore, to get his thoughts on some questions regarding research in the Southeast Asian region.

Q: What are the factors enabling clinical research in our region (Southeast Asia) and what are your thoughts on the factors that need improving to better facilitate clinical research in the region?

A: Southeast Asia is a very diverse region, with 10 countries – 11 if we count East Timor; a large population of around 600 million people; and an economic output of about US\$1 trillion a year. In addition, the region is growing fast – trade and connections are increasing and its populations are aging, making it an attractive destination for clinical research. Scores of pharmaceutical companies and clinical research organizations are already performing studies here.

Several countries have already made significant contributions in the enrollment of patients in clinical trials and several are starting to develop and conduct their own clinical studies. Our institutions in Singapore and Malaysia are involved in developing clinical and health economics and outcome research with both a regional and global perspective.

However, there are myriad challenges [facing research] as countries have different regulatory systems and are at distinct points in the development of their infrastructure.

Q: What can government and non-governmental organizations do to increase the awareness of clinical research?

A: Governments can play a significant role through adequate regulation and promotion of international standards in the conduct of research, as well as the provision of funding through peer-reviewed competitive grants.

Non-governmental organizations have an important role to play in increasing awareness of specific medical conditions that are unique and not usually addressed by our for-profit indus-

try colleagues.

Professional associations should increase their role in the education of healthcare professionals and the public on clinical trials.

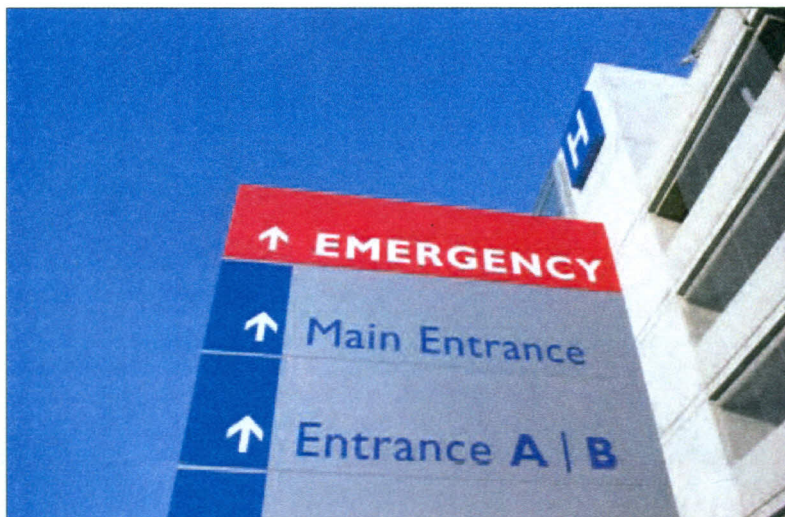
Finally, the industry has a role to play as well, as both pharmaceutical companies and clinical research organizations should continue to bring clinical trials and studies to the region and also assist in providing education opportunities and trial funding for healthcare professionals and investigators in the region.

All these stakeholders should also work on increasing public awareness of clinical studies, helping patients understand what clinical trials are, and what they and society may gain from greater participation. This can be done through public education campaigns in general education sessions.

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Q: Do you think the stakeholders in the region have the basic infrastructure to engage in cancer research? What else can be done to improve the atmosphere for clinical research in the region?

A: Different countries are at different levels of development, but in general, Malaysia, Singapore and Thailand have developed



Institutions in Singapore and Malaysia, including hospitals, are involved in developing clinical and health economics and outcome research with both a regional and global perspective.

an adequate infrastructure for clinical research. Indonesia and the Philippines, as well as Vietnam, are working on increasing theirs. Other countries (in this region) are still focusing on the first steps in the developmental ladder and it will take them a little longer to develop the basic infrastructure.

Q: What types of clinical research are there? What do you think should be the focus for research in the region eg, drug, laboratory, epidemiological/cancer registries?

A: We are living in an interesting time in the region as we already see [an increase in] several cancers that are related to economic development ie, colorectal and breast cancers, while we still see diseases that are more common in countries with lower incomes, such as those of the stomach and liver. Finally, there are diseases such as nasopharyngeal carcinoma that are more common in the region due to epidemiological factors.

As such, all the usual clinical research methods – epidemiological; registries; basic and translation prospective phase I, II, III and IV clinical trials; and health economics and outcomes research – are important. If those are yet to be done, each country should start by establishing can-

cer registries so they can assess their specific situation for planning and action.

It is also imperative that we focus on finding cheaper solutions that can be applied to the resource-limited setting we see in the region. For instance, tobacco control, hepatitis B vaccination, Pap smear screening with or without HPV vaccination and better economic conditions. Greater use of treated water and refrigeration of food are relatively simple measures that can significantly reduce the burden of cancer in countries with more limited resources.

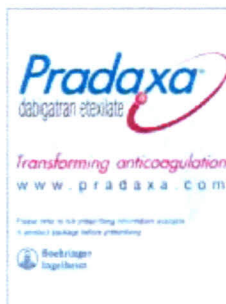
Research on these areas can help raise awareness and improve on current methods.

Q: Do you think cancer research requires major financial investment or skilled manpower or facilities to conduct?

A: Yes. Here, the key is manpower development, as it is only through the creation of well-trained teams that clinical research can be conducted in a meaningful manner.

Q: Does your institution regularly advertise the kind of research that is going on? Is it ethical for institutions to advertise such research for interested patients?

A: We do not advertise directly



to patients, but we do inform physicians and other healthcare colleagues in the country about the clinical trials we currently have open. Here, a simple development that might be extremely helpful is in the

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creation of country-specific websites where physicians and patients can search ongoing clinical trials in their communities.

Q: What are the other legal or clinical considerations for institutions, other than the government or universities, to engage in cancer research?

A: Any institution conducting clinical research needs to create or engage independent ethical review boards and needs to become familiar with the minimum required best practices and documentation requirements. **MI**

The thorny path of clinical research in Malaysia

In the second part of our feature on research, Dr. Thevendran Sadasivam provides *Wendy Loo* with some feedback on clinical research in Malaysia.

Clinical researchers are among those in the frontline in the war against diseases and medical conditions such as diabetes, HIV/AIDS, schizophrenia, etc. However, despite the importance of clinical research, and the ray of hope it gives patients, the path of a researcher is a difficult one, with many obstacles along the way.

There are many research centers globally, with the US, Europe and Japan being at the forefront. But what about Malaysia? How are we faring in this frenzied rush to gather more information especially against deadly diseases?

Nestled unassumingly in the heart of Kuala Lumpur lies a precious research key in Malaysia – the Clinical Research Centre (CRC) of the Ministry of Health (MOH). The CRC conducts clinical trials, clinical epidemiology and economic research, besides managing complex medical databases.

It also plays a role in promoting and supporting investigator-initiated research (IIR), coordinating and facilitating the conduct of contract industrial-sponsored clinical trials as well as developing clinical data resources.

There are two broad classifications of clinical research: IIR and industry-sponsored research (ISR). Both are promoted by the government, and as their names imply,

IIR is started and conducted by researchers, doctors or academicians, whilst ISR is initiated and funded by pharmaceutical companies. The number of clinical trials in Malaysia has been on the increase, with 143 ISRs conducted last year.

Medical Tribune. "The whole team must be committed to ensuring the success of the project, and be detailed in its observations and documentation. This is difficult due to pressures of service, clinic routines and lack of coordination."

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"Clinical research is feasible in Malaysia," said Dr. Thevendran Sadasivam, a CRC spokesperson, "because we have up-to-date facilities, well-trained doctors, and an excellent and large information and referral system within the MOH.

"The amount of projects currently ongoing in the CRC is large and diverse, with oncology, diabetes mellitus, cardiology, infectious disease, psychiatry and hematology being some of the most popular areas of clinical research in Malaysia."

And as with any other path we walk, that of a researcher is strewn with thorns. What are the main stumbling blocks for Malaysian researchers?

"Time and support," Thevendran told

Other pitfalls, he added, include the lack of a research culture, awareness of clinical research, trained research coordinators and facilities at trial sites.

Legal and ethical issues for institutions starting a research project should also be carefully screened and observed. To avoid any legal or ethical entanglements, institutions should form independent ethics committees to vet the clinical research.

Safety is another crucial issue, and institutions must ensure patient safety and also insure any staff involved in clinical trials. The independent ethics committees should not only protect the rights, safety and well-being of study participants, but also ensure that the risks of clinical trials are minimal and that there is potential benefit for patients.

Independent ethics committees should ideally comprise healthcare personnel, other professionals and at least one member who is from a non-scientific field. The committee should go through every aspect of the proposed clinical trial before approving it, including asking for amendments.

"Before they are allowed to be tested on humans, drugs need to undergo rigorous testing, and the preclinical data on animals must be available. Only after the preclinical data from animal testing has been accepted will the drug undergo three phases before it can be registered.

"Phase I trials are usually conducted in small numbers of human volunteers to determine the safety and dosage, and in certain areas (eg, oncology and HIV), can involve a small number of patients," said Thevendran.

As yet, the CRC does not advertise for

subjects, but it does help recruit investigators for clinical trials. In turn, these investigators then go through their case loads for suitable subjects.

An important stakeholder in increasing the awareness of clinical research in Malaysia and, thus, the amount of clinical research being performed, is the media as it is able to increase awareness of:

- The benefits of clinical research.
- The governing ethics of research and guidelines necessary for conducting research.
- How clinical research is conducted.
- How the fully-informed consent process of volunteers is performed.
- How the risks of clinical research are minimized and managed.

It is also important for all parties involved in scientific research to maintain professional and scientific decorum in public places, said Thevendran.

Malaysia is an ideal place to conduct clinical trials due to its multi-ethnic population and diverse cultures, which give clinicians bigger scope in recruiting patients.

Participants are generally kept informed throughout the study and their progress is assessed closely and evaluated at regular intervals. If they wish to do so, participants may opt out of a clinical trial at any time. On the other hand, the medical stakeholders (possibly the research team, the sponsoring company or even the Institutional Review Board) may choose to terminate the trial or remove certain participants and/or patients, depending on the safety and efficacy of the treatment.

Other services provided by the CRC include workshops and courses that can help researchers eg, clinical trial-related and IIR-related courses, and the CRC research consultative clinic for clinicians working in the MOH (primarily those at Kuala Lumpur Hospital).

The research consultative clinic gives advice to clinicians on potential problems in the conduct of clinical research and hopefully offer some solutions as well. Among its services include study design, sample size planning, proposal/protocol development, data management, data analysis and help with statistical software.

For more information, please visit www.crc.gov.my



The entire research team must give its all in ensuring the success of a project.

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Advisory Committee (MDAC), which is supposed to represent all doctors practicing in hospitals and whose function is to ensure that the medical management of patients vests in registered medical practitioners. "Hospitals have many ways and means to dilute the implications of this requirement," said Chow.

Moving on to Part XV of the PHFSA, Chow said contracts between healthcare facilities and managed care organizations (MCOs) must not alter the power of the doctor in providing medical care. Most doctors in the private sector are bound by contracts with

hospitals or MCOs, or directly with employers and companies.

The dilemma now is that when doctors start work at private hospitals, the hospitals themselves may have already entered into contracts with MCOs in which some of the contractual provisions are in contravention of the PHFSA. The doctors themselves have no access to these contracts but, nevertheless, are involuntarily bonded to them by virtue of their contract with the hospital.

"We advise doctors that it is their right to refuse any contract that interferes with their independent medical care of patients. Should they be coerced, FPMPAM will fully sup-

port their action to refer such contracts to the MOH," Chow emphasized.

"The onus is on the MOH to act its part as the regulator. However, the major hospitals are now mainly owned by government-linked companies (GLCs) ie, the government, being the regulator, is also an operator in the industry via its GLCs. In a situation like this, there is clearly a blurring of the line between the regulator and the operator," Chow commented.

In addition, as a measure to boost profits, some hospitals, MCOs and other third parties in healthcare have resorted to extracting mandatory discounts from doctors' profes-

sional fees in their contracts. The FPMPAM calls this 'fee-splitting,' an exercise which is in contravention of the PHFSA and Regulations. "FPMPAM is committed to initiate all action necessary against any party trying to extract such discounts from our doctors."

In the past, Chow said, the FPMPAM had highlighted to the MOH the difficulties doctors were facing with contracts. "We hoped that the MOH would act swiftly and decisively. In 2006, we also proposed important regulations to the PHFSA and Regulations so that all the business components of healthcare are regulated synchronously to protect the public from over-exuberant commercialization." ■