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A Pivotal Moment for China & Vaccine Manufacturing

An Interview with Jiankang (Jack) Zhang

By Claire Topal and Karuna Luthra
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In advance of the June 2011 Pacific Health Summit on vaccines, NBR is conducting a series of interviews on the latest developments and current issues facing the global vaccines and immunization field. This week, we spoke with Mr. Jiankang Zhang (PATH). This interview was published on the NBR website: http://www.nbr.org.

Jiankang ("Jack") Zhang is China Country Program Leader of PATH. Previously, he served as Chief Representative and General Manager of Haemonetics China Subsidiary, a Boston-based blood-processing company. Prior to that, Mr. Zhang worked at the Shanghai Institute of Biological Products (SIBP), a subsidiary of China National Biotec Group (CNBG), where his last position was Deputy Director-General for Operations. While at SIBP, he also served as Director of the Board of SmithKline Beecham Biologicals (Shanghai) Co., Ltd, and as Vice Chairman of the Board of Shanghai Feilong Medical Diagnostic Articles Ltd.

Questions & Answers

The World Health Organization (WHO) announced on March 1, 2011, that the national regulatory authority of China—the State Food and Drug Administration (SFDA), along with affiliated institutions—now meets WHO indicators for a functional vaccine regulatory system. This means that Chinese-made vaccines are now eligible to apply for WHO pre-qualification.[1] Can you give some background on vaccine manufacturing in China and describe the response of the Chinese government and vaccine industry to the announcement?

Currently, China has 36 vaccine manufacturers that produce 49 types of vaccines against 27 diseases. The country's annual manufacturing capacity is nearly one billion doses. WHO's clearance opens the door for these companies to apply for WHO vaccine pre-qualification—a regulatory status that opens the door for United Nations agencies and governments to begin ordering the vaccine— with the aim of becoming eligible for vaccine procurement by the United Nations Children's Fund (UNICEF).

[1] WHO prequalification ensures that vaccines used in national immunization services in different countries are safe and effective for target populations at the recommended schedules, and that they meet particular operational specifications for packaging and presentation. Every year, billions of U.S. dollars-worth of medicines and vaccines are purchased by international procurement agencies for distribution in resource-limited countries. Prequalification is intended to give these agencies the choice of a wide range of quality medicines for bulk purchase. See the WHO website, http://www.who.int/vaccines-documents/DocsPDF06/812.pdf

In order to speed up the process of obtaining WHO pre-qualification, the Chinese government is now offering more support and encouragement to domestic vaccine manufacturers than ever before, particularly to state-owned enterprises such as China National Biotec Group (CNBG) and other leading vaccine companies. This top-down approach has proven to be the most efficient way to move things forward in China.

The announcement will motivate domestic manufacturers to strengthen vaccine development partnerships with international organizations at broader and more strategic levels. More government funding will also pour into companies working toward the goal of WHO pre-qualification. Furthermore, a new interest in vaccine technology will encourage Chinese scientists who are now working overseas to return to the country in order to leverage this opportunity.

The March announcement represents a historic achievement for the Chinese National Regulatory Authority and the Chinese vaccine manufacturing community, as well as for the long-term development of global vaccine markets. On the same day as this WHO announcement, the China SFDA also adopted a new Good Manufacturing Practice code. The new code puts in place stricter requirements for vaccine production, in line with international standards, in order to ensure quality.

What are the implications of the announcement for China's role as an international partner in global health?

Both the Chinese government and Chinese vaccine manufacturers are highly interested in, and motivated to access, the global vaccine market. The potential to be a donor to the GAVI Alliance's[2] immunization programs will position China as an important partner in achieving the Millennium Development Goals and in responding to the Bill & Melinda Gates Foundation's "Decade of Vaccines" initiative. Once the WHO pre-qualification certificate is obtained, the volume of vaccines that Chinese manufacturers will be able to offer to the global vaccine market will be significant. This should contribute to lowering the global procurement price and narrowing supply shortages.

The announcement will motivate the Chinese government to play an increased role in contributing to global health while inspiring Chinese vaccine manufacturers to respond more actively to public-private vaccine-development partnership models. Furthermore, I fully expect that China will create more innovative funding mechanisms that promote public-private vaccine development models between local manufacturer and international organizations.

The Chinese health authority considers the WHO clearance a significant step in China's efforts to contribute to global health, notably to African countries where China has already donated to infrastructure, health systems, and anti-malaria treatment and control programs. The addition of vaccines to this portfolio is truly exciting for the Chinese government.

[2] The GAVI Alliance is a public-private partnership focused on increasing access to vaccines in poor countries. Partners include national governments in developing and developed countries, UNICEF, WHO, the World Bank, the Bill & Melinda Gates Foundation, the vaccine industry in developing and developed countries, public health institutions and civil society organizations (CSOs). Since its inception in 2000, the GAVI Alliance has made available more than U.S.$ 2.5 billion for immunization in GAVI-eligible countries. As a result, vaccination coverage levels have increased dramatically.

What is the timeline you anticipate for Chinese-made vaccines to become WHO pre-qualified and for domestic manufacturers to take on a larger role as international vaccine suppliers?

I am very optimistic about China's long-term role six to ten years from now, but conservative about the country's role in the short term. While Chinese manufacturers have the potential to manufacture WHO pre-qualified vaccines at a low-cost and high-volume to improve access and affordability in developing countries, I believe that there are some huge challenges that must first be addressed:

- Chinese vaccine manufacturers are not yet familiar with the requirements or the process of WHO pre-qualification, UNICEF procurement programs, or GAVI's working mechanisms.
- The China SFDA's regulatory pathways and domestic clinical trials are still in the process of being harmonized with international standards and requirements.
- There will need to be significant English language capacity-building, since English is the working language within the WHO, UNICEF, and GAVI. This is currently a barrier to Chinese vaccine manufacturers, unlike for manufacturers in India.
- Chinese vaccine manufacturers need to quickly attract senior executives and scientists equipped with international work experience and the qualifications to lead companies toward WHO pre-qualification while simultaneously updating old-fashioned work practices.

Obtaining a WHO pre-qualification certificate is complex and can be difficult to maintain. Ultimately, in my opinion, the biggest challenge for China won't be in building infrastructure, but instead in sustaining the commitment of public agencies and encouraging manufacturing executives to strictly comply with WHO requirements and the new Good Manufacturing Practice code. [3]

You mentioned the challenge of sustaining the commitment of public agencies and encouraging manufacturing executives to strictly comply with WHO requirements and the new Good Manufacturing Practice code. Could you elaborate on why this challenge is significant?

As mentioned, obtaining a WHO pre-qualification certificate is very complex, but maintaining it is even more difficult. It takes enduring commitment, effort, and investment. A key factor is the firm political commitment of public agencies to engage in global health, with a special focus on developing countries. The global health community considers China to have great potential as international partner in global health. But that potential has not yet been fully realized.

China's public agencies are currently facing—and will continue to face—challenges around harmonizing with the standards, specifications, processes, and practices of the global health community. These

[3] The new Good Manufacturing Practice (GMP) code, adopted by the SFDA and effective March 1, 2011, aligns with WHO GMP standards, containing stricter requirements for the production of pharmaceuticals (including vaccines). The SFDA has asked that all newly-built pharmaceutical manufacturing enterprises should comply with the new GMP code. Existing factories, which produce sterile drugs, including blood products, vaccines, and injections, are mandated to reach the new code before the end of 2013. The deadline for other plants is Dec 31, 2015. Companies that cannot meet the new requirements before these deadlines will be forbidden from continuing to produce drugs. See SDA website, http://www.sda.gov.cn/WS01/CL0844/59017.html

agencies will start seeing such challenges manifest even more profoundly as they make more of an effort to interpret international standards and specifications and train local manufacturers to comply with the WHO pre-qualification requirements.

With regard to manufacturing executives, they will have to become champions of this process, demonstrating their commitment to learning and adopting WHO requirements by integrating those processes into their operational practices. Leading by example is critical here. It is, however, foreseeable that some executives fear and/or are incapable of leading their staff to reach and maintain these goals right now. In those cases, the job would hopefully become an opportunity for those who have international working experiences and qualifications. Recognizing and leveraging international experience within China's corporate leadership is nothing new, but in the case of vaccine manufacturing, it is critical to China's success as an international supplier.

Chinese vaccine manufacturing executives need to truly understand and be ready to devote lasting efforts to the entire application and maintenance process for WHO pre-qualification. An example from my own experience is PATH's partnership with the Chengdu Institute of Biological Products (CDIBP), a subsidiary of CNBG, since 2004, to expand access beyond China to that company's Japanese encephalitis (JE)[4] vaccine (which CDIBP first developed in 1988). The complexity of the project has ended up being far more nuanced than any of executives originally anticipated when the project was initiated. The ongoing work has proven to be full of blood, sweat, toil, and tears, but with great rewards.

Drawing on your experience working for CNBG as well as for PATH and other international companies in this space, is the March 2011 announcement a milestone for the JE vaccine?

PATH's collaboration with CNBG on JE has provided an important model for applying donor funds toward a neglected disease. At the time of a major JE outbreak in Asia in 2005, the most commonly used vaccine had drawbacks that made it difficult to integrate into national immunization programs in developing countries. Three doses were required, there were side effects, and it was time-consuming and expensive to produce. But then PATH found that China had vaccinated more than 200 million children since 1988 with an effective JE vaccine made from active but weakened virus. Although the Chinese vaccine was safe, effective, affordable, and easy to administer in large campaigns—only one dose was needed—still, language and cultural barriers had prevented information about its potential from being shared internationally.

This special JE effort in China has raised awareness of the disease to an unprecedented level and achieved a lifesaving impact on families and countries burdened by JE. The live attenuated vaccine[5] manufactured by CDIBP has now been registered and used in numerous Asian countries. In India alone, about 76 million have been vaccinated with this vaccine from 2006 to early 2011.[6]

[4] JE is a leading cause of viral encephalitis in Asia, caused by a virus spread by mosquitoes. After a person is infected, the virus invades parts of the central nervous system, including the brain and spinal cord, and symptoms then occur. Countries with JE risk include those in Asia and parts of the Western Pacific Region, from Pakistan and India through China and Japan and south to Papua New Guinea and the islands of the Torres Strait in Australia.

[5] SA 14-14-2 JE

[6] On average, for every 10,000 children vaccinated in JE endemic countries, 6 deaths and 7 disabilities due to JE could be potentially prevented, with a potential to save up to $1,700 in treatment costs associated with JE.

The March 2011 WHO announcement clears the bottleneck for CDIBP to apply for WHO pre-qualification for its JE vaccine, which will make it the first Chinese-made vaccine to be pre-qualified by the WHO. This will not only expand access to and supply for the vaccine in low-resource settings, but it will also set an example for other local manufacturers. PATH is working closely with CDIBP to achieve this goal in the next two to three years.

China has successfully expanded immunization coverage to nearly all Chinese children. Could China's approach to vaccine delivery serve as a potential model for other countries?

China's immunization program has seen great success since the introduction of the WHO's Expanded Program on Immunization (EPI) in 1978. In 2000, China was declared polio-free, and it has been able to maintain this status despite the disease circulating on many of its borders. China has also seen a dramatic fall in hepatitis B infection among children younger than five years old, thanks to an aggressive vaccination program. Finally, China has recently seen a marked decrease in measles cases and is working hard to achieve measles elimination by 2012. Since 2008, the EPI Program in China has expanded from six vaccines against seven diseases to 14 vaccines against 15 diseases, with a 90% immunization coverage rate at the township level.

China's approach to vaccine delivery can indeed serve as a potential model for other developing countries, especially those with large populations. The EPI Program has proven to be one of the most cost-effective public health interventions available for sustainable social development. Hopefully, the March WHO announcement will encourage China and other developing countries to open even more dialogue about international vaccine supplies and other global immunization activities.