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Milestone for China and Global Health

Implications of China's First WHO-Prequalified Vaccine

An Interview with Jack Zhang

By Claire Topal
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Japanese encephalitis (JE) is the leading viral cause of disability in Asia and primarily affects children. Approximately 70% of those who develop the JE illness either die or suffer long-term neurological disabilities. More than four billion people live in JE-endemic regions in Southeast Asia and the Western Pacific, and up to 50,000 cases of JE are reported annually.[1] The World Health Organization (WHO) announced on October 9, 2013, that the Chinese-made SA 14-14-2 JE vaccine has achieved WHO prequalification.[2]

While other JE vaccines exist, the Chinese vaccine, manufactured by Chengdu Institute of Biological Products (CDIBP), a subsidiary of China National Biotec Group (CNBG), is the first single-dose JE vaccine that the WHO has approved for use in children. NBR spoke with Jiankang (Jack) Zhang about why the WHO's announcement marks a historic milestone for both China and global health. He also discusses the implications for China's engagement on health issues in Africa and other parts of the world. Mr. Zhang plays an integral role in the partnership that is helping to make the vaccine internationally accessible.

Jiankang (Jack) Zhang is the China Country Program Leader for PATH, a post he has held since 2007. Previously, he served as Chief Representative and General Manager of Haemonetics China Subsidiary, a Boston-based blood-processing and management company. Prior to that, Mr. Zhang worked at the Shanghai Institute of Biological Products, a subsidiary of CNBG, where his last position was Deputy Director-General for Operations.

Q. The WHO announced on October 9, 2013, that it has granted prequalification status to the Chinese-made JE vaccine. What does this status mean, and why is this announcement important for China?

WHO prequalification is an international regulatory status that enables CDIBP—the Chinese manufacturer of the JE vaccine—to sell the vaccine to governments and international procurement agencies, which purchase billions of dollars of medicines and vaccines every year to distribute in developing countries. The prequalified status is an official seal of approval, ensuring the safety and efficacy of a specific vaccine or medicine. Every product created for international procurement for the developing world must go through WHO's prequalification process, which can take years and be expensive. As of today, WHO has granted prequalification status to 36

1 See World Health Organization (WHO), "Water-related Diseases," http://www.who.int/water_sanitation_health/diseases/encephalitis/en.

2 WHO, "Newly Accessible Japanese Encephalitis Vaccine Will Make Saving Children Easier in Developing Countries," Press Release, October 9, 2013, http://www.who.int/mediacentre/news/releases/2013/japanese_encephalitis_20131009/en/index.html.

vaccines manufactured by 29 companies in 22 countries.[3]

The JE vaccine is the very first Chinese vaccine to be prequalified by the WHO, and this development is a milestone for many reasons. First, it illustrates China's growing role as a global supplier of high-quality vaccines. Second, it showcases the country's commitment to the health of the developing world, where the recipients of the JE vaccine live. Finally, in addition to advancing China's desire to contribute meaningfully to global health, WHO approval is a matter of national pride.

The China Food and Drug Administration (CFDA) has worked very hard to raise its international status by winning the WHO's approval as a functional regulatory authority for vaccines—a costly but hugely valuable process. After unsuccessful attempts in 2001 and 2004, the CFDA became WHO-approved in March 2011. This meant that it officially met WHO criteria for maintaining international standards in vaccine regulation; as a result, CFDA-approved vaccines made in China were eligible to apply for prequalification for specific products. The dedication that CFDA has shown toward achieving this milestone demonstrates its commitment to producing high-quality health products and attracting international recognition for the Chinese vaccine industry.

The recent announcement will motivate the Chinese government to play a larger role in global health and increase its diplomatic efforts in this area. Additionally, since the JE vaccine was developed through a unique partnership between CDIBP/CNBG, the international nonprofit organization PATH, and the Bill & Melinda Gates Foundation, the vaccine's success should inspire other Chinese manufacturers to seek more active engagement in public-private partnership models.

Q. How are you measuring the success of the JE vaccine so far?

In addition to the high quality and low cost of the vaccine, I measure success by the number of people immunized and its effectiveness in averting disease and disability. Outside China, the vaccine has already been licensed or used in eleven Asian countries where JE is endemic, including Myanmar, Cambodia, India, North Korea,[4] South Korea, Laos, Malaysia, Nepal, Sri Lanka, Thailand, and Vietnam. As of September 2013, more than 200 million doses had been distributed to these eleven countries to protect children against JE.

Q. Margaret Chan, director-general of the WHO, and Bill Gates, co-chair of the Bill & Melinda Gates Foundation (which funds PATH's JE vaccine project), have both celebrated China's achievement and noted the opportunity it creates for Chinese leadership in vaccine creation. Can we expect to see prequalification for more Chinese vaccines, and what would be the broader implications of such a trend?

China houses more than 30 domestically owned and operated vaccine manufacturers that together produce 49 types of vaccines against 27 diseases. The country's annual manufacturing volume is nearly one billion doses, with significantly higher manufacturing capacity. The WHO's March 2011 clearance of CFDA opened the door for these companies to apply for WHO vaccine prequalification, and the October 2013 announcement is inspiring both state-owned and private Chinese companies to continue energetically moving forward in this area. It is highly likely that more Chinese vaccines will obtain WHO prequalification in the next five to ten years, including vaccines for seasonal influenza, meningitis, polio, pneumonia, and rotavirus.

More WHO-approved, Chinese-made vaccines will have a strong impact on global vaccine supply, pricing, and accessibility. Historically, a small number of multinational companies have dominated the international vaccine industry, which is worth over $25 billion annually. With companies in China, India, and other emerging countries becoming major manufacturers and now being able to sell to the international market, competition will increase and prices will naturally decrease. This is a very positive development for global health, as governments and international procurement agencies will be able to afford more life-saving vaccines and thus protect more lives.

Q. What is the significance of the WHO's announcement for China from a regulatory standpoint?

For China's regulatory agencies, 2013 has been an important year. The October announcement was preceded by another important announcement on January 1, when the WHO approved the Institute for Biological Product Control—under the China National Institutes for Food and Drug Control—as an official WHO collaborating center for the standardization and evaluation of biological products.[5] This is the seventh center of its kind globally, and the first in a developing country. The other six collaborating centers are located in Australia, Canada, Japan, South Korea, the United Kingdom, and the United States. The January 2013 announcement internationally recognized the quality of China's biological products inspection and research capacity.

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3 WHO, "WHO Prequalified Vaccines," available at http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html.

4 PATH partnered with CDIBP to support North Korea's JE-immunization campaigns in 2009 and 2010, including the donation of 1.5 million doses of JE vaccine.

5 WHO, "New WHO Collaborating Center," http://www.who.int/immunization_standards/en.

Both announcements provide motivation for China to continue its efforts to harmonize the country's regulatory system with the WHO. The government is investing significantly in this area, as are China's state-owned and private companies. For example, CNBG, the manufacturer of the new JE vaccine, has invested more than $1.5 billion to improve its facilities and systems to meet WHO requirements.

Q. We've been talking about China and CDIBP/CNBG, but PATH, a U.S.-based NGO, played a major role in the success of the JE vaccine. How did this partnership come about, and who did what?

Actually there are four key partners, with four key roles: the Bill & Melinda Gates Foundation as donor and advocate; CDIBP as manufacturer; CNBG, which is China's largest state-owned enterprise for vaccine research and development, as manufacturer and supplier, as well as catalyst for political will; and PATH as an integral partner providing critical technical assistance, project-management support, and expanded outreach through advocacy efforts.

PATH established its JE project in 2003 with funding from the Bill & Melinda Gates Foundation. The overarching goal of the project was to eliminate clinical JE and avoid the unnecessary death and disability caused by this disease. Because immunization is the best way to prevent JE, advancing the availability of a safe, affordable, and easy-to-use vaccine has been a key objective.

In search of a solution to help save children from this devastating disease, PATH surveyed the field for a better JE vaccine and discovered that key institutions and individuals in China had already invested twenty years in R&D. Development of the live, attenuated SA-14-14-2 JE vaccine began in the 1970s, led by Dr. Yu Yongxin at the National Institutes for Food and Drug Control. In the early 1980s, the vaccine technology his team developed was transferred to CDIBP, which then produced SA 14-14-2 as a safe, effective, and affordable vaccine for human use. The vaccine was licensed in China in 1989, after which time 200 million children were immunized. It was at this point that PATH reached out to CDIBP.

PATH chose CDIBP as a partner based on its R&D progress, production capacity, pricing structures, and strong commitment at the very top levels of leadership. CDIBP and PATH signed an official collaboration agreement in 2006 to increase access to the JE vaccine in developing countries. Since the inception of PATH's JE project and the organization's collaboration with CDIBP, PATH has established reliable methods of diagnosing and tracking JE to help countries understand the disease, prioritize preventing it, and focus these efforts in regions where children are most at risk. In addition to improving disease surveillance and leading a series of clinical trials to establish the JE vaccine's immunogenicity and safety, PATH provided technical and financial support to ensure that CDIBP could meet the strict standards required for prequalification. This included assisting in the design of a new manufacturing facility to ensure high-quality, adequate, and stable vaccine supply. PATH also negotiated an affordable public-sector price for the vaccine and supported vaccination campaigns in countries that forged ahead even before prequalification.

Q. So the vaccine has actually existed since 1989? Why were so much additional money, collaboration, and time necessary to get the JE vaccine to the international market?

Local Chinese manufacturers have limitless potential to produce more and better life-saving health products. But in many cases their infrastructure, systems, and methods still need to be improved and harmonized with WHO's requirements in order to meet the prequalification standards. As the JE project was unprecedented, there was a learning curve for the entire process, including, but not limited to, gathering supplementary clinical data, bridging study data for the transition of manufacture from an old facility to a new one, and lots of training on behavior changes. However, with the success of the first prequalified Chinese-made vaccine and the ongoing harmonization of CFDA and WHO regulations, new vaccines are expected to take less time and investment to produce.

The Chinese vaccine industry is still in the nascent stages of the WHO prequalification process—the success of one vaccine and one company does not mean that broader China does not still need technical assistance. Yes, the Chinese economy, life-science industry, and population benefit from this assistance. That is why these kinds of partnerships are successful—there are benefits on multiple levels. Similar partnerships exist in emerging economies across the world—and on a much larger scale in India and Brazil, just to name two examples. Some outside observers may perceive this kind of technical assistance to China as hurting foreign industry. To the contrary, more widely available, higher-quality, and less expensive health tools help everyone in the world. I do not think this gives China an unfair advantage.

Q. Why did PATH invest significant resources in such a wealthy company and country?

PATH believed that it was the right time to build partnerships with public and private Chinese companies to develop, manufacture, and supply health products in China for greater public health impact around the globe. The Chinese

public and private sectors are very important players on most global issue and in most industries, and engaging them—leveraging their unique abilities and reach—for global health and development deserves serious consideration and encouragement.

The JE project was by no means a one-way investment but rather was a real partnership. It reflected a perfect fit for both partners. For PATH, the project matched our approach of identifying a promising existing innovation and providing the technical assistance and support needed for wide-scale use. For CDIPB, it represented an opportunity to further scale up production of high-quality vaccines at affordable prices, obtain WHO prequalification, and supply vaccines to international procurement agencies.

Q. Some have asserted that the prequalification of the JE vaccine is a boon for China's global health engagement in Africa. What does a vaccine addressing the leading cause of viral encephalitis in Asia have to do with China's engagement in Africa?

It is not so much the JE vaccine itself that is a boon for China's engagement in Africa. Rather, the announcement creates the opportunity for additional Chinese-made vaccines that could support collaboration between China and Africa on global health to also receive WHO prequalification. China only graduated in 2011 from being a recipient of support from the Global Alliance for Vaccines and Immunization (GAVI)—one of the only countries in the world to make that switch. China's goal is to quickly move from GAVI recipient to GAVI donor.

China is already a generous donor to Africa in the areas of infrastructure expansion, health systems support, and anti-malaria treatment and control programs. The addition of vaccines to this portfolio, once additional Chinese vaccines become prequalified, will be very good for South-South cooperation, as well as for the health of African populations.

This past August, China's National Health and Family Planning Commission, its counterparts in numerous African countries, and representatives from international health and financing organizations convened to endorse the Beijing Declaration of the Ministerial Forum of China-Africa Health Development. The theme of "China-Africa health cooperation in the new era" formally acknowledged health as a central element of cooperation between China and African countries. The action plans resulting from the meeting include supporting the prevention and control of communicable and non-communicable diseases, strengthening the Expanded Program on Immunization, combatting vaccine-preventable diseases, promoting corporate cooperation between China and Africa, and encouraging health technology transfers from China to Africa in order to sustain the supply and increase the affordability of health commodities (e.g., pharmaceuticals, vaccines, and medical devices).[6]

China's National Health and Family Planning Commission is thus making a concerted effort to leverage domestic experience, know-how, technical support, and financial resources to help meet the vaccine and immunization needs of African countries. ~

[6] The original text of the Beijing Declaration of the Ministerial Forum of China-Africa Health Development is available from the China Ministry of Health website, http://www.moh.gov.cn/gjhzs/s3590/201308/da8ad62e487a481f987e631e1318c6fc.shtml.