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Vaccine punch

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The $20 billion global vaccine industry is sitting on a tough decision. Industry is debating whether it is time to move away from the existing 50-year-old production method that relies on chicken eggs and adopt a new method called virus-like particle (VLP) technology. The new technology holds the promise to make production faster and develop better quality vaccines that help prevent against various forms of flu viruses, human papilloma virus (HPV), hepatitis B and diseases endemic to India like dengue fever and chikungunya fever. However, traditional vaccine makers feel that VLP is not yet a licensed technology for H1N1 vaccine so far and is yet to complete the mandatory clinical trials. Hence, their reason to still rely on the time-tested and proven old technology based on embryonated eggs.

From a layman's point of view, traditional vaccines are made of either whole viruses (killed or attenuated) or pieces of pathogens, like surface proteins. The latter, however, don't evoke a strong enough immune response on their own, so vaccine makers add immune enhancers called adjuvants. Ironically, this 50-year-old technology involves injecting the virus into eggs and allowing it to feed on the nutrients in the egg white.

Typically once the fertilised eggs arrive at the vaccine plant, the flu virus is injected into them and allowed to multiply for several days. Then the eggshells are cracked; the virus-laden fluid is extracted, the flu virus is killed and the substance is purified. The inactivated strain is tested to determine purity, potency and yield. From start to finish, the process takes about six months. In normal time, there is usually enough time to get the vaccine to anyone who wants it. But in an all-out epidemic, egg-based production is incapable of producing huge batches quickly. The delays, witnessed recently in the US market for swine flu vaccines, have led to renewed demands for a quicker, more reliable way of producing vaccines than the chicken-egg method, healthcare analysts reveal.

Enter virus-like particle vaccines which are composed of proteins from the viral shell and surface of a pathogen that self-assemble in vitro to resemble an intact virus, but without the potentially infectious viral genetic material (DNA or RNA) of the original virus, then injected as a vaccine. Virus-like particle is a structure similar to a virus but without the genetic material that is responsible for viral replication and infection. Vaccines developed using virus-like particles, once injected into the body trigger an immune response sufficient to protect a person if exposed to the virus.

"Virus-like particle based vaccines have a number of advantages over traditional vaccines. Because they more closely match an individual viral strain, they can trigger a more robust immune response. In addition, as virus-like particles do not contain viral nucleic acids, they cannot replicate, and therefore, they present no threat of infection to a person being vaccinated," says Cadila Pharmaceuticals chairman Indravadan A Modi. "Using the VLP technology, vaccines for swine flu were developed in half the time compared to the conventional egg-based technology. Also, the technology enables quicker mass production," he adds.

Conventional vaccine makers however, have their counter arguments ready. Their rationale: VLP is a scientifically sound technology. However, VLP is not yet a licensed technology for H1N1 vaccine so far. Besides, the efficacy and safety of VLP have to be very closely monitored, since this technology has not yet completed the mandatory regulatory clinical trials.

A more balanced and unbiased opinion comes from KPMG India executive-director, Hitesh Gajaria. "VLP technology

vaccines produce higher levels of therapeutic antibodies as compared with conventional vaccines, therefore generating stronger immune responses. If successful, this technology appears to have advantages over the conventional technologies particularly in terms of faster development and commercialisation of the vaccines," he says.

Curiously while traditional vaccine makers in India as well as overseas are still betting on the time-tested technology based on embryonated eggs, some of the global pharmaceutical majors have gone ahead and launched VLP-based vaccines.

For instance, US drug maker Merck has been the first company to launch VLP-based vaccine called Gardasil in the US market. The vaccine is seen as a preventive medication in women to block four strains of the human papilloma virus that cause the majority of cervical cancers and genital warts. Merck has sold about 50 million doses worldwide, with more than $1.4 billion in revenue last year. Last

October, the US Food and Drug Administration (USFDA) also cleared Gardasil to prevent genital warts in boys.

UK-based GlaxoSmithKline (GSK) is another pharmaceutical major to have embraced the new vaccine production technology for its cervical cancer vaccine, Cervarix. The vaccine has demonstrated high protection against HPV 16 and 18, which are responsible for approximately 70% of cervical cancers worldwide.

Among others, the US-based biotechnology major Novavax has successfully used virus-like particle technology to develop pandemic and seasonal influenza vaccine. The company also plans to apply its particle-based vaccine approach to other viral diseases beyond influenza. Medicago, a Canada-based biotechnology major also initiated its Phase I human clinical trial with its VLP-based H5N1 Avian Influenza vaccine in October 2009.

Closer home, virus-like particle technology is being used by Cadila Pharmaceuticals to develop vaccines. It has formed a joint venture called CPL Biologicals along with Novavax and a 25,000 sq ft facility is coming up at Dholka near Ahmedabad which is expected to be operational by March this year. "The virus-like particle technology is well suited in the development of all types of viral vaccines like HPV and Hepatitis B vaccine. It is also suitable against diseases endemic to India and surrounding regions like dengue fever and chikungunya fever. Currently, there is no vaccine or definitive treatment for dengue fever," says Modi.

Using the virus-like particle technology, Cadila Pharmaecuticals has developed a vaccine for swine flu and is ready to commence clinical trials in the country. "We have applied for conducting the clinical trials and will start the trials as soon as we receive the Drug Controller General of India (DCGI) nod which we feel is overdue. Using the new technology, vaccines for swine flu were developed in half the time compared to the conventional egg-based technology. Also, the technology enables quicker mass production," says Modi.

Buzz around the virus-like particle technology has come to the forefront on account of the ongoing swine flu pandemic. So far, nearly 10,000 people have died of swine flu or influenza A (H1N1) virus in the US, and 50 million people—nearly 17% of the US population—have been affected by the virus. Till date, India has reported over 1,100 deaths due to the contagious virus and over 28,000 people have been infected with the disease till now.

Nevertheless, the domestic vaccine makers have their own take on the tech buzz surrounding the vaccine making process. Their point of view is that there is a pressing need to provide a quick solution to pandemic flu threat rather than engage in scientific possibilities of better or best technologies. "We cannot put human life at risk to uncertainties of technologies. Therefore, we chose a path of time tested sure shot technology based on embryonated eggs," says Rajesh Jain, joint managing director, Panacea Biotec.

Panacea Biotec, Serum Institute of India, Bharat Biotech and Zydus Cadila have got the DCGI's permission to go ahead with the human clinical trials to test the safety and efficacy of their swine flu vaccines. "Bharat Biotech has developed a cell culture based vaccine candidate for influenza, which can serve as a platform technology for both pandemic and seasonal flu vaccines. The company expects to complete the trial in six weeks," says Bharat Biotech chairman and managing director, Krishna Ella.

There is no doubt that vaccines are one of the most effective ways to protect people from contracting illness during influenza epidemics and pandemics. And advancing technologies are encouraging pharmaceutical companies to tackle new vaccine targets. Nevertheless, in the backdrop of the rapid progress made by the virus-like particle vaccine making method, will tech be the game changer in the vaccine world remains to be seen.