

# VAXINNATE

## **VaxInnate's Influenza Vaccine Program**

VaxInnate is developing novel, proprietary vaccines for seasonal and pandemic influenza using a technology platform that substantially improves the potency, manufacturing capacity, and cost efficiency of the vaccines.

This technology physically links a natural component of microbes known as flagellin to vaccine antigens, helping the human immune system to recognize the vaccine as foreign and to respond with a strong, protective immune response. This boost in the immune response appears to overcome the poor potency of seasonal and pandemic influenza vaccines in individuals with less-than robust immune responses, among them the elderly adults.

VaxInnate produces flu vaccine using efficient, low-cost recombinant protein methodologies in bacteria, namely *E. coli*. This recombinant expression of VaxInnate's vaccines alleviates the manufacturing constraints that have long restricted influenza vaccine availability, making it possible to produce sufficient seasonal and pandemic influenza vaccine to meet national and even global needs.

## **BACKGROUND ON INFLUENZA DISEASE AND VACCINES**

### ***Seasonal Influenza***

Influenza is a highly communicable disease, and typically has the most severe impact on children and the elderly. Influenza complications lead to about 200,000 hospitalizations and 36,000 deaths in the United States alone during a typical influenza season. Due to growing awareness of the value of influenza vaccine in preventing disease, the market for influenza vaccines is projected to exceed \$3 billion.

The seasonal nature of influenza, and the virus' ability to mutate and still cause disease, makes it necessary to formulate an entirely new influenza vaccine annually. Seasonal influenza vaccine is based upon a prediction by the Centers for Disease Control (CDC, part of the U.S. government) and the World Health Organization (WHO) of the strains that are likeliest to circulate and cause disease during the next winter's influenza season.

Once the strains are identified, manufacturers race to produce the vaccine so it can be ready before the next influenza season hits. Currently, it takes about six months from the time when the influenza strains are chosen until the first flu vaccine reaches the market. It can take even longer if the strains fail to grow well in eggs, the medium that has been used to produce influenza vaccine since the 1940s. Currently licensed vaccines require a seed virus, which is a reassortant influenza virus that grows well in eggs (or cell culture) and produces high yields of the target HA protein. It takes several months to make the egg-adapted master seed from which stock seeds are derived and then distributed to vaccine producers. After receiving stock seeds, each manufacturer then must develop working seeds, the source for batches of intermediate bulk vaccines. There is growing concern, however, that traditional influenza vaccines may not consistently meet the

demands of seasonal influenza or potential pandemic virus outbreaks due to slow development and production cycles.

Most of the recent efforts to improve influenza vaccine production have focused on the production of influenza vaccine in cell culture. While this approach alleviates the need for eggs, it has its own manufacturing limitations. The focus on cell culture production stems from the historical view that protective forms of HA antigens must be manufactured using cells from animals such as humans, monkeys, dogs and chickens.

### ***Pandemic Influenza***

Novel influenza strains are widely generated in populations of domestic and wild fowl, pigs, and other animals. Fortunately, most strains infect only animals, while many of those that infect humans are easily combated by healthy immune systems.

Occasionally, however, an entirely new strain emerges that spreads from animals to humans. Because humans lack previous exposure to and protection from these novel viruses, a pandemic involving widespread, sometimes severe disease can result. Influenza pandemics generally occur every 30 years. The last pandemic occurred in 2009. Fortunately, the H1N1 swine origin virus was not as lethal as past pandemics. However, one of the worst flu pandemics in memory was one that emerged in the closing days of World War I, causing millions of deaths worldwide.

The recent experience of the H1N1 pandemic in 2009-2010 clearly demonstrated how quickly new pandemic strains can spread globally even with excellent public health precautions. The experience of 2009 highlighted the importance of fast and efficient flu vaccine manufacturing in addressing these circumstances. Even with recent large investments in expanding flu vaccine manufacturing, the pandemic vaccine was slow to get to the public in 2009. The world was fortunate that this H1N1 pandemic strain proved not as highly virulent in most humans as initially anticipated. However new, highly virulent strains of H5N1 avian or bird flu emerged within the last decade and have been circulating in the domestic and wild birds in Asia, Africa, the Pacific, Europe and the Near East. Experts agree that these H5 strains have the potential to cause the next human pandemic, since humans have not developed immunity to this strain. To date, the mortality rate among confirmed human cases of avian influenza has been greater than 50%.

### **VAXINNATE INFLUENZA VACCINE**

VaxInnate's influenza vaccine comprises biopharmaceutical grade purified recombinant proteins that are engineered to be potent in low concentrations, safe, and efficiently manufactured. This product has the attributes needed to address seasonal and pandemic vaccine needs on a global scale.

#### ***Potent, Efficacious and Safe***

This novel approach is designed to meet the demands for seasonal and/or pandemic influenza vaccine by drawing upon new understanding of the way the immune system works. By leveraging both of the two primary mechanisms of immune defense, known as "innate" and "adaptive" responses, VaxInnate's proprietary TLR technology leads to a more effective vaccine against influenza antigens.

Our clinical trials have demonstrated that our recombinant, soluble protein is highly potent and well tolerated as a vaccine in both young adults and the elderly, inducing antibody responses which neutralize the influenza virus. Potency in elderly populations is especially important since this

population is at greatest risk for influenza disease and is the least responsive population to the currently licensed, standard influenza vaccines on the market.

***Highly Efficient and Cost-effective Manufacturing***

VaxInnate's bacterial production method is both more efficient and cost-effective than current influenza vaccine production techniques. Traditional vaccines are generated by growing the virus in eggs in a laborious process that takes up to six months. There are no eggs or animal cells involved in the VaxInnate approach. Instead, VaxInnate grows the necessary proteins in a bacterial expression system, a proven method that is commonly used in the production of other recombinant proteins and biopharmaceuticals.

Experts agree that current levels of influenza vaccine production in the U.S. have been inadequate for pandemic events. By producing a high-yield, more robust vaccine that does not rely on egg- or cell-based technology, VaxInnate reduces or eliminates many of the bottlenecks in the current influenza vaccine production process. Cell culture and egg-based systems grow the whole virus, which must be harvested, purified and then inactivated. By contrast, VaxInnate produces individual recombinant proteins, eliminating several steps in the production process.