

Flu Preparedness AHEAD of Pandemic - New Approach

Influenza (Flu) Pandemics:

- Unknown virus
- Unknown timing
- Unknown outbreak location
- Potentially high morbidity & mortality worldwide
- Substantial economic losses

Pandemic Flu Vaccines – Why?

- Cost effective in term of life years saved if given within 6 months of outbreak⁴
- Mitigates macroeconomic costs, the key parameter being school closures³
- 'Dampens' burden of disease⁵ even if low efficacy⁶

Pandemic Vaccination Today – Limited Preparedness

- Matching vaccine expected only up to 6 months after outbreak
- Limited production capacity

BiondVax's Pandemic Strategy – Preparedness AHEAD of all pandemics

Upon outbreak: administer BiondVax's universal flu vaccine as primer from national stockpile, relevant whatever pandemic strain

Within 6 months: administer pandemic-specific vaccine

Net result: considerably reduced pandemic illness and economic losses

Competitive Advantages of BiondVax's Universal Flu Vaccine as Universal Pandemic Primer

- Easy & cost effective to manufacture & stockpile (unchanging formulation & manufactured using bacteria)
- Relevant whatever pandemic flu strain emerges
- Enhances & broadens activity of pandemic-specific flu vaccines and enables pandemic-specific vaccine sparing without requiring adjuvant

Background: the flu (influenza) virus changes unpredictably and frequently, making it hard for our immune system to recognize new strains, with the result that flu is the most common infectious disease and periodically, the cause of devastating pandemics. It is estimated that 5-15% of the global population suffer flu and around half a million people die from flu-related diseases each year. Pandemics occur when a substantially altered flu virus becomes contagious in humans and can potentially result in over 300 million deaths - if the virus is deadly¹, which appears to be case for the H5N1 and H7N9 flu strains circulating locally in animals and humans today.

In addition to human suffering, flu disease represents a huge economic burden. The annual cost of seasonal flu in the US alone is estimated at over \$90B². Remarkably it is estimated that a severe pandemic, with an infection rate of 10-50%, could result in a GDP loss of up to 8%³.

Pandemic Preparedness Today – Too Little, Too Late: certain governments stockpile vaccines designed to target potentially pandemic strains that are circulating in animals and humans locally, but the identity of the actual future pandemic strain is unknown and unpredictable. Pandemic-specific vaccines are expected to be available only up to **six (6) months after** outbreak, as this is the time taken to characterize the actual pandemic strain, manufacture and distribute a matching vaccine. During this long period the population is exposed to a possibly deadly pandemic virus, with costly human and economic consequences.

Pandemic Preparedness – Ahead of outbreak: BiondVax's universal flu vaccine offers a solution for this dangerous period when the world population is under threat. For the first time ever, health authorities worldwide will have a comprehensive strategy to prepare populations ahead of flu pandemic outbreaks!

Our new strategy is based on the discovery that BiondVax's universal flu vaccine improves the activity of all pandemic-specific vaccines tested to date and more generally, on the principle that effective protection against a disease typically requires a vaccination schedule with multiple administrations, such as for HPV and Hepatitis B. Since the pandemic strain is unknown until it starts spreading among humans rapidly, as soon as the pandemic outbreaks, we propose to vaccinate the population twice with our universal flu vaccine. **The vaccine will be available from national stockpiles maintained during inter-pandemic periods.** The third vaccination in this anti-pandemic campaign will be the pandemic-specific vaccine, which can be expected to be available up to 6 months after outbreak. This whole-of-community, proactive preparedness strategy will considerably reduce pandemic illness and economic losses.

¹ Stockpiling pre-pandemic influenza vaccines: a new cornerstone of pandemic preparedness plans. Jennings et al. Lancet Infect Dis 2008. 8:650

² The imperative of influenza vaccines for elderly individuals - an evolving story. Poland and Mulligan. J Infect Dis 2009. 200:161

³ The macroeconomic costs of a global influenza pandemic. Keogh et al. In press

⁴ Vaccination strategies for future influenza pandemics: a severity-based cost effectiveness analysis. Kelso et al. BMC Infect Dis 2013, 13:8

⁵ Options for design and financing of an H5N1 vaccine stockpile. Bill and Melinda Gates Foundation 2009.

⁶ Safety and Immunogenicity of Influenza A H5 subunit vaccines: effect of vaccine schedule and antigenic variant. Belshe et al. 2010, 2011:203