Modeling H1N1 US vaccine demand – another multibillion dollar issue

LONDON, UK----21st May 2009----ExpertREACT. As of 19th May 2009, the World Health Organisation (WHO) decided it was premature to recommend that commercial scale production of H1N1 vaccine should start immediately. Although this stance may change in the coming weeks, **VacZine Analytics** believes now is a good time to review the issues and deciding factors. We also estimate that US authorities will need to spend >$1 bn at least procuring the new H1N1 vaccine.

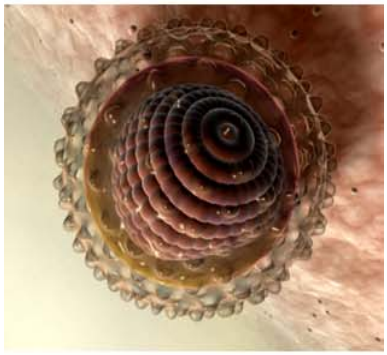
As of 20th May 2009, the novel triple reassortant H1N1 influenza A, virus previously referred to as "swine flu" has caused over 10,000 laboratory confirmed cases of infection with 80 deaths **(1).** 41 countries have reported infection with over half of the cases being identified in the continental United States. Currently, H1N1 has similar transmissibility to that of seasonal influenza viruses although observed clinical disease severity has been mild in most infected persons. H1N1 has caused the World Health Organisation (WHO) to lift its pandemic alert status to level 5 and is widely expected to be raised to 6 if "community-level sustained transmission" occurs in another region of the world. Significantly, Japan is currently also experiencing a spread of the virus with the closure of ten schools in the Kobe City area.

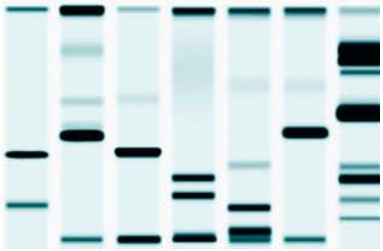
Because sera from individuals vaccinated with recent seasonal influenza (07/08 or 08/09) vaccines do not appear to neutralize the novel H1N1 virus, experts are concerned that the majority of the population, especially younger groups do not have sufficient pre-existing immunity. Furthermore, in a recent MMWR report describing hospitalized cases in California (30 patients, median age, 27.5 yrs) a large proportion of individuals had underlying medical conditions including chronic lung disease **(2).** These early observations suggest that, although H1N1 appears relatively mild in terms of disease severity, as the confirmed case number increases, its impact on public health especially "at risk" groups still is of concern.

H1N1's spread has naturally prompted discussion of whether manufacturers should initiate large scale production of H1N1 pandemic specific vaccine. This action has many important considerations in terms of potential safety concerns of the new vaccine, impact on standard influenza vaccine production and eventual deployment. As of 19th May 2009, the WHO considered it premature to recommend that commercial-scale production of influenza A (H1N1) vaccine should start immediately. Moreover, because of steps required to generate and characterize H1N1 seed viruses manufacturers would not be ready to switch production before mid-July 2009, if required.

What assumptions can be made at this stage regarding a potential H1N1 vaccine and vaccination program if initiated? Firstly, it appears that the candidate vaccine is likely to be monovalent, given separately to the seasonal vaccine and most likely composed of two doses. Previous experience with H5N1 pre-pandemic vaccines demonstrated that some influenza viruses for production purposes have low growth potential, sometimes 50% less than that obtained for seasonal vaccines. If the novel H1N1 virus has these same characteristics, then the available supply will be difficult to predict and possibly limited. This could be compounded further if immunogenicity of the vaccine is low. Again, the first H5N1 vaccine (Sanofi Pasteur) used for the current US pre-pandemic stockpile was a whole vaccine requiring a high antigen amount of 90mcg per dose. Such higher antigen amounts necessary to induce protective immunity put increased demands on production, hence the drive towards antigen sparing technologies such as adjuvantation. Adjuvantation in turn elevates safety concerns, especially in the US where authorities have not yet approved a novel vaccine adjuvant.

Despite these many potential variables and considerations with H1N1 vaccine production, some of the large vaccine manufacturers have begun to take orders for H1N1 specific vaccine. GlaxoSmithKline, the first company to submit a "mock-up" dossier for an egg-based vaccine in the EU, announced that it has been contacted by the UK, French, Belgium and Finland government to supply potential H1N1 vaccine **(3)**. Again, the company is keen to promote the use of its AS03, MPL-containing adjuvant which they state will lessen the antigen amount required and possibly protect against "drift" of the H1N1 virus.





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Sanofi Pasteur, another major player in influenza vaccines had previously stated that it stood ready to aid the H1N1 vaccine effort and had been contacted by national governments although there are less specific details publically **(4).** Like GSK, the company also has a proprietary adjuvant, AF03 but is further behind in terms of development when compared to rivals. It is therefore likely the company will focus on a traditional vaccine approach (if required for H1N1) currently favoured by US regulators.

Although current orders so far indicate that governments wish to vaccinate their whole populations, the considerations that have been discussed in this article make it a likely possibility that H1N1 vaccine supply will initially be limited and phased according to population priorities decided by each countries national health authority. A good example is the vaccine allocation guidance previously published for H5N1 pandemic specific vaccine by the US Department Health and Humans Services (US HHS) **(5).** Using these priorities for a H1N1 vaccine, and assumptions previously gathered for H5N1 and seasonal vaccines, **VacZine Analytics** has modeled specific demand scenarios (per quarter) in the US. It is clear at this early stage, that US authorities will need to spend at least >$1 bn procuring the new H1N1 vaccine **(6).** This sum is unfortunately in addition to the vast sums already spent on H5N1pandemic preparedness. Indeed, influenza continues to be a dangerous, troublesome and expensive virus to deal with.

References:

1) World Health Organisation (WHO). Influenza A (H1N1) – update 34. Available at: http://www.who.int/csr/don/2009_05_20/en/index.html. Accessed May 2009

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5) US Department of Health and Human Services (HHS) and US Department of Homeland Security. Guidance on allocating and targetting pandemic influenza vaccine. Available at: http://www.pandemicflu.gov/vaccine/allocationguidance.pdf. Accessed May 2009

6) MarketVIEW: H1N1 vaccine – US demand (CAT No: VAMV006), published by **VacZine Analytics 2009.**

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