Influenza Vaccine Research & Development

Last Update: October 2006

IMPROVEMENTS	RATIONALE	APPROACHES
Increased efficacy of seasonal vaccines in immunocompromised patients, elderly, very young and high risk groups	Boosting immune response may be required for certain populations in order to provide increased efficacy and longer duration of protection - even for a strain-matched vaccine.	1) Adjuvantation of injected inactivated vaccines to boost immune response 2) Intra-nasal live virus vaccines
Increased efficacy of pandemic vaccines in all age groups	Everyone will be naïve to a pandemic strain and have no immunity to it. Trials have indicated that inactivated vaccines alone do not produce an acceptable immune response unless multiple doses and increased antigen doses and/or adjuvants are employed.	1) Adjuvantation of injected inactivated vaccines to broaden immune response 2) Intra-nasal live virus vaccines 3) DNA vaccines
Increased protection against Strain Drift in seasonal vaccines	Every few years a drifted strain arrives too late to be included in the seasonal vaccine (e.g. Fujian), reducing vaccine efficacy due to partial strain mismatch. Increased protection against Strain Drift would reduce necessity of annual update for small drifts.	1) Adjuvantation of injected inactivated vaccines to broaden immune response 2) Intra-nasal live virus vaccines 3) DNA vaccines
Increased protection against Strain Drift in pandemic vaccines	Pre-pandemic vaccines may be stockpiled to cover the early stages of a pandemic, before supplies of an exact matching pandemic vaccine become available. It is possible that the pandemic strain may have drifted from the strain used in the pre-pandemic vaccine.	1) Adjuvantation of injected inactivated vaccines to broaden immune response 2) Intra-nasal live virus vaccines 3) DNA vaccines
Increased protection against Strain Shift in seasonal vaccines (the "Universal Vaccine")	Vaccines which provide protection against Strain Shift may avoid the need for multi-strain vaccines and reduce the need for annual re-vaccination, if it provides long-term protection.	1) M2 conserved antigen – DNA 2) M2 conserved antigen – protein 3) M2 conserved antigen - VLP 4) Multiple epitope - peptide based 5) Conserved –oligonucleotide
Increased protection against Strain Shift in pandemic vaccines (the "Universal Vaccine")	Vaccines which provide protection against Strain Shift are particularly relevant, because a pandemic strain is by definition a strain shift from the seasonal strains; the seasonal vaccine could also confer protection against pandemic strains - i.e. would also be the pandemic vaccine.	1) M2 conserved antigen - DNA 2) M2 conserved antigen - protein 3) M2 conserved antigen - VLP 4) Multiple epitope - peptide based 5) Conserved –oligonucleotide

Increased acceptability of influenza vaccines	Market research into the reasons for healthy individuals declining influenza vaccination consistently cites dislike of needles as one of the principal reasons, particularly among children and young adults.	1) Intranasal vaccines 2) Transdermal patch 3) Intradermal injection 4) Epidermal powder injection
Increased accessibility to influenza vaccines	Needle administration of flu vaccine occurs once a year, so requires access to a healthcare professional - a time and cost constraint and waste management. The ability of some patients/parents to self administer flu vaccines could overcome this barrier.	1) Intranasal vaccines 2) Transdermal patch 3) Intradermal injection 4) Epidermal powder injection
Development of alternatives to egg based manufacture of antigens	Egg supply is at risk during avian flu outbreaks and may not be suitable to grow avian strains such as H5N1 (although Reverse Genetics to generate non-pathogenic seed virus can overcome this problem) and cannot be scaled up quickly to respond to increased demand. Also, the presence of microbial contaminants in eggs can lead to quality problems and supply interruptions, particularly with the phasing out of thimerosol from the production process. Egg waste disposal can be a problem.	1) Mammalian cell culture 2) Insect cell culture 3) DNA & other processes
Development of Mammalian Cell Culture	These processes have been developed to produce split or subunit antigens similar in nature and performance to those produced in egg. However, the production processes are better controlled, more easily scalable to respond to increased demand and can be used if necessary to grow pandemic strains in wild virus form, due to the high levels of biosafety employed.	1) MDCK Adherent 2) Vero 3) MDCK Suspension 4) Per.C6
Development of Insect Cell Culture	Insect cell culture system has been developed to produce recombinant hemagluttinin (HA), rather than the viral components produced in split or subunit processes, hence the vaccine is different from those currently marketed. The above cell culture process advantages v egg should also apply.	Baculovirus