

Update on vaccine efficacy, safety and regulatory issues

Timelines for availability of data to support licensure, and licensing processes

Extraordinary meeting of SAGE

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**World Health
Organization**

Regulatory preparedness

- regulatory authorities are generally well prepared and have responded vigorously to the need to facilitate rapid development of H1N1v vaccines, whilst retaining a proportionate degree of independent oversight of quality, safety and efficacy of candidate products
- through WHO there is, and continues to be, real-time international information exchange and consensus-building between authorities
- communicating the scientific basis for regulatory decision-making is key to this effort



Quality related issues

- candidate H1N1v vaccines will be expected to comply with quality specifications for seasonal influenza vaccines
- reagents to calibrate the majority of candidate vaccines using conventional potency tests are likely to be available (just) in time prior to initiation of clinical trials
- in some cases candidate vaccines will be available ahead of the reagents; authorities are being flexible and validated alternative potency tests are being considered to enable clinical trials to proceed
- H1N1v vaccines will be presented in multi-dose vials; preservatives will be required by regulators
- Regulators will expect to see expiry dates on vial labels



Efficacy related issues

- all authorities expect clinical trials be done by manufacturers to confirm that the selected dose and schedule is likely to be immunogenic; criteria for assessment of immunogenicity as per WHO guidance ("Regulatory preparedness document")
- if a strain change is necessary (better yielding strain for example), authorities will not expect additional clinical trials to be done, unless the HA or NA antigens have to be manipulated to obtain improved yields
- not all questions will be answered by the manufacturer's clinical trials and additional studies by public health authorities will be necessary to answers to questions such as interchangeability of vaccines; effect of concomitant administration of flu and non-flu vaccines are needed for the decision-making process



Safety related issues

- there is relatively little experience with population-wide use of adjuvanted influenza vaccines; special attention will therefore be needed to monitor the safety of such vaccines as they are deployed on a large-scale
- international collaboration on influenza-vaccine specific safety surveillance and risk communication post-large scale use of H1N1v vaccines will be essential and is being developed at present
- guidance on stopping rules in case of adverse events following immunization needs to be developed



Regulatory data requirements

- in general, regulatory data requirements to inform benefit-risk evaluations inversely vary with the severity and incidence of natural infection; for a natural infection of "moderate severity" several key authorities will require a full data package, but provide interim opinions as data become available, in case of urgent public health need for the vaccine
- as countries may experience different disease burdens for H1N1v natural infections, regulatory authorities may vary in their benefit-risk decisions concerning the use of the vaccine; data sharing between countries, especially any early introducer countries, will be very beneficial; mechanisms to rapidly and efficiently share such data need further development
- WHO prequalification will be available for H1N1v vaccines and will address the needs of countries receiving vaccine via UN supply






Expected timelines for regulatory submissions and opinions

- authorities will implement "rolling reviews" of submissions - i.e review of the Q data package as it is received and ahead of receipt of the clinical data package
- the timelines for regulatory authorities to provide opinions will vary with the registration status of similar vaccines from the same company; opinions will be faster (days) for previously registered products with similar product profiles compared to companies with no previously registered similar products (weeks or months)
- if vaccines are needed in Sep/Oct 09, most public health authorities will need to make decisions on their use before having human clinical trial data available



Estimated data availability for one regulatory authority

ESTIMATED DATA AVAILABILITY FOR THREE MOCK-UP MAS *via* VARIATION

Jul 09	Aug 09	Sep 09	Oct 09	Nov 09	Dec 09	Jan 10	Feb 10
		Quality data					
		First/ interim adult clinical data					
		First/ interim paediatric data					
 Range of quality data submission times  First/ interim adult clinical data  First/ interim paediatric data							
<p>The timelines given covers the range of submission dates proposed by the companies concerned and are still estimates as we need to further discuss with these companies the precise submission dates and data packages All vaccines are monovalent A(H1N1)v vaccines</p>							

