

GACVS draft report (version, 23 June 2009) intended for publication in WER

Preparing for novel influenza vaccine safety

The session on pandemic influenza preparedness focused on a review of Guillain-Barré (GBS) and swine influenza vaccines, and adjuvants for influenza vaccines. The swine influenza vaccines used in the U.S. in 1976 were associated with a small but significant risk of GBS in the 8 weeks following immunization. The attributable risk among vaccinees was approximately 1 case per 100,000 persons vaccinated. The underlying reason for the association is unknown. Studies of other influenza vaccines since 1976 have shown no association with GBS or in some studies, a very small risk (e.g., attributable risk of less than 1 per million vaccinations). Because the new H1N1 influenza virus is in part derived from a swine lineage, GACVS discussed the importance of preparing for active surveillance of GBS cases in individuals vaccinated with the novel H1N1 vaccines. This should include developing common protocols, case definitions, and assessments to learn more about GBS. It will be important to obtain baseline rates in unvaccinated populations, particularly in developing countries, and to be prepared to assess whether there is an association between GBS and vaccination with novel H1N1 vaccines, as well as between GBS and influenza illness caused by the novel H1N1 virus. There should be collaboration and communication among the health authorities in countries capable of active surveillance for GBS to develop common approaches and share results with WHO so that other countries using similar vaccines can benefit from the information. It may also be possible to expand acute flaccid paralysis surveillance programs to all ages in an effort to capture GBS cases in some low and middle income countries. However, GACVS emphasized that such assessment should be limited to settings where the assessment would not adversely affect polio surveillance programmes. There was also discussion on additional laboratory assessments that might be done in clinical trials of novel H1N1 vaccines to potentially elucidate mechanisms of aberrant immune responses that may predispose to GBS.

With regard to adjuvants for influenza vaccines, there was discussion regarding: limited safety data in certain populations, e.g. young children (< 3yr) and pregnant women; limited information of preservative/oil-in-water adjuvant interactions, and post-marketing surveillance requirements for the vaccines. It was noted that there may be significant challenges in addressing certain potential concerns, such as auto-immune adverse events, if there is a long latency period between vaccination and such potential event. Another issue raised is whether there could be an increased risk of febrile convulsions in young children, given the increased reactogenicity of adjuvanted vaccines and potential need for monitoring. At the moment there are no safety or immunogenicity data on interchangeability of adjuvanted/non adjuvanted influenza vaccine use for either 1st or 2nd dose.

It is anticipated that the range of H1N1 vaccines will be heterogeneous in formulation, antigen presentation and substrate used for manufacturing, therefore these vaccines may significantly differ in their safety profiles. In view of likely widespread use in all age groups and required two dose schedule, there may also be differences to current well established safety profiles of licensed seasonal influenza vaccines. The choice of post-marketing surveillance strategy to be applied with H1N1 vaccines will depend on available time to institute modified AEFI monitoring systems and capacity of the

countries to do active surveillance for selected serious adverse events in addition to GBS. In addition, baseline background rates for other conditions that are anticipated to occur coincidentally in the populations targeted for vaccination should also be obtained.

In view of H1N1 vaccine utilization, countries should carefully assess capacity of current systems to monitor vaccine effectiveness and safety, and enhance rapid detection of potential signals. Robust and efficient mechanisms for AEFI case notification that link with global networks for analysis and risk communication are of paramount importance. Strengthened monitoring for seasonal influenza offers an opportunity to test the functionality of the systems. Reporting timeliness, and rapid cycle monitoring and analysis are of utmost importance. With regard to utilization of H1N1 in subpopulations, auxiliary monitoring systems may be required, such as perinatal registries capturing pregnancy outcomes of immunized pregnant women, or monitoring of HIV positive vaccinees.