Summary of oral evidence: Professor Robert Belshe

10 April 2006

Professor Robert Belshe, Director of the Center for Vaccine Development St Louis University, gave evidence to the working group by teleconference. The views expressed were the personal views of Professor Belshe.

Members of the working group present were: Sir John Shekel (chair), Professor Barry Furr, Dr John McCauley, Professor Andrew McMichael, Professor Karl Nicholson and Professor Robin Weiss.

Key points

Influenza vaccines and clinical trials

Professor Belshe described his ongoing clinical trials using standard egg-produced vaccines where past experience has shown that unexposed adults/children need two doses of vaccine to produce a suitable antibody response. The development of novel vaccines is affected by regulatory processes and novel vaccines have a high regulatory burden. Changing the strain of antigen in an existing vaccine is not classified as a novel vaccine and has relatively little regulatory burden, but adding an adjuvant to an existing vaccine is considered novel and requires efficacy data for licensing.

Professor Belshe told the group that there has been a boost recently in adjuvant research. He is involved in an ongoing dose-finding clinical trial which he hopes will help identify if the use of adjuvant is dose-sparing. The trial has 9 arms using no adjuvant, MF59 (Novartis Vaccines), alum and a combination of both adjuvants. The study is being conducted in young adults aged 18-64 with at least 30 patients in each group. He is also working on trials examining vaccine administration routes and described an ongoing study in St Louis with a trivalent vaccine. The study is comparing intradermal (ID) administration at doses of 0.1, 0.2 and 0.3ml vaccine volume (3,6,9 micrograms) compared with intramuscular (IM) administration at doses of 3, 6, 9 or 15μg with all appropriate controls. The study aims to identify a more precise dose response comparing IM and ID in young people.

Professor Belshe described ongoing work with live attenuated vaccines for H5 and H9 in humans in collaboration with John Hopkins University. Live attenuated viruses with modified haemagglutinin are easy to produce and are dose sparing as one egg can produce up to 1000 to 10,000 doses rather than the maximum of one dose from one egg in inactivated vaccines.

Vaccines produced by reverse genetics are being considered by the FDA in a formal application. These vaccines provide an opportunity not to require clinical isolate and their manufacture is likely to be faster that egg production.

Professor Belshe was asked about the use of avian vaccines in the US. These are not generally used in the US which instead enforces a strict and aggressive culling policy including strict boarder controls with Mexico.

Antiviral drugs and therapy

The US is developing a stockpile of Tamiflu but is behind Europe in ordering and receiving the drug. There is still ongoing debate on how to select who receives it and how it is distributed. Professor Belshe told how the major use will most likely be for treatment of symptoms and not prophylaxis. Prophylaxis is not being

considered practical by Professor Belshe in the US as the population of 300 million people makes this impossible with a limited supply of drug.

Professor Belshe was asked about the potential use of monoclonal antibodies or immunoglobulin treatment. He told the group that there is interest but it is not considered a timely response due to the time needed to obtain a licence for therapy. They are also expensive options and Professor Belshe told the group that the use of monoclonal antibodies in children for RSV infection costs $3000 per month, although it may be an option in high risk patients.

Diagnostics

Professor Belshe believes that diagnostics are of value to identify the strain of influenza circulating in the community but not for individual patients. Currently, Americans returning from China may be tested for H5 if they develop a flu-like illness, but this is a cell culture test taking 3 to 4 days. Five rapid diagnostic tests for influenza have been approved for use the US but they are of little use in hospitals as a bedside diagnostic as their sensitivity is only 60-70%.

Intensive care provision and infection control policy

Professor Belshe was asked about the impact of an epidemic on hospitals and ITU in the US. He told the group about local planning in St Louis to identify the need for equipment such as ventilators. Equipment is currently seen as the limiting factor in preparedness but the hospital has not bought new machines to date. No policy exists for treating ITU staff prophylatically with Tamiflu and policies on the use of masks are in place but of limited value.

Emergency panning

The group asked Professor Belshe about plans to stabilise the community in a pandemic. The Government will not close national boarders in the event of a pandemic. Recently, one day regional state meetings have been held which have brought together fire and police departments, teachers, healthcare workers etc to discuss pandemic preparedness. The meeting discussed basic epidemiology, what to do in a pandemic and general panning.

Professor Belshe believes that the US Government have made a slow response to the threat of an influenza pandemic but are now investing large amounts of money into large research programmes. He believes that the Government need to be seen to be acting decisively in the wake of the hurricane Katrina disaster, although he doesn't consider the Government's response well planned.

Vaccine manufacturers are building more production facilities but it will be several years before capacity is expanded sufficiently. However, increasing vaccine manufacturing capacity is important in the long term. The US is moving to vaccinate all children under the age of 5 in the near future for seasonal influenza, which will then be extended to the age of 9 and then 18 which will drive the need to invest in manufacturing capacity.