Emerging Drug List
VACCINES FOR AVIAN INFLUENZA

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Generic (Trade Name): Influenza A/H5N1 prototype vaccine

Manufacturer: Vaccines are being developed by Chiron Corporation (Emeryville CA), CSL Limited (Commonwealth Serum Laboratories, Australia), GlaxoSmithKline (UK), sanofi pasteur (Swiftwater PA), and Sinovac Biotech Ltd. (China). ID Biomedical, now part of GlaxoSmithKline Biologicals (Belgium), was awarded a contract with the Canadian government to produce a prototype H5N1 flu vaccine for clinical testing in Canada. Delivery of the prototype is expected in the late summer or early fall of 2006.1

Indication: Prototype vaccines are being developed against the H5N1 influenza virus, which is thought to pose the greatest threat for a potential pandemic.

Current Regulatory Status: No vaccines have been approved to protect humans against the H5N1 virus. The manufacturers have identified potential prototype vaccines, and expect to seek regulatory approval for them before the end of 2006.2,3

Description: The World Health Organization’s (WHO) Global Influenza Surveillance Network characterized several influenza viruses that were isolated from humans infected with the H5N1 virus during the 2004 to 2005 outbreak in Asia.4 These viruses have been used to develop recombinant H5N1 influenza strains thought to resemble a potential pandemic strain. This work has involved subjecting the viruses to reverse genetics, a technique used to lower their pathogenicity.5

Three recombinant prototype H5N1 virus strains have been made available for use in vaccine development: A/Vietnam/1194/04, A/Vietnam/1203/04, and A/Hongkong/213/03.4 The prototype vaccines based on the A/Vietnam/1203/04 strain are being produced by growing the inactivated H5N1 strains in live chicken eggs. This is the traditional method used for vaccine production. To hasten the production cycle, the manufacturers are developing methods to produce the vaccines using cell cultures instead of chicken eggs.6

Current Treatment: Interim guidelines for the clinical management of human cases of avian flu have been issued by WHO.7 The guidelines advocate treatment with antiviral medications including the neuraminidase inhibitors, oseltamivir (Tamiflu) and zanamivir (Relenza), as early in the clinical course as possible. WHO is also recommending inoculating with seasonal influenza vaccine those at increased risk of exposure to the H5N1 avian influenza virus circulating in Asia (e.g., poultry farm workers and health care workers).7 Although seasonal influenza A vaccines do not protect against the H5N1 avian influenza virus, vaccination may reduce the chance of simultaneous infection with human H1 and H3 influenza A subtypes. Co-infection with the human and avian influenza viruses may result in genetic reassortment, and is seen as the greatest risk for the emergence of a new influenza virus with pandemic potential.8

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Cost: In the event of an avian influenza pandemic, it is expected that vaccines will be provided free to those at high risk for infection. According to the Canadian Pandemic Influenza Plan, health care workers, paramedics, ambulance attendants, and public health workers would be vaccinated first, followed by essential service workers, then persons at high risk of severe or fatal outcomes after influenza infection. A decision to vaccinate healthy adults and healthy children would depend on having an adequate supply of vaccine.

Evidence: Chiron expects to begin clinical testing of its vaccine in early 2006 in the US and Europe. Chiron will also evaluate its vaccine adjuvant, MF59. Previous studies have found that adding the MF59 adjuvant to an H5N3 vaccine (against the non-pathogenic H5N3 avian influenza virus) induced productive antibody titres against the H5N1 strain, even at the lowest dose tested.

CSL Ltd. began a clinical trial to evaluate their H5N1 prototype vaccine in October 2005. The study is expected to enrol 400 healthy adults who are 18 to 45 years old.

GlaxoSmithKline has announced that it plans to release initial clinical study results for its investigational H5N1 prototype vaccine in 2007. The manufacturer is also planning to test its alum adjuvant with the H5N1 vaccine, which could allow for treatment at lower doses. The low dose formulation would result in a greater supply, if needed.

Sanofi pasteur began a phase I clinical trial of a prototype avian influenza vaccine in April 2005. The trial, which is intended to investigate the safety of the vaccine and its ability to generate an immune response, randomly assigned healthy adult volunteers to receive two intramuscular injections of saline placebo (N=50), or 7.5 μg, 15 μg, 45 μg, or 90 μg of the influenza A H5N1 virus vaccine (N=100/dose group). Preliminary data from 113 of 452 participants showed that two 90 μg doses of the H5N1 candidate vaccine, given four weeks apart, generated the highest immune response. A follow-up phase II clinical trial is underway to determine if a third dose, administered five months after the second dose, provides more immunity than two doses. Sanofi pasteur reported preliminary trial results in December 2005. These results suggest that the use of an adjuvant (alum) to boost the immune response may help to stretch the supply of vaccine for H5N1 avian influenza by a modest amount. The 300-patient trial showed that two 30 μg doses of the vaccine, given with the adjuvant, produced an immune response comparable to that achieved with seasonal flu vaccines. Sanofi pasteur has also begun recruiting healthy elderly adults to participate in a phase I-II dose range finding study of the influenza A H5N1 vaccine. Approximately 240 adults aged 65 and older will be enrolled. The trial began in October 2005, and is expected to last approximately 15 months.
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Beijing-based Sinovac Biotech Ltd. received approval from China’s State Food and Drug Administration (SFDA) on November 22, 2005, to begin human clinical trials of a pandemic H5N1 influenza prototype vaccine. The SFDA fast-tracked Sinovac’s application. Researchers in the clinical trials will examine safety and immunogenicity in humans, and establish ideal dosages and immunization schedules.

Adverse Effects: Preliminary data from sanofi pasteur’s phase I trial suggest that the H5N1 prototype vaccine is safe and can be tested in other populations, including healthy elderly adults and children.

Commentary: As of November 25, 2005, there have been 132 confirmed cases of human H5N1 avian influenza virus infections in Asia, resulting in 68 deaths. Most cases of H5N1 infection have occurred among poultry farm or market workers. The risk for human-to-human transmission of the H5N1 virus has been limited. If a human-to-human strain of H5N1 influenza virus emerges, the experience gained from the production and clinical testing of prototype vaccines should permit fast development and mass production of an H5N1 pandemic vaccine. It remains to be seen if the virus that emerges will look like the prototype viruses, and if the vaccines produced will be effective. Because few countries have pandemic preparation plans, the implementation of an appropriate vaccine delivery strategy may prove to be challenging.

References:


This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

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