

# Regulation of H1N1 Pandemic Influenza Vaccine

The H1N1 pandemic influenza vaccine virtual product information leaflet will be available on the Health Canada Website at the following links:

English: <http://web.hcsc.gc.ca/dhpmpps/prodpharma/legislation/interimorders-arretesurgence/index-eng.php>

French: <http://web.hc-sc.gc.ca/dhp-mpps/prodpharma/legislation/interimorders-arretesurgence/index-fra.php>

The Biologics and Genetics Therapies Directorate (BGTD) Branch of Health Canada is responsible for the regulation of the H1N1 Pandemic Influenza Vaccine.

## Challenges of Developing Pandemic Vaccine

- Vaccine cannot be developed until the pandemic strain is isolated.
- Vaccine is usually needed immediately upon manufacture.
- There can be either no time, or only a limited time for traditional clinical trials for safety (which typically last up to seven years).
- There is no way to verify that the vaccine is actually effective in humans. It may be possible to determine that the vaccine produces antibody (immune response), the determination that the immune response is protective against infection can only be determined with lengthy clinical trials or actual use of the vaccine.

## Regulatory Process in Canada

Canada has a contract with GlaxoSmithKline Canada (GSK) for pandemic vaccine. Through the contract between Canada and GSK an ongoing process during the pre-pandemic period has been the development and regulatory evaluation of a “mock” (prototype) adjuvanted H5N1 vaccine. The use of adjuvant vaccine is consistent with the World Health Organization’s (WHO) recommendation to use a dose-sparing approach to the development of pandemic vaccine. The development and regulatory evaluation of a “mock” vaccine has allowed Canada to validate the process of developing an actual pandemic vaccine because of the ability to review non-clinical and clinical studies with the “mock” vaccine and prepare for the regulatory evaluation of an actual pandemic vaccine.

Production of the pandemic vaccine against the H1N1 strain of influenza virus was initiated by GSK in July 2009 following the declaration of a pandemic by the WHO. Health Canada has communicated to GSK that the following information is needed to issue the authorization for sale:

- Safety and other data from the review of the H5N1 mock vaccine (completed)
- Updated quality assurance data to support the strain change from H5 to H1 (submitted October 12<sup>th</sup>, 2009 for review).
- Preclinical challenge study in an animal model in lieu of human studies of effectiveness (preliminary data will be accepted in October, 2009 or post-market).
- Immunogenicity and safety data from small clinical study of approximately 120 patients (submitted for review October 12, 2009).

True effectiveness data in humans will only be obtained with actual vaccine use.

### **Quality Evaluation Process in Canada**

A quality evaluation process for the development of pandemic H1N1 vaccine is needed in Canada to ensure that the vaccine has been manufactured according to standards and does not contain; live influenza virus, bacterial or viral or other contaminants, or any chemicals that could harm the vaccine recipient. Similarly the regulatory and evaluation process must ensure that the vaccine is of correct potency, purity and composition.

### **The Canadian Pandemic Vaccine Regulatory Pathway**

The Canadian pandemic vaccine regulatory pathway is the process that authorizes a pandemic vaccine for use in the absence of effectiveness data. This pathway is specifically designed to provide an appropriate degree of regulatory oversight to ensure the safety, efficacy and quality of the pandemic vaccine in a timely manner that permits the earliest possible access to the pandemic vaccine if needed. Options for authorization of the pandemic vaccine in this unique situation are available from the *Food and Drugs Act*.

#### **1. Interim Order**

The *Food and Drugs Act* permits the federal Minister of Health to make an Interim Order if the Minister believes that immediate action is required to deal with a significant risk, direct or indirect, to health, safety or the environment. The Interim Order is written to give authority for the Minister to take an action which is not possible under the regulations. Interim Orders become effective once signed by the Minister and remain in effect for 14 days unless approved by the Governor in Council. Once approved by the Governor in Council the Orders are valid for one year.

An Interim Order was needed and was issued to address the specific regulatory challenges associated with the pandemic H1N1 influenza vaccine.

#### **2. International Status**

Health Canada is working in close collaboration with US FDA, EMEA and TGA on licensure and sharing of data. Both US and EMEA have more flexible legislation which allows them to authorize products with limited clinical data.

The United States, Europe, and Australia have already licensed Pandemic H1N1 vaccine.