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United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

Center for Veterinary Biologics

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CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 09-10

TO: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics
Veterinary Services Management Team
Area Veterinarians in Charge
State Veterinarians

FROM: Richard E. Hill, Jr. /s/ Byron E. Rippke, for Director
Center for Veterinary Biologics

SUBJECT: Availability of H1N1 Influenza Virus

I. PURPOSE

The purpose of this notice is to inform interested parties that the Center for Veterinary Biologics (CVB) will provide licensed biologics manufacturers with pre-approved Master Seed Virus (MSV) for use in development of a conditionally licensed, multi-dose, monovalent novel H1N1 swine influenza virus (SIV) product for the protection of swine in the United States.

The availability of the pre-approved H1N1 MSV does not preclude development of novel H1N1 MSVs by individual firms, but is meant only to expedite licensure and production of vaccines to protect swine against the novel H1N1 virus. By providing all interested manufacturers with the same approved H1N1 MSV, APHIS will eliminate the need for each manufacturer to focus resources on developing its own master seed that would then require CVB confirmatory testing. Instead, while the "global" MSV is undergoing tests at CVB, each interested manufacturer can begin working immediately on the next steps involved in novel vaccine production. In the event that the virus appears to be an emerging disease in swine, the availability of the pre-approved MSV will facilitate a more rapid response should vaccine production be warranted. Because the novel H1N1 virus has, to date, not been detected in the U.S. domestic swine population, the incorporation of the virus into autogenous or existing multivalent products is not authorized.

The MSV will be available as soon as it is fully characterized and tested. The MSV should be ready for distribution in mid-July of 2009.

II. BACKGROUND

In March of 2009, Mexico first noticed an increase in influenza-like illness in humans. The number of human cases steadily rose during April. On April 24, 2009, the World Health Organization issued a statement indicating that the United States and Mexico had confirmed several cases of human influenza virus H1N1. The number of confirmed and suspect cases rapidly spread through the United States, Canada, and Europe. On May 2, 2009, the Canadian Food Inspection Agency reported that the virus had been confirmed in a swine herd located in Alberta, Canada. The virus strain causing the current outbreaks is a novel H1N1 virus that has not been observed previously in either humans or animals. The H1N1 virus genome contains eight segments which can readily reassort if more than one type of influenza virus infects a single cell. Through this reassortment capability, the current human H1N1 virus contains human, swine, and avian gene segments.

Historically, cross-protection against new SIV strains has not always been observed in vaccinated pigs. In the fall of 1993, the CVB licensed the first SIV vaccine. The vaccine contained the classical SIV H1N1. A new strain of SIV emerged in the late 1990s in the swine population, and was identified as SIV H3N2. Several vaccines were licensed to protect against this strain. In 2000, a variant of the classical SIV H1N1 was observed in swine herds in the United States. Studies conducted by the USDA Agriculture Research Service (ARS) found the products effective in protecting against classical H1N1 disease did not provide sufficient protection against the variant SIV H1N1. Preliminary results from work conducted at the ARS's National Animal Disease Center (NADC) in response to the 2009 H1N1 situation seem to indicate little to no serologic cross-reactivity between classical SIV H1N1 and the novel H1N1 identified this year. Therefore, current SIV vaccine products may not provide adequate protection against the novel H1N1 strain identified in 2009. APHIS and ARS continue to run additional tests to determine if any vaccines currently available protect against the 2009 H1N1 strain.

The new H1N1 MSV candidate is a pig-passaged virus derived from a sample acquired from the Centers for Disease Control and Prevention (CDC) through collaboration between the ARS's NADC and APHIS's CVB.

III. ACTION

Biologics firms that wish to obtain H1N1 MSV samples from CVB for research purposes should do the following:

A. Complete and Submit VS Form 16-3 – Complete an application form, VS Form 16-3, "Application for Permit to Import Controlled Material or Import or Transport Organisms or Vectors", and submit it to the National Center for Import

and Export (NCIE), along with the current user fee. The form can be obtained by any one of the following methods:

1. Access NCIE's website at: *www.aphis.usda.gov/import_export* and select "Find a VS Form," then "Application for Permit to: Import or Transport Controlled Material or Organism or Vectors."
2. Call NCIE's main phone line at (301) 734-3277 and request an application form and instructions.

B. Obtain Approval of the State Veterinarian – The applicant must obtain approval from the State Veterinarian to transport SIV H1N1 into the State where the applicant's facilities are located.

C. Ensure Adequate Facilities and Procedures for Containment – NCIE requires firms to demonstrate that they have adequate facilities and procedures to ensure containment of the novel H1N1 MSV before issuing an organism and vectors permit for interstate transport.

Additionally, due to the human health concerns, safety measures must be described for employees working with the MSV. The CDC recommends growth of the virus be performed in a Biosafety Level (BSL) 2 laboratory, with BSL-3 practice, including implementation of the recommendations on the CDC website at *www.cdc.gov/h1n1flu/guidelines_labworkers.htm.* NCIE will contact CVB Inspection and Compliance for information regarding whether facilities and practices at the firm are adequate to meet these specifications.

D. Procedures for requesting the new MSV from the CVB are described in Veterinary Services Memorandum 800.97 Section VI. Specific information regarding production methods are provided by the CVB in all reagent shipments. The CVB will also provide a material transfer agreement (MTA) to parties interested in obtaining the pre-approved H1N1 MSV. The CVB will require a signed MTA to be submitted prior to shipment of the pre-approved MSV. The MTA will include details regarding how the MSV may be used.

Further authorization from APHIS will be required in order to do animal studies.