USDA-APHIS SURVEILLANCE PROGRAM FOR INFLUENZA IN SWINE

Sharing of data and virus isolates through the USDA Swine Influenza Virus Surveillance System is encouraged so that the industry, practitioners, animal health officials, researchers and manufacturers will be equipped with information and materials that are as contemporary as possible. The surveillance program, designed by APHIS, ARS, industry stakeholders and public health officials, began in 2010. For detailed information visit: *www.aphis.usda.gov/animal-health/swine-health-surveillance.*

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A Review of Optimal Use of Diagnostics and Vaccines for Control of Influenza A Virus Infection in Swine

INFLUENZA A virus in swine (IAV-S) is an economically important pathogen for the United States pork industry. In addition, incidents of zoonotic influenza transmission raise concerns. The vaccines currently available are often incapable of providing adequate protection against the diverse circulating strains. Diagnostic tools can supply critical data about local IAV-S isolates – information that will help determine the best choice of vaccine, even when all options fall short of ideal. Importantly, the USDA national surveillance program can identify new strains for selection to update existing vaccine platforms as well as develop new platforms to further improve vaccine choices.

IMMUNITY TO INFLUENZA

VIRUS NEUTRALIZATION	Antibodies that bind to specific regions of hemagglutinin (HA) protein can block viral attachment and entry, which is the most direct way to prevent infection. Viruses carrying HA gene mutations that disrupt antibody-HA binding can escape the neutralizing antibodies.
ANTIGENIC DRIFT	The accumulation of antibody-evading mutations in HA and neuraminidase (NA).
CROSS-PROTECTIVE IMMUNITY	Broader immunity can be provided by T cells that recognize portions of the virus's internal proteins. Cytotoxic T lymphocytes (CTL) recognize and kill infected cells.
MODE OF VIRUS EXPOSURE	Infection induces a balanced response of antibodies and T cells, including local antibodies in the respiratory tract. Vaccines consisting of inactivated/killed virus induce primarily circulating IgG antibodies to virus surface proteins, which are likely to neutralize the homologous virus. Replicon particle vaccines deliver viral HA genes for expression in the immunized pig, which induces circulating antibodies.
MATERNAL IMMUNITY	Passive antibodies can neutralize antigenically similar strains, protecting piglets until the maternal antibody titers wane. Even when maternal antibodies reduce disease severity in piglets, they sometimes fail to prevent viral shedding and transmission. Lingering maternal antibodies can interfere with young pigs' active antibody responses if they receive an IAV-S vaccine.

IAV-S VACCINES AVAILABLE IN THE UNITED STATES

CONVENTIONAL LICENSED IAV-S VACCINES: contain inactivated/killed virus.

- Multiple strains are formulated with an adjuvant, and sometimes also bacterial antigens.
  - Early multivalent IAV-S vaccines contained two strains (H1N1 and H3N2).
  - Updated products contain 4-5 strains of IAV-S. Strains were added to protect against new antigenically distinct variants within subtypes H1 and H3.
- Stimulate protective immunity against antigenically identical or very similar strains. In the ideal situation, the vaccine induces antibodies that can neutralize the virus.
- IAV-S strains are diverse and continually evolving, so it is difficult for manufacturers to maintain formulations that match all contemporary strains encountered in the field.

ALPHAVIRUS-LIKE REPLICON PARTICLES (RP): a viral vector vaccine technology approved by USDA as a vaccine for IAV-S.

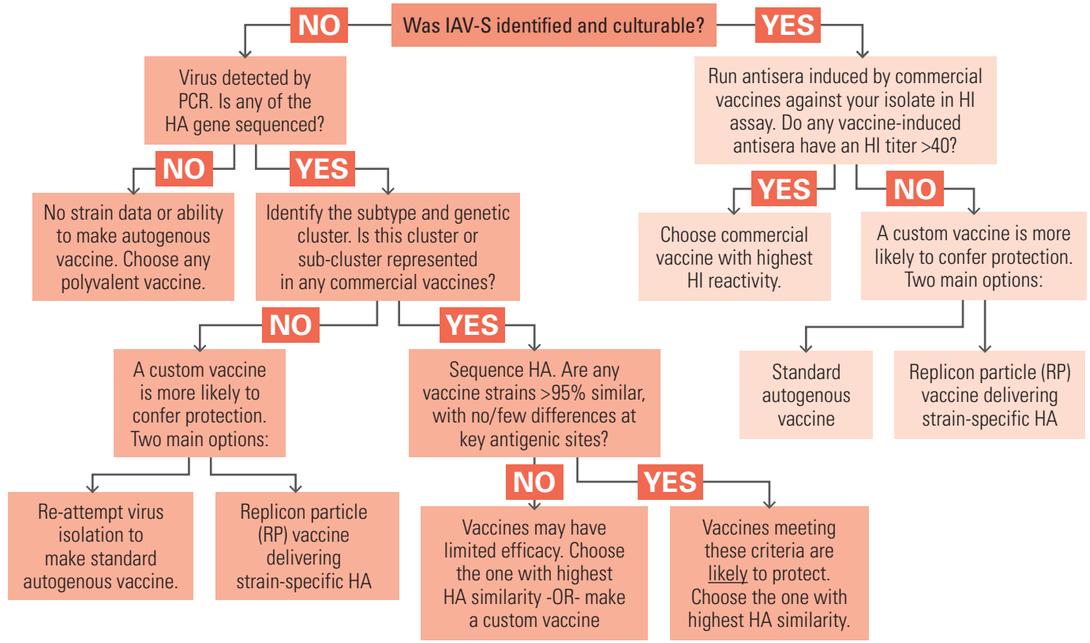
- The RP vaccine initially licensed by USDA contains RNA encoding HA of a cluster IV H3N2 virus, which is expressed in vivo after intramuscular injection.
- Similar RP-HA vaccines induced systemic antibodies, a cell-mediated immune response, and protection against homologous challenge infection.

AUTOGENOUS/CUSTOM IAV-S VACCINES

- Autogenous vaccines are an option if the virus has been isolated from the herd or from another herd that is linked epidemiologically. The virus must grow efficiently in cell culture.
  - Advantage: Provides antigens identical to strains that were isolated on the same premises in a recent time frame.
  - Disadvantages: Lag time for vaccine to be produced, lack of efficacy and potency testing.

MAJOR IAV-S VACCINE MANUFACTURERS provide some veterinary diagnostic laboratories with swine antisera raised against each proprietary IAV-S strain in their polyvalent vaccines. This enables the laboratories to compare the serum antibodies induced by those vaccines for cross-reactivity to the field isolate(s), and then report the closest match. The serological approach could also use swine antisera induced by the complete polyvalent vaccines, given in accordance with the product labels. This would be more efficient because it only requires one test for each of the available vaccines. Hemagglutination inhibition tests showing significant reactivity against a field isolate (such as a titer >40) suggest that the commercial vaccine will be effective.

FIGURE 1. DECISION TREE FOR SELECTION OF IAV-S VACCINE STRATEGY TO CONTROL A SPECIFIC HERD ISOLATE.



OPTIMIZING CHOICE OF IAV-S VACCINE TO ADDRESS SPECIFIC FARM OUTBREAKS

The best choice of IAV-S vaccine requires information about the local strain(s). HA and NA gene sequence from the isolates can be a helpful indicator. Nucleotide sequence data can be used to:

- Indicate the subtype, phylogenetic cluster, and evolution of the HA genes from herd isolates. The polyvalent commercial vaccines contain slightly different combinations of the co-circulating HA clusters (Table 3 of the full white paper*), so cluster classification is the first step to indicate which vaccine is better matched.
- Determine the percentage of amino acid sequence homology with strains in different vaccines. Manufacturers share HA sequences of each strain in their polyvalent IAV-S vaccine with qualified veterinary diagnostic laboratories. The labs analyze submitted field isolates for HA similarity with strains in the commercial vaccines.

'The white paper based on a literature review is available at www.cfsph.iastate.edu/Species/swine.php.

Evaluating cross-reactivity of field isolates and vaccine strains by serology is an excellent complementary test that may give a more definitive estimation of antigenic similiarity. This requires antisera against the commercial vaccine strains, which major manufacturers already make available to some diagnostic laboratories (see sidebar). Tests to identify the subtype and genetic cluster of an isolate can be performed simultaneously with HI assays to evaluate the efficacy of commercial vaccines against that isolate.

VACCINE ASSOCIATED ENHANCEMENT OF RESPIRATORY DISEASE (VAERD)

In experimental studies, piglets vaccinated with whole-inactivated, adjuvanted IAV-S and later challenged with an antigenically divergent strain developed more severe lesions and clinical disease than control groups that received no vaccine. It is not known if VAERD occurs in vaccinated swine under field conditions with commercial or autogenous vaccines. The higher the similarity between vaccine antigen and circulating influenza strains, the lower the predicted risk of VAERD.