American Association of Swine Veterinarians position statement on pandemic (H1N1) 2009 influenza

AASV issues recommendations on A/H1N1 2009 pandemic influenza virus

The American Association of Swine Veterinarians (AASV) Board of Directors has approved the adoption of a series of position statements regarding the A/H1N1 2009 pandemic influenza virus. The document was developed by the AASV H1N1 Influenza Working Group chaired by Dr Joe Connor.

While pork continues to be safe to eat, concerns have arisen regarding the potential cross-species transmission of the novel virus. Recognizing the necessity to protect both animal and human health, the AASV Executive Committee created the working group, which it charged with examining the influenza issue and developing recommendations based on the best available current knowledge and pertinent published literature.

In response, the working group developed a series of recommendations to address concerns in four broad topic areas: protection of swine workers, vaccination of swine herds, vaccine development, and movement of animals from herds infected with the novel virus. The specific recommendations are outlined below.

The emergence of the pandemic (H1N1) 2009 influenza virus has reminded us of the potential for cross-species transmission of influenza viruses. As veterinarians, we believe that protecting human health is of primary importance, and all reasonable measures should be taken to avoid any unnecessary risk to human health. The "One Health Initiative" of the American Veterinary Medical Association and the American Medical Association recognizes the impact that animals have on human health and vice versa.[1] An essential component of protecting human health is providing a safe, high quality, and affordable food supply.

Influenza recommendations for pork-production staff, veterinarians, and harvest-plant workers

To protect both human health and the food supply, the AASV strongly advises that all personnel working in the pork-production industry be vaccinated against seasonal influenza annually and against any novel human influenza A viruses as they emerge.[2-5] Vaccination enhances protection for personnel while minimizing the likelihood of viral transmission from personnel to pigs.

Therefore the AASV recommends that:

- **Swine owners continue to encourage, facilitate, and financially support employee vaccination against seasonal influenza viruses.**
- **All personnel associated with pork production and harvest in North America be given high priority for vaccination against any novel influenza virus that emerges in the human population.**
- **The Centers for Disease Control and Prevention, state departments of health, and local health departments work in close cooperation with, solicit input from, and collaborate in the decision-making process with USDA-APHIS, state animal health officials, and local veterinarians through the establishment of working groups and defined communication channels to facilitate the implementation of vaccination plans across North America.**
- **All personnel associated with pork production and harvest intensify basic hygiene and biosecurity practices.**

Influenza vaccination recommendations for swine

While humans have taken the approach of annual vaccine strain updates in attempts to minimize influenza illness and death, control of influenza in swine herds has been less flexible. Vaccination of swine with killed virus vaccines has been employed with varying degrees of success since the mid-1990s. As more strains of SIV emerged, biological companies have added contemporary strains to their existing, commercially licensed vaccines, resulting in bivalent and trivalent vaccines carefully balanced to induce immunity to all subtypes of SIV in the vaccine. Alternatively, autogenous killed influenza virus vaccines have gained in popularity to better match the antigenic and genetic differences of new SIV strains when compared to the commercial vaccine virus strains. A change in vaccine strain is generally recommended when issues such as antigenic correctness, timing, adjuvant, and co-infections have been properly addressed. More often, the decision to use an autogenous vaccine is driven by a need to more immediately respond with a specific and rapid solution to the problems unsolved by the use of commercial vaccines.

The AASV recommends:

- **Vaccination with currently approved vaccines for the control of swine influenza should continue to be used to control clinical signs of disease due to swine influenza virus as recommended on each product's label.**
- **Vaccination of swine against the pandemic (H1N1) 2009 influenza virus should be implemented if scientific evidence demonstrates that vaccination reduces virus shedding and the risk of transmission to pork-production personnel.**
- **Increased funding and research on novel delivery methods and vaccines to rapidly develop and introduce safe, effective vaccines against novel influenza viruses that not only minimize the risk of transmission between species but also overcome maternal immunity.**
- **Increased funding and research on the utilization of technologies, such as core matrix, that would enable the rapid updating of influenza vaccines to incorporate emerging strains, promote cross-protection against multiple influenza strains and facilitate the development of a differential vaccine.**

Development of a national influenza vaccine strain selection system for swine

To protect both human health and the food supply, the AASV recognizes that minimizing the risk of cross-species transmission of influenza A viruses is critically important. Vaccination has been a useful tool for control of clinical disease due to influenza in humans. However, there is conflicting data regarding the use of currently available killed influenza vaccines in swine to control shedding or transmission of influenza between pigs. The AASV believes that it would be useful to have a vaccine strain selection system for swine production that is similar to the World Health Organization (WHO) system used for human vaccines. However, there are several barriers preventing implementation of this system in animals.[6-16]

Therefore, the AASV recommends:

- **The development of a system modeled on the WHO system for strain selection that facilitates the production of national or regional influenza vaccines for swine.**
- **Increased government funding and infrastructure to support the surveillance of influenza strains of swine and the development of vaccine strategies that reduce influenza risk.**
- **That the Center for Veterinary Biologics (CVB) promote new technology and streamlined vaccine approval methods to enable the timeliness of market entry, given the potential frequency of influenza antigenic drift and shift.**
- **That universities, diagnostic laboratories, and commercial organizations release their rights to ownership of influenza genetic material for the purpose of production of a national influenza vaccination program for swine.**

Swine movements in herds infected with novel type A influenza virus

To protect both human health and the food supply, the AASV recognizes that minimizing the risk of cross-species transmission of influenza A viruses is critically important. Slowing the rate at which swine herds are infected and the total number of herds infected with a novel type A influenza is an important "One World, One Health" control strategy. Historically, limiting movements between production sites early in an outbreak has been an accepted measure to contain a disease outbreak and minimize or stop introduction into new herds. Practically, these measures have been of limited value in situations where there is a high degree of mobility of potentially infected animals or people and where shedding of the organism occurs prior to significant clinical signs. This was the case in the recent introduction of the pandemic (H1N1) 2009 influenza infection in humans, where infection spread to multiple countries before it was detected and accurately diagnosed.

Therefore the AASV recommends that:

- **Pork producers cooperate fully and actively participate in the development and implementation of surveillance programs established by federal, state, and local governments to promote a full understanding of the extent of a novel virus spread in the US swine herd.**
- **Producers consult with and implement the recommendations of their veterinarian to fully understand any potential new infections in their herds, and veterinarians use the best available information to make science-based decisions on appropriate control measures for those herds.**
- **Movements of animals originating from infected herds are continued under the supervision of the herd veterinarian(s) in accordance with state and federal regulations (refer to USDA's H1N1 Response Guidelines) and standard industry procedures.**
- **The discovery of novel influenza strains in pork production systems be confidential regarding owner and location and that producers be protected by indemnity if quarantine or depopulation methodologies are employed by local, state, or national health control officials.**

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*Non-refereed references.

BACKGROUND

Influenza recommendations for pork production staff, veterinarians, and harvest plant workers

Vaccination of people working in pork production and harvest is critically important because of the risk of human-to-swine transmission of influenza virus is quite high. The two dominant influenza A hemaglutanin (HA) types circulating in the North American swine population today are of human origin. The Sw/H1 virus (A/Sw/Iowa/1930/H1N1) likely originated from the 1918 human H1N1 virus. The original H3 HA gene segment (A/Sw/Texas/1998/H3N2) originated from the 1976 H3 human virus and appears to have been introduced to the North American swine population in the late 1990's. Historically, there have been isolated cases of swine-to-human transmission, but subsequent human-to-human transmission of these viruses has been limited. The current pandemic (H1N1) 2009 is a single example where there has been more extensive person-to-person spread due to further host adaptation in humans.

The best means to minimize the risk of swine-to-human transmission of influenza A is to lower the risk of introducing novel viruses into the swine population thereby reducing the risk of viral reassortment with passage back to humans. The pork industry has taken numerous steps over the last 20 years to minimize the risk of novel influenza introductions. They include:

- Preventing bird and pig interactions through the adoption of bird proof, indoor housing
- Strict protocols to limit human transmission of disease into swine herds that include showering and changing clothes prior to entering swine rearing facilities, limiting visitors to swine production facilities, and strictly enforcing time away from other livestock for all people entering the production facility
- Promotion of seasonal influenza vaccination of all animal caregivers through facilitation and financial support of vaccination for pork industry employees and families

While the pork industry has been very proactive in the implementation of prevention strategies for their herds, there is a need for additional strategies designed to protect workers from influenza. Pork production workers should be considered high priority for receiving novel influenza A strain vaccination. Animal caregivers, veterinarians, and harvest plant workers are critical in the attempt to reduce the risk of pandemic (H1N1) 2009 influenza virus introduction into the North American swine herd.

The AASV recognizes the importance that swine can play in promoting the transmission of a novel influenza virus. In the spirit of the "One Health" initiative, the AASV strongly encourages everyone involved in human and animal health to promote and facilitate vaccination of personnel involved in pork production.

Influenza vaccination recommendations for swine

It has been demonstrated that commercial SIV vaccines have failed to significantly reduce viral replication or shedding following a challenge, although the vaccines have proven to be beneficial in reducing clinical signs and lung lesions. This failure could be critical in the epidemiology of swine influenza viruses, possibly increasing the risk of transmission to susceptible animals and humans, favoring genetic mutation and generation of virus variants. If the current vaccines are insufficient in controlling the spread of virus variants, the variant viruses may continue to change and infect pigs, or even reassort with other influenza viruses that could infect humans and other animals. Therefore, further genetic and serologic evaluations of currently circulating SIV strains should be done, and upon review of the information obtained from such analyses, it may become evident that updating and improving commercial SIV vaccines is necessary.

While improving the commercial SIV vaccines through yearly updates with relevant strains may help, it may be more beneficial to seek new vaccine technologies with the intent of providing heterologous, cross-protective immunity against the many influenza viruses circulating globally in both the human and hemispherical swine populations. One novel technology that has been shown to be efficacious in experimental settings is the use of vectored vaccines.

The growing complexity of influenza viruses at the animal-human interface and the isolation of viruses with a seemingly high affinity for reassortment make the U.S. swine population an important reservoir of influenza A viruses. Therefore, finding a vaccine or control technology that can enhance the immune system, greatly reduce the shedding of virus, and improve clinical outcome of the disease in both animal and human populations will help reduce the interspecies transmission potential of influenza A viruses.

Development of a national influenza vaccine strain selection system for swine

There are several challenges to developing a "national" swine flu vaccine for the US swine herd that resembles the human seasonal flu vaccine strategy.

1) **Lack of government funding and infrastructure.**
   The US veterinary and veterinary biologics industry lacks the government-funded infrastructure to follow the human model for selecting and generating updated influenza vaccine seed strains. In the human model, government-funded influenza centers characterize viruses and epidemiologic data and once strain selection is made for a vaccine update, the human biologic firms are provided with the master seed strains to use. Use of this model requires a centralized government-funded surveillance program to include virologic characterization as well as epidemiologic investigation to identify the prevalent subtypes, strains, and geographic differences – information that is essential to Center for Veterinary Biologics (CVB) for strain selection.
2) **Efficacy tests are required for commercial swine influenza virus vaccines.**
   Animal vaccines require that efficacy challenge studies or immunogenicity studies be done in swine prior to approving the vaccines. The stipulations are described in Veterinary Services Memorandum No. 800.111, and a summary of

the requirements are attached. The efficacy and other tests required by CVB make updating swine flu vaccines by veterinary biologic companies cost prohibitive on an annual basis. This is in contrast to seasonal human influenza vaccines which require no efficacy tests in the human host for manufacturers that have previously provided data to CDC on immunogenicity of their vaccine formulations. We therefore recommend that CVB apply the same regulatory guidelines used for the production of seasonal human influenza vaccines to the manufacture of veterinary biologics to facilitate the rapid updating of swine influenza vaccines.

3) **Lack of easily transferable biologic material to and from veterinary biologic companies.**
The majority of influenza virus isolation and characterization is performed at university laboratories. Many universities consider viruses and their genetic information as part of the university's intellectual property. In addition, some veterinary-client-patient data is considered confidential and is also not freely shared. Efforts should be made to modify these policies to facilitate the transfer of biologic material necessary for the development of effective diagnostics and vaccines.

Summary of new USDA-APHIS-CVB Guidance on Swine Influenza Vaccines (Killed Virus), Veterinary Services Memorandum No. 800.111

Process	Policy
Addition, substitution, or deletion of strains	• Proposals for additions or substitutions of new strains, or deletions of current strains, must be reviewed and approved by CVB prior to changing the licensed product.
	• Up to two strain substitutions for each subtype may be made at any one time.
	• Based on adequate justification additional strains of each subtype may be added.
	• A licensed product may not contain more than 3 strains of a subtype.
	• A reassortant virus arising from the existing HA and NA subtypes (HIN1 or H3N2) is not considered a "new" subtype (HIN2).
Manufacturing methods	• The antigen concentration per dose of each new strain must not be less than the minimum concentration established for the strains in the currently licensed vaccine.
	• The manufacturing methods must not be significantly altered from those approved for the currently licensed vaccine.
Master Seed Viruses	• Genetic and antigenic characteristics of SIV vaccine strains should be justified by epidemiologic data and scientific literature.
	• Master Seed Virus testing requirements unchanged, as per 9CFR 113.200.
	• Master Seed characterization must include H and N subtype designations and sequence data.
Immunogenicity and Safety	• Immunogenicity of new strains (of the same subtypes) is established by demonstrating that the revised product generates an immune response that is not less than the original formulation.
	• Full-scale field safety not required.
	• Antigen interference does not need to be demonstrated for previously-licensed combination products.
	• Efficacy of a lower antigen dose for existing subtypes, or for the addition of a new subtype, must be demonstrated by an acceptable host animal challenge study.
Labeling	• Label includes subtype and strain designations made to accepted standards of influenza virus nomenclature.
Conditional License	• Requirements for application for a conditional license remain unchanged (9 CFR 102.6 and VS Memorandum No. 800.75)

Swine movements in herds infected with pandemic type A influenza virus

While conventional wisdom would promote the closure of herds infected with a novel agent, the science does not support this measure in the case of the pandemic (H1N1) 2009 influenza initially discovered in 2009 in humans in Mexico and California. Specifically, there are numerous challenges to making herd closure effective in controlling the spread of this or any novel influenza including, but not limited to, the significant delay between infection and detection with laboratory diagnosis, a high degree of interconnectedness between sites, the frequent movements of livestock between sites, and the potential for aerosol transmission of the virus between sites in swine dense areas.

The time from infection to clinical signs is between 3 to 5 days in an individual animal and it is often over 7 days before herd level infections are detected with clinical signs. Assuming that the caregivers are very observant, and that the veterinarian responds very quickly, any sampling for an influenza herd infection would be 7 days following the index case. Because influenza is endemic in the US swine population, mild cases may go unreported for several additional days or unreported altogether. It is highly likely that there would be a 14-day delay from the herd index case before samples would be collected for diagnostic testing. Once samples are collected there will be an additional 24-hour delay before test results are available. In many cases, the time from sample collection to results will be 72 to 96 hours if the clinical presentation appears mild and seasonal influenza like. It cannot be overemphasized that an infection with the pandemic H1N1 virus will not initially be recognized clinically because of the high annual rate of swine influenza virus infections in herds. In addition, by the time a pandemic H1N1 influenza infection is recognized by laboratory confirmation, notification will potentially occur long after numerous contacts between an infected herd and other herds have occurred. These additional herd exposures are often not geographically confined. The lack of recognition of a novel infection coupled with a significant delay from infection to laboratory confirmation renders positive herd closure to movements of little value in controlling the national spread of pandemic (H1N1) 2009 virus or other novel influenza viruses.

The multiple site structure of the US swine industry limits the use of herd closure as a control or eradication tool. The advent of three- and multi-site production in the US in the 1990's has been a boon to swine health and has been very valuable in controlling many economically important diseases. This change in production systems has allowed breeding herds to be located away from growing pig sites, which has dramatically improved pig welfare through the elimination of lice, mange, many internal parasites, and many diseases such as *Actinobacillus pleuropneumoniae*, atrophic rhinitis, Aujeszky's disease, and in some cases porcine reproductive and respiratory syndrome (PRRS) in breeding and growing pig herds. This production strategy also promoted the opportunity to establish breeding herds and growing pig populations with significant geographic separation. While highly beneficial for improving swine health, multiphase production has created a situation where pigs are commonly moved multiple times per week from breeding herds to growing pig sites and between growing pig sites. Because of significant early detection limitations, multiple herds will always have had contact through animal movements prior to recognition of infection. Thus it will be impractical to limit the spread of influenza virus through herd closure procedures.

Finally, the potential for lateral transmission between sites between the time of exposure and identification of infection is significant in swine production areas of the country. The US pork industry is concentrated in several regions to take advantage of the economic benefits of input costs and available markets. Areas such as northern Iowa and southern Minnesota have very high concentrations of swine from multiple breeding herd sources. Many of these sources are imported from other areas of the country and Canada making them "melting pots" of production systems, and therefore potential melting pots of disease. Within each region, there is a high degree of direct or indirect contact between sites through human exposure. This contact is a result of both vectors (pigs and people) and fomites (maintenance equipment, waste spreading equipment, delivery of supplies, and removal of dead stock through rendering). These interconnections exist between common owners and across systems. The modern industry structure, while greatly improving swine health, welfare, and food safety, severely limits the effectiveness of test and quarantine disease control methodologies.

A pig-adaptable, novel influenza is likely to become endemic within a very short period of time and well ahead of any herd quarantine implementation. This situation is not unlike the abandonment of travel restrictions, mass school or other public gathering closures, or other extreme measures as a means of infection control by public health officials to prevent spread of the pandemic (H1N1) 2009 in humans. This approach was deemed ineffective. The same assumption should be made for pork production. Herd quarantines would only increase economic losses for the industry while providing no benefit for human or animal health. Control methods using vaccination, production management practices such as all in/all out movement of animals, and medical treatments to alleviate clinical signs should be the focus of efforts to prevent spread of this virus among the swine population. Continued efforts enforcing biosecurity procedures and worker vaccination and hygiene are most effective in reducing the risk of transmission between herds and between humans and pigs. However, even with control measures and enhanced biosecurity procedures, it is likely that this virus will spread among swine herds. Therefore, it is of utmost importance that the welfare and care of sick animals be considered and any preventive measures that will aid in amelioration of clinical signs or severity of the disease in animals be implemented.