

NAHEMS GUIDELINES: VACCINATION FOR CONTAGIOUS DISEASES

APPENDIX B: VACCINATION FOR CLASSICAL SWINE FEVER

FAD PReP

**Foreign Animal Disease
Preparedness & Response Plan**

NAHEMS

**National Animal Health
Emergency Management System**



United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

The Foreign Animal Disease Preparedness and Response Plan (FAD PRéP)/National Animal Health Emergency Management System (NAHEMS) Guidelines provide a framework for use in dealing with an animal health emergency in the United States.

This FAD PRéP/NAHEMS Guidelines was produced by the Center for Food Security and Public Health, Iowa State University of Science and Technology, College of Veterinary Medicine, in collaboration with the U.S. Department of Agriculture Animal and Plant Health Inspection Service through a cooperative agreement.

These draft guidelines are under ongoing review. During the review process, which ends on **April 13, 2012**, please send questions or comments to:

Center for Food Security and Public Health
2160 Veterinary Medicine
Iowa State University of Science and Technology
Ames, IA 50011
Phone: 515-294-1492
Fax: 515-294-8259
Email: cfsph@iastate.edu, subject line FAD PRéP/NAHEMS Guidelines

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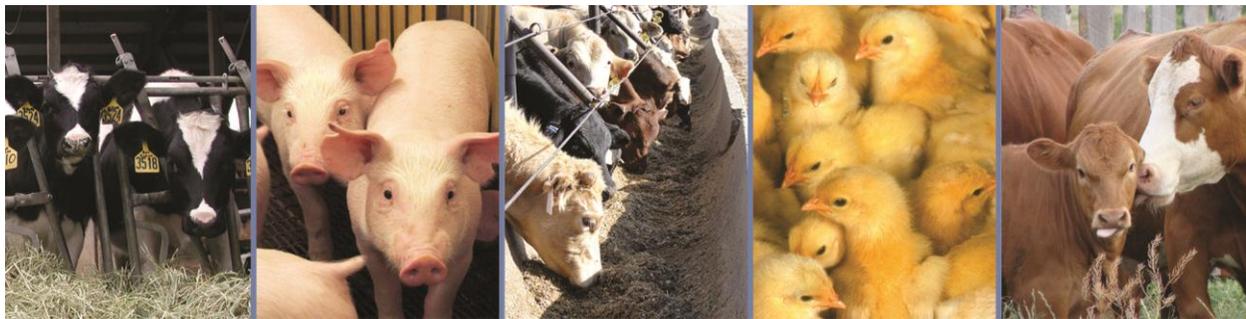
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THE IMPERATIVE FOR FOREIGN ANIMAL DISEASE PREPAREDNESS AND RESPONSE

Why Foreign Animal Diseases Matter

Preparing for and responding to foreign animal diseases (FADs), like highly pathogenic avian influenza (HPAI) and foot-and-mouth disease (FMD), are critical measures to safeguard our nation's animal health, public health, and food supply.

There are significant potential consequences of an FAD outbreak in the United States. In addition to the economic impact, the social and psychological impact on both producers and consumers could be severe. The FMD outbreak in the United Kingdom had an estimated impact of between \$12–18 billion. Studies have estimated a likely national welfare loss between \$2.3–69 billion¹ for an FMD outbreak in California, depending on delay in diagnosing the disease.²



Challenges of Responding to an FAD Event

An FAD outbreak will be challenging for all stakeholders. For example, there will be disruptions to interstate commerce and international trade. Response activities are complex, and significant planning and preparation must be conducted before an outbreak. Outbreaks can become large and widespread. Large, geographically dispersed and diverse teams will need to be assembled rapidly and must react quickly. The response effort must have the capability to be rapidly scaled up, involving many times more resources, personnel, and countermeasures. As such, responding to an FAD—large or small—may be a very complex and difficult effort.

Lessons Learned from Past FAD Outbreaks

Past outbreaks both in the United States and in other countries offer important lessons that can be applied to preparedness and response efforts. To achieve successful outcomes in future FAD response, it is vital to identify, understand, and apply these lessons learned:

- Provide a unified State-Federal-Tribal-industry planning process that respects local knowledge.
- Ensure the unified command sets clearly defined and obtainable goals.
- Have a unified command that acts with speed and certainty to achieve united goals.
- Employ science-based and risk-management approaches that protect public health and animal health, stabilize animal agriculture, the food supply, and the economy.
- Ensure guidelines, strategies, and procedures are communicated and understood by responders and stakeholders.

¹ Carpenter TE, O'Brien JM, Hagerman AD, & McCarl BA. 2011. "Epidemic and economic impacts of delayed detection of foot-and-mouth disease: a case study of a simulated outbreak in California." *J Vet Diagn Invest.* 23:26-33.

² Estimates based on models may vary: Ekboir (1999) estimated a loss of between \$8.5 and \$13.5 billion for an FMD outbreak in California. Ekboir JM. 1999. "Potential Impact of Foot-and-Mouth Disease in California: the Role and Contribution of Animal Health Surveillance and Monitoring Services." *Agricultural Issues Center.* University of California, Davis.

- Acknowledge that high expectations for timely and successful outcomes require the:
 - Rapid scale-up of resources and trained personnel for veterinary activities and countermeasures, and
 - Capability to quickly address competing interests before or during an outbreak.
- Rapid detection and FAD tracing is essential for the efficient and timely control of FAD outbreaks.

FAD PReP Mission and Goals

The significant threat and potential consequences of FADs, and the challenges of and lessons learned of effective and rapid FAD response have led to the development of the Foreign Animal Disease Preparedness and Response Plan, also known as “FAD PReP.” The mission of FAD PReP is to raise awareness, expectations, and develop capabilities surrounding FAD preparedness and response. The goal of FAD PReP is to integrate, synchronize, and de-conflict preparedness and response capabilities as much as possible before an outbreak, by providing goals, guidelines, strategies, and procedures that are clear, comprehensive, easily readable, easily updated, and that comply with the National Incident Management System.

In the event of an FAD outbreak, the three key response goals are to: (1) *detect, control, and contain the FAD in animals as quickly as possible*; (2) *eradicate the FAD using strategies that seek to stabilize animal agriculture, the food supply, the economy, and protect public health*; and (3) *provide science- and risk-based approaches and systems to facilitate continuity of business for non-infected animals and non-contaminated animal products*. Achieving these three goals will allow individual livestock facilities, States, Tribes, regions, and industries to resume normal production as quickly as possible. They will also allow the United States to regain FAD-free status without the response effort causing more disruption and damage than the disease outbreak itself.

FAD PReP Documents and Materials

FAD PReP is not just one, standalone FAD plan. Instead, it is a comprehensive US preparedness and response strategy for FAD threats. This strategy is provided and explained in a series of different types of integrated documents, as illustrated and described below.

FAD PReP Suite of Documents and Materials



Note: APHIS = Animal and Plant Health Inspection Service, NAHEMS = National Animal Health Emergency Management System, SOP = standard operating procedures.

- Strategic Plans—Concept of Operations
 - *APHIS Foreign Animal Disease Framework: Roles and Coordination*: This document provides an overall concept of operations for FAD preparedness and response for APHIS, explaining the framework of existing approaches, systems, and relationships.
 - *APHIS Foreign Animal Disease Framework: Response Strategies and Activities*: This document provides significant detail on response strategies and activities that will be conducted in an FAD outbreak.
 - *National Center for Animal Health Emergency Management (NCAHEM) Stakeholder Coordination and Collaboration Resource Guide*: This guide describes key stakeholders with whom NCAHEM collaborates.
 - *NCAHEM Incident Coordination Group Plan*: This document explains how APHIS headquarters will organize in the event of an animal health emergency.
- NAHEMS Guidelines
 - These documents describe many of the critical preparedness and response activities, and can be considered as a competent veterinary authority for responders, planners, and policy-makers.
- Industry Manuals
 - These manuals describe the complexity of industry to emergency planners and responders and provide industry a window into emergency response.
- Disease Response Plans
 - Response plans are intended to provide disease-specific information about response strategies. These documents offer guidance to all stakeholders on capabilities and critical activities that would be required to respond to an FAD outbreak.
- Critical Activity Standard Operating Procedures (SOPs)
 - For planners and responders, these SOPs provide details for conducting 23 critical activities such as disposal, depopulation, cleaning and disinfection, and biosecurity that are essential to effective preparedness and response to an FAD outbreak. These SOPs provide operational details that are not discussed in depth in strategy documents or disease-specific response plans.
- Continuity of Business (commodity specific plans developed by public-private-academic partnerships)
 - *Secure Egg Supply (SES) Plan*: The SES Plan uses proactive risk assessments, surveillance, biosecurity, and other requirements to facilitate the market continuity and movement of eggs and egg products during an HPAI outbreak.
 - *Secure Milk Supply (SMS) Plan*: Currently under development, the SMS Plan will help facilitate market continuity for milk and milk products during an FMD outbreak. This Plan also will employ proactive risk assessments.
 - *Secure Pork Supply (SPS) Plan*: Currently under development, the SPS Plan will help facilitate market continuity for pork and pork products during an FMD, classical swine fever, swine vesicular disease, or African swine fever outbreak.
 - *Secure Turkey Supply (STS) Plan*: Currently under development, the STS Plan will help facilitate market continuity for the turkey sector during an HPAI outbreak.
- Outbreak Response Tools
 - Case definitions, appraisal and compensation guidelines and formulas, and specific surveillance guidance are examples of important outbreak response tools.
- State/Tribal Planning
 - State and Tribal planning is essential for an effective FAD response. These plans are tailored to the particular requirements and environments of the State or Tribal area, taking into account animal populations, industry, and population needs.

- Industry, Academic, and Extension Planning
 - Industry, academia, and extension stakeholder planning is critical and essential: emergency management is not just a Federal or State activity.
- APHIS Emergency Management
 - APHIS directives and Veterinary Services Memorandums provide critical emergency management policy. APHIS Emergency Management documents provide guidance on topics ranging from emergency mobilization, to the steps in investigating a potential FAD, to protecting personnel from HPAI.

These documents are available on the FAD PReP collaboration website: <https://fadprep.lmi.org>. For those with access to the APHIS intranet, they are available on the internal APHIS FAD PReP website: <http://inside.aphis.usda.gov/vs/em/fadprep.shtml>.

PREFACE

The Foreign Animal Disease Preparedness and Response Plan (FAD PReP)/National Animal Health Emergency Response System (NAHEMS) Guidelines provide the foundation for a coordinated national, regional, state and local response in an emergency. As such, they are meant to complement non-Federal preparedness activities. These guidelines may be integrated into the preparedness plans of other Federal agencies, State and local agencies, Tribal Nations, and additional groups involved in animal health emergency management activities.

This Appendix B: Vaccination for Classical Swine Fever is a supplement to FAD PReP/NAHEMS Guidelines: Vaccination for Contagious Diseases, and covers the disease-specific strategies and general considerations of vaccination. Both documents are components of APHIS' FAD PReP/NAHEMS Guideline Series, and are designed for use by APHIS Veterinary Services (VS), and other official response personnel in the event of an animal health emergency, such as the natural occurrence or intentional introduction of a highly contagious foreign animal disease in the United States.

Appendix B: Vaccination for Classical Swine Fever, together with the Vaccination for Contagious Diseases Guidelines, provide guidance for USDA employees, including National Animal Health Emergency Response Corps (NAHERC) members, on principles of vaccination for classical swine fever for animal health emergency deployments. This Appendix B: Vaccination for Classical Swine Fever provides information for Vaccination Group Supervisors and other personnel associated with vaccination activities. The general principles discussed in this document are intended to serve as a basis for understanding and making sound decisions regarding vaccination in a classical swine fever emergency. As always, it is important to evaluate each situation and adjust procedures to the risks present in the situation.

The FAD PReP/NAHEMS Guidelines are designed for use as a preparedness resource rather than as a comprehensive response document. For more detailed vaccination information, see plans developed specifically for the incident and consult the FAD PReP Standard Operating Procedures (SOP): 16. Vaccination.

APHIS DOCUMENTS

Key APHIS documents complement this “Appendix B: Vaccination for Classical Swine Fever, Strategies and Considerations” and provide further details when necessary. This document references the following APHIS documents:

- APHIS Foreign Animal Disease Framework documents
 - Roles and Coordination
 - Response Strategies and Activities

These documents are available on the FAD PReP collaboration website at: <https://fadprep.lmi.org>
Username and password can be requested.

For the full listing of all references, including other APHIS documents, see section 25. References.

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Appendix B: Vaccination for Classical Swine Fever *Strategies and Considerations*

1. PURPOSE

This Appendix is intended to provide relevant information for federal and state officials and other interested parties who will participate in making decisions related to use of vaccine as an aid to control an outbreak of classical swine fever (CSF) in the United States (U.S.). The following topics are presented and discussed:

- Important characteristics of CSF
- Characteristics of vaccines
- Strategies for vaccine use
- Various factors that must be considered when designing an effective vaccination program

2. BACKGROUND

The United States eradicated the last case of CSF in August 1976 [1]. A possible disease introduction continually threatens the U.S. swine herd. This concern has been heightened with the actions on September 11, 2001. The intentional release of CSF virus (CSFV) into the U.S. swine herd is a real concern. We also have to accept that an unintentional introduction is possible. Employees and owners of hog production systems who travel all over the world as well as visitors who arrive from countries with endemic CSF could unintentionally expose the pigs they care for or come in contact with. The clinical signs associated with CSF resemble many endemic diseases, so diagnosis may be delayed which in turn makes control even more difficult. Tens of thousands of pigs are being moved daily in the U.S. Conservative industry estimates place over 625,000 swine in trucks on the road every day [2]. During transport, any pig exposed to CSFV would have the potential to spread the disease to another location before it is diagnosed. Artificial insemination is a technology which has greatly benefitted the U.S. swine industry; however, if a boar stud becomes infected with CSFV, infected semen could be distributed throughout the country unknowingly [3]. Feral swine continue to thrive in several states in the U.S. If CSFV would infect feral swine, then CSF would be even more difficult to eradicate from the U.S. Therefore, an appropriate and usable response plan needs to be in place before a diagnosis is confirmed if the swine industry is to be able to respond effectively to such an event.

CSF is endemic in many parts of the world. CSF is found in several countries in Asia, Africa, South and Central America and in some Caribbean islands [4]. Specifically, according to the OIE World Animal Health Information Database, Mexico last reported new cases of CSF in the period of January-July 2009 with the disease being absent July- December 2010. CSF was reported in Haiti in 2011 and the Dominican Republic and Cuba in 2010 (2011 data not available on OIE website for the Dominican Republic and Cuba). This disease has been eradicated from the U.S., Canada, New Zealand, Australia, and from domestic swine operations in most of western and central Europe.

Outbreaks in countries free of CSF have resulted in CSF infection on multiple farms with significant economic losses for swine industries in those countries. In 1994, Germany reported 117 farms infected, and Belgium reported 48 farms tested positive for CSFV [5]. During the outbreak from 1997-1998, 429

farms in the Netherlands were infected with an estimated \$423 million in losses and \$596 million in losses for related industries [5]. Terpstra et al. [6] estimated greater losses in the Netherlands totaling over \$2 billion. Paarlberg et al. [7] calculated potential economic losses during a CSF outbreak in the U.S. Eleven million hogs are destroyed in this scenario, with losses ranging from \$2.6 billion to \$4.1 billion when considering the value of destroyed animals, the effect on breeding herd numbers, product demand and effect on exports.

Controlling CSF infections in areas that are pig dense has proven to be very challenging. Measures to control CSF outbreaks in The Netherlands, England and Belgium did not include CSF vaccination. Although the measures of stop animal movement, isolation and stamping-out helped to control the outbreak in the Netherlands, it was at a great economic loss [8]. For countries of the European Union (EU), utilizing CSF vaccination is prohibited unless the affected country requests and is granted permission to carry out emergency vaccination in addition to control measures already underway, according to Article 19 of EU Directive 2001/89/EC [9]. For example, beginning in 2006, Romania determined that in order to eradicate CSF, vaccination would be beneficial. In order to utilize vaccination, they would have to receive approval from the European Commission. The contingency plans including the use of CSF vaccine submitted by Romania to the Commission on 9 November 2006 for the control of classical swine fever were approved under Directive 2007/19/EC[10]. Emergency vaccination was allowed to be used in Romania in order to eradicate CSF.

While stopping the movement of pigs may help to contain the spread of CSF, preventing animals from moving can create welfare concerns. With the management practices of the U.S. swine industry, many animals remain on a site until a specified weight or age. For example, pigs may be placed in a nursery from weaning at about 3 weeks of age until they reach about 50 pounds body weight. At that time, they are to be moved into a finishing building. If a stop movement were in place, the animals would continue to grow becoming overcrowded. Also, young animals that need to be weaned cannot be transported onto that site or building if it hasn't been emptied. According to Plumiers et al. [8], during the outbreak in the Netherlands during 1997-1998, the welfare of the pigs during a stop movement was a concern. As animals became overcrowded and pigs began to suffer health problems, authorities implemented a buy-out plan and carcasses were destroyed. In 2004, participants in the World Organization for Animal Health (OIE) International Conference on the Control of Infectious Animal Diseases by Vaccination in Buenos Aires, Argentina concluded that mass slaughter is no longer acceptable as the main technique for disease control and eradication, due to ethical, ecological and economic concerns [11]. They recommended that methods for disease prevention, control and eradication be reviewed, and advised an increased emphasis on vaccination.

When initial control measures such as stamping-out, quarantine, and stop movement do not contain a CSF outbreak, the use of vaccine needs to be considered. According to DeHaven [12], "The decision to use, or not to use, a vaccine in the face of a foreign animal disease outbreak can be complex and have far-reaching socio-economic consequences. Incorrect decisions or delays occurring during the actual outbreak can be costly." Several factors to consider include the number of herds affected, how quickly the disease is spreading, personnel available to assist in the response effort and the number of feral swine in the area.

3. OVERVIEW OF CLASSICAL SWINE FEVER (CSF)

Summary

Classical swine fever virus (CSFV) is a member of the genus *Pestivirus* and family Flaviviridae.

The small enveloped, single stranded RNA virus is closely related to the ruminant pestiviruses that cause bovine viral diarrhea and border disease. Only one serotype exists, although variability has been shown.

All species of domestic (*Sus scrofa domesticus*), feral and wild pigs, including European wild boar (*Sus scrofa scrofa*) and collared peccaries, are thought to be susceptible. Humans and other livestock species do not appear to be affected by CSFV.

Virus shedding can begin before the onset of clinical signs, and occurs throughout the course of acute or subclinical disease. Chronically or persistently infected pigs can shed virus continuously or intermittently for months.

Sows can be infected at any stage of gestation and the virus may cross the placenta and infect the fetuses. The outcome of the fetal infection depends on the strain virulence and the time of gestation when the infection occurs. Pigs born to sows infected with CSFV during gestation may be stillborn, aborted or mummified. Those pigs born alive may be persistently infected.

Persistently infected pigs born alive may appear asymptomatic initially; however, a congenital tremor may develop. These piglets may survive past 6 months, rarely up to a year, meanwhile shedding the virus and acting as a source of infection for other pigs.

Cerebellar hypoplasia is evident more frequently in pigs born to sows infected prior to 43 days of gestation.

Clinical signs may vary depending on the stage of infection and type (acute, subacute, chronic or persistent/late onset) and virulence of the strain. Clinical signs with an acute infection of a highly virulent strain include a high fever, huddling, weakness, drowsiness, anorexia, conjunctivitis, and constipation followed by diarrhea. Clinical signs are generally less severe with the subacute form due to infection with lower virulence strains. The chronic form presents with clinical signs similar to the acute form except pigs lose weight as severe lesions develop in the ileum and rectum.

Transmission between pigs occurs mainly by the oral or oronasal routes, via direct or indirect contact. Virus can be shed in saliva, lacrimal secretions, blood, urine, feces, and semen. Transmission may occur through feeding uncooked contaminated garbage containing pork products, or may be spread by genital transmission or artificial insemination. The virus can also be transmitted on fomites and by mechanical spread. Airborne transmission seems to be possible over short distances; however, the maximum distance the virus can spread is unclear.

The incubation period for acute disease can range from 2 to 14 days, depending on the virulence of the strain, the route of infection and the dose.

CSFV is easily transmitted due to its ability to survive in the environment and in pork products. CSFV survival time in chilled pork is up to 3 months, up to 4 years in frozen pork and pork products, and 17-180 days in salted or smoked meat.

3.1 Serotypes and Strains

Classical swine fever virus (CSFV) is a member of the genus *Pestivirus* and family *Flaviviridae* [13]. The small enveloped, single stranded RNA virus is closely related to the ruminant pestiviruses that cause bovine viral diarrhea and border disease [14]. Only one serotype exists, although variability has been shown [15]. The structure of the virus is made up of the Protein C and glycoproteins Erns, E1, and E2 [16]. CSFV strains can vary considerably in virulence.

3.2 Species Affected

All species of domestic (*Sus scrofa domesticus*), feral and wild pigs, including European wild boar (*Sus scrofa scrofa*) and collared peccaries, are thought to be susceptible. Humans and other livestock species do not appear to be affected by CSF.

3.3 Pathogenesis

Infected pigs are the only reservoir of this highly contagious virus. The most common form of CSFV transmission in pigs is oronasal [17]. If pigs are intranasally infected with CSF virus, it will replicate primarily in the tonsils before spreading to other lymphoid organs [18-20] including regional lymph nodes, and then into the peripheral blood, bone marrow and visceral lymph nodes [17]. Blood, oronasal and lacrimal secretions, urine, feces, semen and tissues contain infectious virus [3, 21, 22]. Spread of the virus within the animal usually occurs in 5-6 days [23]. Virus shedding can begin before the onset of clinical signs, and occurs throughout the course of acute or subclinical disease [24]. Chronically or persistently infected pigs can shed virus continuously or intermittently for months [22, 25].

3.3.1. Persistent Infection (sometimes referred to as the Prenatal Course or 'late onset CSF')

When sows were infected with CSFV on either day 22 or 43 of gestation, pigs born showed a variety of clinical signs including tremors [26]. Of those with tremors, 83% of those pigs had cerebellar hypoplasia. Several piglets died within a few days of birth. Pigs from sows infected after day 72 of gestation did not exhibit severe tremors, although a majority of these piglets were either mummified or stillborn [26]. Tremors became less evident as the pigs grew older and continued to shed CSFV. Van Oirschot et al. [27] produced different results upon infecting four sows each at 40, 65 and 90 days of gestation with a low virulent CSFV. Transplacental transmission did not occur in two of the four sows infected at 40 days gestation and two of four sows infected at 90 days gestation. Two different sows infected at 40 days gestation gave birth to pigs which all tested positive for virus at birth, and one of four sows infected at 65 days gestation also gave birth to pigs all of which tested positive at birth [27]. Concerning persistently infected animals, Van Oirschot et al. [27] concluded from this experiment that sows that are infected with this low virulent strain of CSFV at an earlier stage of gestation will produce a greater number of persistently infected pigs. Dahle et al. [28] inoculated sows between 70 and 90 days gestation and observed persistently infected pigs born to these sows.

3.4 Clinical Signs

For official control purposes, the World Organization for Animal Health (OIE) defines the incubation period for acute infection of CSF as 2-14 days and in cases of chronic infection up to 3 months [29]. Pigs infected with CSFV may show a variety of clinical signs depending on the stage and type of infection (acute, subacute, chronic or persistently infected) and virulence of the strain.

3.4.1 Acute Infection

Clinical signs associated with an acute infection include a high fever, huddling, weakness, drowsiness, anorexia, conjunctivitis, and constipation followed by diarrhea [17, 30, 31]. Purple discoloration of the skin in the abdomen, inner thighs or ears may be visible, or hemorrhages may be evident. Vomiting bile may occur, or respiratory signs may develop. Pigs may show neurologic signs such as incoordination or unsteadiness, which may progress to posterior paresis or convulsions in the terminal stages [4, 31]. If bloodwork is conducted, the clinician may find severe leukopenia. Pigs in the acute stages of CSF often die within 10-20 days after infection [24].

3.4.2 Subacute Infection

Moderately virulent strains of CSFV can cause subacute disease in which the clinical signs are less severe. However, the fever may persist for two to three weeks. Survival of pigs with subacute classical swine fever varies as some survive longer periods; while others die within a month [24].

3.4.3 Chronic Infection

When the immune system cannot eliminate the CSFV, pigs develop the chronic form of the infection. The clinical signs are similar to those associated with the acute form; however, pigs lose weight as severe lesions develop in the ileum and rectum [31].

For animals infected with a moderately virulent CSF virus, chronic infection may occur [25, 32]. Animals that have been chronically infected with CSF do not always demonstrate a clear antibody response following a CSF infection. Chronically infected pigs shed CSF virus [33]. While these animals may not show clinical signs, they may harbor the virus and shed it. Pigs developing the chronic form may survive 2-3 months before they die [17].

3.4.4 Persistent Infection (sometimes referred to as the Prenatal Course or 'late onset CSF')

Sows can be infected at any stage of gestation, with the virus crossing the placenta and infecting the fetuses. The outcome of the infection will depend on the virulence of the strain and the time of gestation [31]. If infected in early pregnancy with a strain of moderate or low virulence, pigs may be aborted, stillborn, or mummified. Infection of the sow around 50-70 days of gestation may result in persistently infected pigs, depending on the strain virulence [31]. While these pigs are born alive, they may develop a congenital tremor while others are asymptomatic at birth [27, 31]. Persistently viremic animals may not show signs, such as stunted growth, for several months [31, 34]. Some pigs will survive for more than six months, rarely surviving past one year, while shedding the virus, potentially spreading the disease [22].

Differential diagnosis includes African swine fever, salmonellosis, porcine dermatitis and nephropathy syndrome, erysipelas, porcine circovirus associated disease, hemolytic disease of the newborn, porcine reproductive and respiratory syndrome, pasteurellosis, actinobacillosis, *Haemophilus suis* infections, thrombocytopenic purpura, anticoagulant (e.g. warfarin) poisoning, salt poisoning, pseudorabies, parvovirus infections and eperythrozoonosis [4, 31].

3.5 Transmission

Classical swine fever is highly contagious. Transmission between pigs occurs by the oral or oronasal routes, via direct or indirect contact [17, 31, 35, 36]. Some experts regard direct contact as the most important route of CSF transmission [37]. Virus can be shed in saliva, lacrimal secretions, blood, urine, feces and semen [3, 21, 27, 38, 39]. CSFV can be spread by genital transmission or artificial insemination as boar semen may contain CSFV[3]. In the 1997-98 CSF outbreak in the Netherlands, two AI studs became infected. Because the boar studs were allowed to continue shipping semen, they were suspected of potentially infecting 21 sow herds [6]. Infected carrier sows may give birth to persistently infected pigs.

CSFV may be transmitted when uncooked contaminated garbage containing pork products is fed to pigs [36]. Because pork products may be smuggled into the U.S. from countries with endemic CSF, this would represent a possible long-distance route of transmission. Garbage feeding has been suspected in other countries as a means of CSF introduction. In Bulgaria, non-vaccinated pigs fed uncooked table scraps tested positive for CSFV in March 2000 [40]. According to Kleiboeker [41], a hiker feeding part of a ham sandwich to a sow herd was suspected to introduce the CSF virus in the United Kingdom in 2000. Transmission occurred in these cases due to the survival period of CSFV in pork products. CSFV survival time in chilled pork is up to 3 months[42-44], up to 4 years in frozen pork and pork products [45] and 17-180 days in salted or smoked meat [4, 43, 45-47].

Fomites and mechanical spread involving insects, birds, pets and other wild or domesticated animals can also play a role in virus transmission. Dorset et al.[48] reported stableflies and houseflies can transmit CSFV from sick pigs to healthy pigs. While they have been suspected, it is still unclear if birds play a role

in transmission [37]. The role cats, dogs, and rodents have played in spread of CSFV has been questioned. Research by Dewulf et al. [49] provided evidence that cats, dogs and rats do not serve as a reservoir of CSFV; although transmission may still be possible. Feral swine roam in many states throughout the U.S. If CSFV infects feral swine, they would threaten the health of the U.S. domestic herd. In Germany, direct or indirect contact with CSFV infected wild boar was found to be the cause of CSFV transmission to domestic swine [36].

While Dewulf et al. [50] demonstrated airborne transmission is possible under experimental conditions, the maximum distance the virus can spread is unclear. While aerosol transmission was documented only within a radius of 250 meters in some studies, transmission did occur up to 1 km in another [37].

Transportation vehicles pose a threat in transmitting CSFV when not properly cleaned and disinfected. Although it hasn't been proven, transportation vehicles are thought to have introduced CSFV into The Netherlands during the 1997/1998 CSFV outbreak [51]. Swine transport trucks are suspected to have come in contact with CSFV virus in Germany and carried it back to the farm where the primary outbreak later occurred in The Netherlands. The very cold weather made properly cleaning and disinfecting the transport vehicles difficult.

Estimates of its survival in pens and on fomites under field conditions vary. Weesendorp et al. [52] utilized the highly virulent strain Brescia and the moderately virulent strain Paderborn to investigate CSFV survival in urine and feces. In their model, virus was no longer detectable in the feces after 42 days when pigs were infected with the Paderborn strain and after 64 days when pigs were infected with the more virulent Brescia strain. However, when testing the urine, neither strain of the virus could be detected after 18 days post infection [52]. While initial concentrations and strain of the virus in feces will affect the survival time, using this model, at 20°C, the virus was inactivated in feces within 3 (Paderborn strain) to 5 days (Brescia strain) and 15-20 hours at 30°C [52]. The incubation period can range from 2 to 14 days, depending on the virulence of the strain, the route of infection and the dose [4]. The OIE listed incubation period ranges from 2 to 14 days [29]; Pasick reports 3 to 4 days may be typical [15]. Under field conditions, the disease may not be diagnosed in a herd for 2 to 4 weeks as the clinical signs resemble domestic diseases. In the Netherlands, on January 15, 1997, a practitioner observed atypical disease clinical signs in finishing pigs [51]. He suspected pneumonia and prescribed antibiotics. When the pigs did not respond to treatment, the practitioner suspecting Porcine Reproductive and Respiratory Syndrome (PRRS), submitted two pigs to the diagnostic laboratory on January 21. The laboratory diagnosed CSFV on February 4, 1997, over 2 weeks after the pigs began to show clinical signs.

3.5.1 Vaccination and Virus Transmission

Effective vaccination can decrease transmission between animals by 1) decreasing the susceptibility of animals to infection, and 2) reducing virus shedding, if a vaccinated animal becomes infected.

4. DETECTION OF INFECTED ANIMALS

Summary

Diagnosing CSFV based on clinical signs alone is almost impossible.

Several OIE-approved tests are available with the preferred sample of whole blood or serum for live animals and tonsil, ileum or additional acceptable tissues if the pig is necropsied.

The CSFV virus or viral antigens are detected by direct immunofluorescence (FAT or FATST test), enzyme-linked immunosorbent assays (ELISAs), virus isolation, reverse transcription-PCR (RT-PCR) and real time RT-PCR (qRT-PCR).

The fluorescent antibody test (FAT) utilizes the tonsil, spleen, kidney, lymph nodes or distal portions of the ileum to detect CSF antigen. The tonsil is the preferred sample 2 to 15 days post infection whereas the ileum will provide more accurate test results for subacute and chronic cases. Vaccine administration and infection with ruminant pestiviruses may affect FAT test results in some cases.

When ruminant pestiviruses are suspected, a panel of monoclonal antibodies (MAbs) can be used to differentiate CSF from ruminant pestiviruses.

The antigen-capture ELISA is a good test to use on live animals in herds suspected of CSF infection.

While virus isolation is a more sensitive test, it takes longer to complete. When using the PK-15 or SK-6 cell line, cultures are examined by FAT after 24 to 72 hours, or in 4- to 5-day-old cultures when utilizing immunoperoxidase staining. Samples for virus isolation should be refrigerated but not frozen; they should be kept cold during shipment to the laboratory.

Reverse-transcription polymerase chain reaction (RT-PCR) is especially useful in preclinical diagnosis of CSF due to its high sensitivity. Blood samples from live pigs or tissues samples, including tonsil, spleen, ileum and lymph node, collected during necropsy can be utilized with results in 48 hours.

Serology is used for diagnosis and surveillance. Antibodies develop after 2 to 3 weeks, and persist lifelong. The most commonly used OIE-approved tests are virus neutralization tests, which include the neutralizing peroxidase-linked assay and the fluorescent antibody virus neutralization test, and various ELISAs.

Performing virus neutralization tests or ELISAs that use monoclonal antibodies provides for differentiation of CSFV infections from ruminant pestiviruses.

Several countries and the European Union accept the use of RT-PCR in suspect CSF cases as it is sensitive and can be performed rapidly. However, as false positive results may occur, another test such as virus isolation should be performed when an initial CSF positive may signal a CSF outbreak.

Diagnosing CSF based on clinical signs alone is almost impossible. The clinical presentation of CSF is similar to many U.S. endemic diseases including salmonellosis, porcine reproductive and respiratory syndrome, porcine circovirus associated disease, erysipelas, pasteurellosis, actinobacillosis, and *Haemophilus parasuis*. African swine fever, which is a foreign animal disease, produces clinical signs similar to those of CSF also. Therefore, diagnostics need to be performed to confirm CSF. Several OIE-approved tests are available with the preferred sample of whole blood or serum for live animals and tonsil, ileum or additional acceptable tissues if the pig is necropsied [34].

An overview of CSF diagnostic methods, as described in by the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2009 [34], is given below.

4.1 Detecting Acutely Infected Animals by Identifying the CSF Virus

Classical swine fever can be diagnosed by detecting the virus, its antigens or nucleic acids in whole blood or tissue samples. Viral antigens are detected by direct immunofluorescence (FAT test) or enzyme-linked immunosorbent assays (ELISAs). If isolating the virus, the pig kidney (PK-15) cell line may be used. Polymerase chain reaction (PCR) is also commonly performed [34].

4.1.1 Fluorescent Antibody Test

CSFV antigen can be detected using the fluorescent antibody test (FAT). This rapid test utilizes frozen sections of tonsils, spleen, kidney, lymph nodes or distal portions of the ileum [34]. Detecting CSF virus in the tonsil is more likely 2 to 15 days post infection when animals are showing clinical signs of CSF compared to animals that have been infected for a longer period of time [21, 53]. Testing the ileum will provide more accurate test results for subacute and chronic cases [17]. If a FAT result is negative and CSF is still suspected, virus isolation in cell culture ((e.g. pig kidney [PK-15]) or another cell line of pig origin) should be attempted [34].

Vaccine administration and infection with ruminant pestiviruses may affect FAT test results in some cases. Administration of the MLV vaccine may cause pigs to test positive on the FAT test for 2 weeks following vaccination [34, 54, 55]. Ruminant pestiviruses can also interfere with CSFV testing causing false-positive FAT reactions. Pigs infected with ruminant pestiviruses from congenital infections can have the same clinical signs and lesions as pigs with chronic CSF [56-58]. To differentiate infections from CSFV versus ruminant pestiviruses, animals can be tested for neutralizing antibodies to the virus [34].

4.1.2 Immunoperoxidase Staining

As stated previously, ruminant pestiviruses can produce a false-positive FAT test. When ruminant pestiviruses are suspected, a panel of monoclonal antibodies (MAbs) can be used to differentiate CSFV from ruminant pestiviruses [34]. CSF antibodies are tagged with an enzyme and the chemical reaction that follows CSFV antigen and antibody binding produces the colored product [59]. Monoclonal antibodies can also be used to determine if CSF positive test was due to field or vaccine strains. Obviously, these MAbs do not need to be used if vaccine had not been administered [34].

4.1.3 Antigen-Capture ELISAs

When testing a herd suspected of being infected with CSFV, the antigen-capture ELISA is a good tool for early diagnosis in live pigs [17]. Blood, tissues, plasma or serum specimens can be tested [59]. Because this test is less sensitive than PCR or virus isolation, in mild or subclinical cases, the test would be most valuable if all clinical animals are tested. For this reason, antigen-capture ELISAs are best used for herd testing when CSF is suspected and not as a surveillance tool in healthy herds or to diagnose a single animal [34]. In 2008, the NVS Classical Swine Fever Countermeasures Working Group (CSFCWG) [59] concluded that “there is a need for useful pen-side tests that can be used in an outbreak situation to make rapid decisions in the field about the status of a test herd.”

4.1.4 Virus Isolation

Virus isolation is a more sensitive test than FAT and ELISA. The tonsil is the tissue of choice for virus isolation, although spleen, kidney, ileum, or lymph nodes can be used [34]. Blood, plasma and tonsil scrapings can also be tested from live animals [59]. When using the PK-15 or SK-6 cell line, cultures are examined by FAT after 24 to 72 hours, or in 4- to 5-day-old cultures when utilizing immunoperoxidase staining [34, 59]. Samples for virus isolation should be refrigerated but not frozen; they should be kept cold during shipment to the laboratory [60].

While virus isolation is the test of choice when diagnosing/confirming CSFV due to its high sensitivity, it may not be preferred during an outbreak to test a large number of samples as it is labor intensive and takes too long to complete [17].

4.1.5 Reverse Transcription- PCR

Reverse-transcription PCR (RT-PCR) is especially useful in preclinical diagnosis of CSF [34]. It is accepted for CSF testing by the EU and other nations [34, 61]. The OIE recommends that it be used with a confirmatory test due to the risk of false positives from laboratory contamination. It is more sensitive than the CSF antigen-capture ELISAs or virus isolation in this situation [34]. Harding et al. [62, 63]

developed a reverse-transcriptase PCR procedure with a reported sensitivity of 100%. Blood samples from live pigs or tissues samples, including tonsil, spleen, ileum and lymph node, collected during necropsy can be utilized [17] with results in 48 hours [61].

PCR protocols are being used in laboratories around the world to both detect CSFV and to differentiate it from ruminant pestiviruses [34]. In some situations if feral swine are found dead and the tissue autolyzed, PCR might be the test of choice [61].

4.1.6 Real Time RT-PCR

Real time RT-PCR (qRT-PCR) is more rapid as results can be available within 2 hours after the samples are prepared, and can be used when confirming a test result or in surveillance [59]. These assays have been adapted using automation. Although a risk of false negative and positive results still exists, qRT-PCR has the potential to replace the Fluorescent antibody test and Antigen-capture ELISAs; however, virus isolation still will be necessary to isolate the virus for further testing [59].

Tonsil scrapings, tonsil, spleen, lymph node, blood and nasal swab are all samples that can be tested using qRT-PCR [64]. LSI (TagVet CSF) and ADIAGEN (Adiavet CSF) have developed kits which have been validated on pooled serum, blood and tonsils [59, 65]. Leifer et al. [66] developed real-time RT-PCR assays to differentiate CSFV field strains from either CP7_E2alf (discussed in section 5.6) or the C-strain “Riems” which could be used to immunize feral swine.

4.2 Detecting Infected Animals by Serological Assays

Serology is used for diagnosis and surveillance, especially when infection with a CSFV strain of low virulence is suspected [34]. Also, it is useful in the final phase of CSF eradication when trying to detect any positive animals that might remain in a breeding herd [34]. Antibodies may not be detected until 2-3 weeks post-infection and can be present for the life of the animal [34, 67]. Congenitally infected pigs are immunotolerant and do not produce antibodies detectable on serology [26].

When testing for antibodies, the most commonly used tests are virus neutralization tests, which include the neutralizing peroxidase-linked assay [68] and the fluorescent antibody virus neutralization test [69], and various ELISAs [34, 67]. The definitive test for differentiation from ruminant pestiviruses is the comparative neutralization test.

4.2.1 Virus Neutralizing Tests (VNTs)

Due to the possibility that breeding herds may be infected with ruminant pestiviruses, tests that can differentiate ruminant pestivirus and CSF infections are necessary [34]. Performing virus neutralization tests (VNT) or ELISAs that use monoclonal antibodies provides for this differentiation. VNTs can be used to test both serum and plasma samples. When compared to ELISA, VNT is more sensitive especially when used for detecting antibodies in samples 10-14 days post infection [53]. The VNT recognizes all CSF genotypes, but the test is more sensitive when the same strain or a closely related viral strain is used to produce the test [53]. However, VNTs cannot differentiate between antibody titers produced from a field strain of CSFV versus those produced following administration of a modified live CSF vaccine [67]. Laboratories need to have high biocontainment facilities in order to perform this test [59].

4.2.1.1 Neutralizing Peroxidase-Linked Assay (NPLA)

This prescribed test for international trade is preferred as it is easier to read than the Fluorescent antibody virus neutralization test [34]. Neutralizing peroxidase-linked assay is performed using the constant-virus/varying-serum method. The test utilizes cell cultures; however, CSFV is noncytopathic. Because of this characteristic, non-neutralized virus must be detected by an indicator. Immunoglobulin conjugated with Horse Radish Peroxidase reacts with a chromogen-substrate solution to allow visualization of

infected cells. Samples can sometimes be read with the naked eye, although use of an inverted light microscope is preferred.

4.2.1.2 Fluorescent antibody virus neutralization test (FAVN)

The fluorescent antibody virus neutralization test is similar to the assay described above and involves the observation of infected cells. However, the conjugate used allows for fluorescence of infected cells and must be detected by fluorescence microscopy.

4.2.2 Antibody ELISAs

Many techniques can be used as long as they minimize cross reactions with ruminant pestiviruses [34]. The only samples which can be used with antibody ELISAs are serum or plasma from individual pigs [34]. The USDA's National Veterinary Stockpile (NVS) for the U.S., established in 2004, exists to help provide for state and local resources to fight 17 of the most dangerous animal diseases of which CSF is fifth on the list. In 2008, the NVS Classical Swine Fever Countermeasures Working Group (CSFCWG) [59] expressed concern that no currently available ELISA is fully capable of distinguishing between CSFV-specific antibodies and antibodies to other pestiviruses. In 2008, according to the CSFCWG report [59], the following five CSF-ELISA kits were commercially available: Herdcheck CSFV Antibody test kit (IDEXX Laboratories), Chekit-CSF-Sero and Chekit-CSF-Marker ELISAs (former Dr. Bommeli AG), Ceditest CSFV and Ceditest CSFV 2.0 test kits (Cedi-Diagnostics). As it detects Erns antibodies, the Chekit CSF Marker ELISA is a companion test for the Intervet E2 marker vaccine and proves to be more useful when used at the herd level [59].

4.2.3 Serological Assays in Development

In 2008, the NVS CSFCWG [59] recommended several additional diagnostic tests be improved or developed including tests to differentiate vaccinated animals from animals infected with the field strain as well as CSFV infection from exposure to ruminant pestiviruses.

The companion DIVA tests for E2 subunit "marker" vaccines are ELISAs which detect antibody to the Erns protein [70, 71]. Having received approval from the European Commission [72], these tests are utilized to determine if a herd vaccinated with an E2 marker vaccine may also have been exposed to field virus. According to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animal [34], neither discriminatory ELISA was able to consistently detect individual marker-vaccinated, CSF-challenged weaner pigs. Therefore, this technology was recommended to only be used at the herd level.

4.3 The Use of Diagnostic Tests in Outbreaks

Several countries and the European Union accept the use of qRT-PCR in suspect CSF cases as it is sensitive and can be performed rapidly [34, 61]. However, as false positive results may occur, another test should be performed when an initial CSF positive may signal a CSF outbreak.

Serological tests have limitations when utilized during a CSF outbreak. Antibodies may not be detected until 2-3 weeks post-infection, but can be present for the life of the animal [34, 67]. Therefore, serological tests may miss cases if samples are collected from animals which have not been exposed to CSFV long enough to produce antibodies. However, they are useful when monitoring for CSF cases or in surveillance programs [61].

In the 1997-98 CSF outbreak in the Netherlands, over 2 million samples were tested for CSF using several diagnostic tests [73]. FAT was utilized on tonsils to detect 74% of the positive tests. Over 140,000 blood samples were tested using virus isolation. In Korea in 2003 [74], antibody and antigen ELISA and RT-PCR tests were utilized to detect CSF positive animals.

Real-time RT-PCR assays have been developed that show great potential to differentiate CSFV field strains from either CP7_E2alf (discussed in section 5.6) [66, 75] or the C-strain “Riems” when used to immunize feral swine[66]. Therefore, in European countries which are trying to eliminate CSFV from their wild boar populations, utilizing this DIVA technology may become more widely utilized.

5. CSF VACCINES

Summary

Inactivated whole virus vaccines are not effective or available for use.

Live Attenuated Virus (LAV) vaccines or Modified Live Virus (MLV) vaccines, made from attenuated CSFV strains, are the most widely used vaccines in countries with endemic CSF. In countries where CSF has become endemic in the feral swine population, oral vaccination of feral swine has been practiced using a LAV vaccine.

Countries free of CSF may not allow the use of LAV vaccines because it is impossible to differentiate animals vaccinated with LAV vaccines from animals infected with the field strain using serology.

Subunit ‘marker vaccines’ induce antibodies that can be distinguished from those produced by animals infected with the field strain utilizing an accompanying serological test.

The ‘marker vaccines’ which have been marketed previously use the CSFV major envelope glycoprotein E2 produced in a baculovirus recombinant system. These vaccines have the potential to allow the Detection of Infection in Vaccinated Animals (DIVA).

Because the E2 marker vaccine is produced by infecting insect cells with a baculovirus containing the E2 CSFV gene, they do not contain live CSFV. Therefore, the final preparations contain the baculovirus which has been chemically inactivated and adjuvanted with mineral oils as a double or single emulsion using water and oil. Additional regulatory considerations may be applicable when discussing vaccines produced through biotechnology.

For the U.S. National Veterinary Stockpile (NVS), in 2008 the CSFCWG recommended stockpiling CSF LAV Strain C vaccine and CSF E2 marker vaccine with the hope in the long term of adding a second generation CSF vaccine which is as effective as the CSF LAV vaccine strains but with DIVA capabilities. If marker vaccines are added to the NVS, the companion DIVA tests would need to be stockpiled also.

A large number of LAVs are being marketed. Two E2 marker vaccines were registered in the EU, although only one manufacturer is currently producing this vaccine.

For a vaccine to be given a full product license, the manufacturer must conduct extensive efficacy, purity and safety testing.

Steps in the licensing of vaccines in the U.S. include a review of the data from the manufacturer to support the product and label claims; inspections of manufacturing processes and practices; confirmatory testing of the biological seeds, cells and product; post-licensing monitoring including inspections and random product testing; and post-marketing surveillance of product performance.

Researchers utilized several different approaches when creating chimeric pestivirus marker vaccines with varying degrees of success when administering intramuscularly, intranasally, and oronasally.

5.1 Types of CSF Vaccines

Inactivated whole virus vaccines are not effective or available for use [34]. In the past, when CSF vaccines have been utilized, LAV vaccines have been the only option available. Recently, however, a CSF E2 marker vaccine has been developed (but not currently marketed), and experimental vaccines continue to be developed and evaluated.

5.1.1 CSF Live Attenuated Virus (LAV) Vaccines - also known as Modified Live Virus (MLV) Vaccines

LAV vaccines, made from attenuated CSFV strains, [34] are the most widely used vaccines in countries with endemic CSFV according to Blome et al. [53]. Countries free of CSF may not allow the use of these vaccines because it is impossible to serologically detect infection in vaccinated animals (DIVA) when LAV vaccines are used [34]. This inability to detect infection by field virus in vaccinated animals may result in strict international trade restrictions on pork and pork products [59]. LAV vaccines may be used if CSF eradication is not possible so as to prevent the spread of the virus on a production site. Examples of such attenuated vaccines are the Chinese lapinised strain (CLS), sometimes called the C, K or LPC strain; the Japanese guinea pig cell-culture-adapted (GPE-) strain; the Thiveral strain (the French PK-15 cell-adapted strain); and the Mexican PAV strain (the most common being the PAV-250 strain, from the 250th passage of the A-PAV-1 strain) [15, 53].

According to Blome et al. [53], the most widely used strain is the Chinese strain. The Japanese GPE-strain vaccines are used in Asian and Pacific countries, the Thiveral strain vaccines are produced in France, and the Mexican PAV strain vaccine is licensed in Mexico.

5.1.1.1 LAV Administered Orally

LAV vaccines can be administered orally, in addition to parenterally. In countries such as Germany where CSF has become endemic in feral swine, oral vaccination of feral swine has been practiced [76]. Baits containing vaccine were set on the ground and covered up. Younger animals did not consume the baits as well as the older animals, and because a LAV vaccine was utilized, the uptake of oxytetracycline was used to help differentiate vaccinated animals from animals infected with the field strain [76]. When feral swine consume the baits containing oxytetracycline, oxytetracycline can be found in the bones for at least 4 months [76]. A fluorescence microscope was used to detect oxytetracycline from the foot, rib or breastbone.

Kaden et al. [76] studied the use of oral vaccination of wild boar in field trials from 1993-1995. Animals initially received 2 doses approximately 14 days apart with booster doses every 6 months [76]. While the overall rate of uptake of the baits was between 85-100%, less than 50% of the younger animals took the baits and became immunized [76].

Several studies have been conducted since the 2000 Kaden et al. study, in an attempt to improve the immunization of wild boar. In 2010, Rossi et al. [77] reported on a double vaccination protocol tested in France from 2005-2007. Each year, 500,000 baits were buried by hunters on wild boar feeding grounds. Rossi et al. reported that the effectiveness of the vaccination effort could not be improved by increasing the number of baits per wild boar. However, they did confirm that preventative vaccination is an important part of a CSF control program. Research needs to continue to determine the best strategy for immunizing feral swine/wild boars.

Refer to section 13. for field experiences with oral vaccine in Germany and Romania.

5.1.2 CSF E2 Marker Vaccine

DIVA vaccines (also called “marker” or “subunit” vaccines) contain one or more protective antigens, but do not contain one or more viral antigens that induce antibodies when vaccinated animals are exposed to wild-type virus. Each marker vaccine has an accompanying serological test which must be able to distinguish that vaccinated herds are not infected with the field virus [34].

The ‘marker vaccines’ which have been marketed previously used the CSFV major envelope glycoprotein E2 produced in a baculovirus recombinant system [78, 79]. Of the three envelope glycoproteins, E2 is believed to be the most immunogenic, inducing a neutralizing antibody response in pigs [79-82]. Researchers have developed E2 subunit CSF marker vaccines in which neutralizing antibodies are formed against the E2 glycoprotein only [82]. Therefore, any antibodies formed against other proteins of the CSF virus would have been formed due to infection with a field strain [70]. If the test result is negative, the pig was either seronegative, naïve or had been vaccinated whereas a positive result indicated the pig had been exposed to the field virus [59]. This is the basis for the companion discriminatory tests which detect antibodies to the E2 glycoprotein [70, 83]. These DIVA tests are not sufficiently sensitive to reliably detect individual animals that are infected. They are used on a herd basis.

In one study by de Smit et al. [84], when a single dose of an E2 marker vaccine was administered followed by challenge, some pigs developed a fever and two of eighteen became viremic, however, the virus was not transmitted from vaccinated and challenged pigs to unvaccinated sentinel pigs. E2 marker vaccines demonstrate protection two weeks after an initial and booster vaccination or six weeks following a single vaccination [53, 78, 81, 85]. This delay in the onset of a protective immune response against CSF infection makes these vaccines less useful when faced with an outbreak [59].

These marker vaccines are safe as they do not contain any CSFV and the baculovirus is inactivated [34]. Bouma et al. [86] tested the stability of an E2 marker vaccine and documented that the vaccine was stable at 4°C for at least 18 months after being produced, and retained its full potency.

Marker vaccines continue to be developed and improved [34]. Two marker vaccines have been registered in the EU. PORCILIS[®] PESTI (Merck-Intervet Schering-Plough Animal Health) is one of the commercial vaccines available with its accompanying discriminatory ELISA Chekit Marker[®]. The PORCILIS[®] PESTI vaccine is temporarily off the market due to technical issues. The second commercial vaccine is BAYOVAC[®] CSF Marker (Bayer) with its accompanying discriminatory ELISA Ceditest Marker[®]. The Bayer vaccine is also not available at this time.

5.2 Production of CSF Vaccines

5.2.1 Live Attenuated Virus Vaccines

OIE requirements for Containment Group 4 need to be met when CSFV is used to produce CSF vaccine [34]. In the United States, CSF is listed on the National Select Agent Registry. According to APHIS Select Agents Regulations (9 CFR Part 121), classical swine fever poses a potential threat to animal health. Vaccine production tends to be driven by market demand, and currently, the U.S. does not have a market for CSF vaccine. Therefore, because CSF is listed on the National Select Agent Registry and the lack of demand for the CSF vaccine, CSF vaccine is not manufactured in the U.S. Conditions for the production of LAV vaccines are addressed in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals [34].

5.2.2 E2 Marker Vaccines

Because the E2 marker vaccine is produced by infecting insect cells with a baculovirus containing the E2 CSFV gene, they do not contain live CSFV [34]. Final preparations contain chemically inactivated baculovirus, adjuvanted with mineral oils as a double or single emulsion using water and oil.

Additional regulatory considerations may be applicable when discussing vaccines produced through biotechnology. The National Environmental Policy Act (NEPA) of 1969 requires the review and approval by the appropriate federal agency that is necessary to evaluate the potential impact of an organism containing recombinant DNA on the environment [87]. The Institutional Biosafety Committee (IBC) will review experiments performed for licensure when they are performed within a facility; whereas the USDA Center for Veterinary Biologics (CVB) must give the approval when those experiments are field trials conducted prior to licensure that involve environmental release [87].

5.3 Vaccine Banks

Vaccine banks (also known as antigen banks or strategic reserves) store a variety of vaccines which can be used if an outbreak occurs. Banks may contain either ready-to-use vaccines or vaccine antigens that will be formulated, if needed, into complete vaccines.

Some experts agree that when a contingency plan includes the possible use of CSF vaccine in an emergency vaccination protocol, CSFV vaccine banks should be established [78, 88]. For the European Union Vaccine Bank, recommendations include at least 2 million doses of LAV vaccine, possibly E2-marker vaccine or a new modified live marker vaccine provided the vaccines prove effective [88]. With E2 marker vaccine or live marker vaccine, the companion diagnostic test would be necessary.

[59]. For the U.S. National Veterinary Stockpile, in 2008 the CSFCWG [59] recommended stockpiling CSF LAV Strain C vaccine and CSF E2 marker vaccine (Merck-Intervet) with the hope in the long term of adding a second generation CSF vaccine which is as effective as the CSF LAV vaccine strains but has DIVA capabilities. The addition of marker vaccines to the NVS would require the companion DIVA tests to be included in the stockpile to take advantage of the DIVA properties. Therefore, the CSFCWG [59] also recommended stockpiling the Chekit CSF Marker ELISA (Merck-Intervet) as well as a PCR test, Nucleic acid extraction kits and supplies, and PCR reagents and supplies. The long term goal for the NVS would be to have a pen side test kit available for use during an outbreak to rapidly detect any CSFV field strain.

According to the NVS fact sheet[89], the NVS contains two CSF vaccines. One vaccine is a LAV vaccine. The second vaccine is a DIVA-compatible E2 antigen-based CSF vaccine utilizing killed baculovirus vector technology.

5.4 CSF Vaccines from Commercial Manufacturers

A large number of LAVs are being marketed. Table 1 lists many of the vaccines by the manufacturer producing each vaccine. Generally speaking, LAV vaccines protect against challenge beginning 4 days post vaccination, lasting more than one year and maybe even lifelong [38, 90]. C-strain vaccine and chimeric vaccines have prevented clinical signs and transmission when vaccinated pigs are challenged 7 days post vaccination [30, 91].

Two E2 marker vaccines were registered in the EU. Both vaccines were produced with the baculovirus expression system [92]. PORCILIS[®] PESTI (Merck Intervet Schering-Plough Animal Health) was one of the commercial vaccines available with its accompanying discriminatory ELISA Chekit Marker[®].

During a transmission experiment, PORCILIS® PESTI was not able to prevent clinical signs or block transmission when vaccinated pigs were challenged 7 days post vaccination [30]. The second commercial vaccine was BAYOVAC® CSF Marker (Bayer) with its accompanying discriminatory ELISA Ceditest Marker®.

Table 1. Vaccine Manufacturers, Classical Swine Fever

Manufacturer	Product Name	Type	Strain/Subtype	Adjuvant	Licensed Countries
Agrovét	Classical Swine Fever (LK-VNIIVVIM)	Live	LK-VNIIVVIM	None	Russia
	Classical Swine Fever (VGNKI)	Live	K	None	Russia
	Subivac	Unknown	Unknown	None	Russia
Bestar Laboratories Ltd.	BSL-HC	Live	GPE	Unknown	Singapore
BIO-TONG S.A.	Colertong	Live	Chinese (lapinized)	None	Peru
Bioveta	Pertisen C	Live	Chinese	None	Czech Republic
Ceva Sante Animale	COGLAPEST®	Live	Unknown	Unknown	France, United Kingdom
Chengdu Tianbang Bio-Products Ltd. Corp.	Name Unknown	Live	Unknown	Unknown	China
ChoongAng Vaccine Laboratories Co., Ltd.	SuiShot® HC	Unknown	Unknown	Unknown	South Korea
	SuiShot® HE (Classical Swine Fever, Swine Erysipelas)	Unknown	Unknown	Unknown	South Korea
Empresa Colombiana de Productos Veterinarios S.A. (Vecol)	COLERVEC®	Live	Chinese (lapinized)	None	Colombia

Manufacturer	Product Name	Type	Strain/Subtype	Adjuvant	Licensed Countries
Institut Pasteur	Pestivac	Live	IP-77	None	Romania
	Pestruvac (Classical Swine Fever, Swine Erysipelas)	Live	VR 2 (SE)	None	Romania
Komipharm International Co., Ltd.	HC-VAC	Live	LOM	None	South Korea
Kyoritsu Seiyaku Corporation	Classical Swine Fever Vaccine	Live	GPE	None	Japan
LABIOFAM	Vacuna Colera Porcino	Live	China	None	Cuba
Laboratorio de Diagnostico Y Prevencion Veterinario (LaDiPreVet)	Peste V	Live	China	None	Argentina
Malaysian Vaccines and Pharmaceuticals	MVP Swine Fever GPE	Live	GPE	Unknown	Malaysia
Merial Philippines	Pestiffa®	Live	Chinese	None	Philippines
Merial Russia	Pestiffa®	Live	Chinese	None	Russia
Merial SAS (France)	Pestiffa®	Live	Chinese	None	Belgium, Bulgaria, Colombia, Dominican Republic, Former Yug. Rep of Macedonia, France, Germany, Hong Kong, Indonesia, Malaysia, Netherlands, Peru, Philippines, Russia, Spain, Sri Lanka, Thailand, Venezuela, Vietnam

Manufacturer	Product Name	Type	Strain/Subtype	Adjuvant	Licensed Countries
MSD Animal Health (Merck)	PORCIVAC®	Live	PAV-250	None	Mexico
	PORCILIS CSF Live	Live	GPE-	Unknown	Netherlands, Philippines
	PORCILIS Pesti	Marker	CSFV-E2	Oil	Peru, Philippines, Russia, Venezuela
National Biologicos Producers Veterinarios (PRONABIVE)	Pav Plus 250	Live	PAV-250	None	Mexico
Philippines Bureau of Animal Industry	Hog Cholera Vaccine	Live	Unknown	None	Philippines
Romvac	Rompestivac	Live	RP93	None	Romania
State Research Institution (SRI)	Classical Swine Fever Vaccine	Unknown	LK-VNIIIViM	Unknown	Russia
VETERINA Animal Health Ltd.	Plivak®-KS	Live	Chinese	None	Belarus, Bosnia and Herzegovina, Croatia, Former Yug. Rep. of Macedonia, Serbia and Montenegro, Slovenia, Vietnam

1. Adapted from the Center for Food Security and Public Health, Vaccine List, Classical Swine Fever. Available at: http://www.cfsph.iastate.edu/Vaccines/disease_list.php?disease=classical-swine-fever&lang=en

5.5 Vaccine Licensing

The USDA CVB, the USDA NVS, and other agencies may be involved in evaluating and purchasing vaccine antigen concentrates and/or finished routine or emergency use vaccines [93]. NVS may also contract with manufacturers for immediate access to existing stocks of licensed emergency use vaccines. Vaccines may be licensed by the CVB and distributed with a full product license, or they may receive a conditional biologics license for use in specific conditions, e.g., if the product will be used by or under the supervision of the USDA in an emergency animal disease outbreak [93].

For a vaccine to be given a full product license, the manufacturer must conduct extensive efficacy, purity and safety testing [93, 94]. Steps in the licensing of vaccines in the U.S. include a review of the data from the manufacturer to support the product and label claims; inspections of manufacturing processes and practices; confirmatory testing of the biological seeds, cells and product; post-licensing monitoring including inspections and random product testing; and post-marketing surveillance of product performance [93]. In standard licensing, the seed materials, product ingredients and final product must be

completely characterized and tested for purity. Safety and efficacy tests must also be done, and product stability as well as duration of immunity (DOI) must be evaluated. All of these steps may not be possible during an animal disease emergency. The USDA has mechanisms for expedited product approval, and can exempt products from some of the regulatory requirements for full product approval during emergencies [93]. However, every attempt is made by the CVB to establish a reasonable expectation of purity, safety, potency and efficacy prior to the use of any vaccine. In addition to potential harm to animal, human and environmental health, the risk of lawsuits if problems occur must be considered [93].

5.6 Experimental Vaccines

5.6.1 Chimeric Pestivirus Marker Vaccines

Researchers utilized several different approaches when creating chimeric pestivirus marker vaccines. Van Gennip et al. [95, 96] replaced antigenic regions of the CSFV with genes from the BVDV II strain 5250. These chimeric viruses protected animals against CSFV during challenge. The animals challenged with these chimeric viruses produced antibodies that could be discriminated from those produced by animals infected with the field strain using specific ELISAs [59, 95, 96].

The modified live vaccine CP7_E2alf was produced by replacing the E2 region of BVDV strain CP7 with the E2 region of CSFV strain Alfort 187 [96-98]. This vaccine protected against challenge and vaccinated animals were negative for anti-CSFV Erns antibodies when tested with its companion diagnostic test, the PRIONICS CSF-specific Erns antibody ELISA [59, 96]. The effectiveness of the C-strain vaccine was compared to CP7_E2alf, which was administered oronasally [99]. CP7_E2alf was isolated from the tonsil as early as 4 days following vaccination and induced an immune response lasting up to 98 days following oronasal administration. In comparison, the C-strain vaccine was isolated from the tonsil as early as 3 days following vaccination and also induced an immune response lasting up to 98 days [99].

Reimann et al. [100] constructed a new BVDV chimera utilizing the previously created CP7_E2alf. The chimeric pestivirus CP7_E1E2alf_TLA was created by substituting BVDV E1 and E2 into the E1 and E2 regions of CSFV strain Alford 187. The antigenic epitope CSFV-specific TAVSPTTLR was then exchanged with the E-2 epitope of BVDV strain CP7 in order to be able to differentiate vaccine from field strain when performing serology [100]. Following vaccination with CP7_E1E2alf_TLA and challenge with CSFV strain Koslov 28 days post-vaccination, pigs had a short increase in body temperature. This chimera was not able to protect pigs as effectively as the C-strain vaccine, and did not provide total differentiation between vaccinated animals and those infected with the field strain.

As only live vaccines can be administered orally, chimeric marker vaccines may be useful when attempting to immunize feral swine against CSFV when using baits [98].

Holinka et al. [101] reported the development of a CSFV antigenic marker live attenuated CSFV strain Flag T4v, containing a positive antigenic marker, synthetic Flag® epitope, and a negative marker created with the removal of an epitope recognized by monoclonal antibody WH303 (mAbWH303). It was created by combining RB-C22 [19] and T4[18] CSF Brescia viruses [59]. Flag T4v has been administered both intranasally and intramuscularly. Complete protection against CSF strain Brescia at 3 and 28 days post infection occurred when Flag T4v was administered intranasally and starting at 2 days post infection when administered intramuscularly [101]. Animals given FlagT4v can be differentiated from animals infected with wild CSFV, as those immunized will respond serologically against the Flag epitope [59, 101] and will not respond to the negative marker.

Another approach undergoing investigation has been to utilize viral vector systems with viruses such as pseudorabies (PRV) [80, 85, 102, 103], porcine adenovirus [104-107], and swinepox virus [96, 108].

When pigs have been immunized with pseudorabies vector system with glycoprotein E1 inserted from the CSFV, pigs were protected against both CSFV and PRV [80].

6. VACCINE MATCHING, POTENCY AND SAFETY

Summary

While vaccine matching is commonly used with Foot and Mouth Disease, the process isn't utilized with classical swine fever as strain variation requiring different vaccines for different strains does not occur with CSFV.

Vaccine potency is determined through a dose response study.

Overall, CSF LAV (Chinese lapinized strain (C, K or LPC), GPE strain and the Thiverval strain) vaccines are considered safe to be administered intramuscularly or orally to all ages of pigs including neonatal and pregnant swine.

Marker vaccines are generally considered to be low-risk for animal safety, aside from occasional tissue reactions at the injection site.

6.1 Vaccine Matching

Vaccine matching is used to determine whether a given vaccine is likely to provide good protection against a field strain. While vaccine matching is commonly used with Foot and Mouth Disease, the process is not utilized with classical swine fever as strain variation requiring different vaccines for different strains does not occur with CSFV.

6.2 Vaccine Potency

Potency is traditionally expressed as the number of 50 percent swine protective doses (PD_{50}) within each dose of vaccine recommended on the label. The PD_{50} determination is a dose response study. Two groups of 6-8 week old pigs, with 5 piglets per group, are used [34]. The groups are vaccinated intramuscularly with two different partial doses (a 1/40 and a 1/160 dilution). Two additional animals are nonvaccinated controls. All animals are challenged with 10^5 PID₅₀ (50% porcine infectious dose) of a CSF virulent strain administered intramuscularly 2 weeks after vaccination. Within two weeks, the nonvaccinated control animals should die. Using the numbers of animals that live and do not demonstrate any clinical signs due to CSF, statistical calculations will determine the number of PD_{50} in the vaccine [34]. As reviewed by Biront et al. [38], Leunen and Strobbe [109] vaccinated animals intramuscularly with the C-strain vaccine and challenged 14 days post vaccination with the Behring strain. Results of this study lead European Pharmacopeia to require a potency of at least 100 PD_{50} per dose. When animals were again challenged with the Behring strain by Biront et al. [38], animals vaccinated with 160 PD_{50} were protected by one week post vaccination according to the review by Blome et al. [53].

If a manufacturer can prove a 'distinct and reproducible relationship' between the amount of virus in their vaccine and the protection for the challenged pigs, the manufacturer may be allowed to replace the in vivo potency test with an in vitro cell infectivity assay [34].

6.3 Vaccine Safety

In general, safety assessments for vaccines vary with the type of vaccine (inactivated or live, bacterial or viral), the adjuvants used, and the history of similar products in use, as well as the dose, vaccine claims, usage regimen and animal factors such as the species [110]. The 'worst case' scenario is usually assessed even if it is unlikely, assuming that the product will be used at its maximum potency and quantity, in animals of the highest sensitivity. Safety concerns include both manufacturing errors and user errors that could cause problems [110].

Overall, CSF LAV (Chinese lapinized strain (C, K or LPC), GPE strain and the Thiverval strain) vaccines are considered safe to be administered intramuscularly or orally to all ages of pigs including neonatal and pregnant swine [59, 90, 111]. Marker vaccines are generally considered to be low-risk for animal safety [110], aside from occasional tissue reactions at the injection site [78, 86, 112, 113]. CSF E2 marker vaccines, however, are only given parenterally, not orally [111].

In the U.S. the USDA Center for Veterinary Biologics will determine the recommended ages for vaccine administration, whether it is approved for use in pregnant swine and recommended revaccination frequency. This information will accompany the vaccine.

Adjuvants and other vaccine ingredients may cause local or systemic reactions in some animals [110]. The E2 marker vaccine has produced a local tissue reaction at the injection site [86]. Contamination of vaccines by extraneous pathogens could also cause morbidity or mortality [110], for example a C-strain vaccine was contaminated with another pestivirus [57, 78]. Consideration should be given to the possibility of interactions with other vaccines [110].

Risks to people who administer or contact the vaccine should also be assessed. The LAV CSF vaccine will not replicate in humans. However, local reactions from oil adjuvants, other ingredients, or infection at the injection site may occur [110].

7. VACCINE WITHDRAWAL TIMES IN MEAT

Because vaccination does not usually result in harmful residues or immune responses that differ from natural immune responses, countries do not necessarily require a withdrawal period for the antigen component in a conventional vaccine, unless it is a live virus zoonotic agent [110]. Other vaccine components such as adjuvants and excipients must also be considered in the safety evaluation, and may require withdrawal periods [110]. Prior experiences with these components in other vaccines should be considered [110]. Marketed internationally, the two previously available CSFV marker vaccines both listed zero withdrawal times.

However, in the U.S., withdrawal times before animals may be slaughtered after vaccination with specific products are established by the USDA Center for Veterinary Biologics, and will be found on the vaccine label. Due to regulatory requirements, all vaccines for food animals in the U.S. must be labeled with a minimum slaughter withdrawal time of 21 days.

8. VACCINES AND DIVA TESTS AVAILABLE IN THE U.S.

In 2008, the National Veterinary Stockpile (NVS) CSFCWG [59] conducted an in-depth analysis of available measures to control and eradicate CSFV if an outbreak were to occur in the U.S. They recommended stockpiling CSF LAV Strain C vaccine and CSF E2 marker vaccine (Intervet) with the hope in the long term of adding a second generation CSF vaccine which is as effective as the CSF LAV vaccine strains but has DIVA capabilities. If marker vaccines in the NVS are used to control an outbreak, companion DIVA tests would need to be available also. Therefore, the CSFCWG also recommended stockpiling the Chekit CSF Marker ELISA (Intervet) as well as a PCR test, Nucleic acid extraction kits and supplies, and PCR reagents and supplies [59]. A long term goal for the NVS would be to have a pen-side test kit available for use during an outbreak to rapidly detect any CSFV field strain.

9. EFFECTS OF VACCINATION ON VIRUS TRANSMISSION

The main purpose of emergency vaccination is to end or reduce virus transmission. This can be accomplished by vaccines that increase the minimum infectious dose of virus, and/or decrease virus shedding from animals that become infected.

The reproduction ratio or R value estimates the ability of a vaccine to reduce transmission of the virus in a field situation. If vaccination decreases R to less than one, the epidemic will die out and only minor outbreaks are expected (however, some transmission is still expected to occur until the epidemic ends) [114]. If R remains higher than 1, there can be major outbreaks and the epidemic may continue to grow. Reproduction ratios can be estimated within herds (R₀) and between herds (R_h).

A baculovirus vector E2 marker vaccine produced by Moormann et al. [115] administered as a single dose prevented virus transmission to unvaccinated in-contact animals when challenged 3 weeks after vaccination. A transmission experiment was designed to estimate the R value of the virus. At one week after vaccination, the R value was >1, whereas in another challenge 2 weeks after vaccination, the R value was <1. Transplacental transmission of the challenge CSFV was prevented in 8 out of 9 animals when a single vaccination was administered; however, transmission to offspring was prevented when the sow received two vaccinations, then challenged 70 days after the second vaccination [115].

Dewulf et al. [30] compared a C-strain LAV vaccine and an E2 marker vaccine in preventing illness and virus transmission at 7 days after vaccination. The C-strain vaccine prevented illness and virus transmission in all pigs challenged via CSF inoculation, and prevented illness in vaccinated pigs in contact with CSFV-inoculated animals. However, all the pigs vaccinated with the E2 marker vaccine became clinically ill when challenged at 7 days and many of the vaccinated pigs in contact with the CSFV-inoculated animals became viremic [30].

Another concern during an outbreak is the infectivity of rendered animals. When animals are vaccinated with a LAV vaccine, then infected at least 4 days later with CSFV, the carcass has very little risk of infecting other animals with CSFV [111].

10. ONSET OF PROTECTIVE IMMUNITY

The onset of protective immunity varies between vaccination with LAV vaccines and E2 marker vaccine. Protective immunity can be induced within a few days when LAV strains C, GPE, Thrival and PAV-250 are utilized [59]. A single vaccination may protect animals by day 5-6 [90, 116] with neutralizing antibodies detectable by day 7-10 post vaccination [90]. While LAVs induce immunity within a few days, E2 marker vaccines may not protect animals from challenge until two to three weeks after vaccination with a single injection [59, 86, 115, 117] although a second injection is recommended.

The onset of protection for chimeric virus vaccines may differ with route of administration. Holinka et al. [101] investigated intranasal and intramuscular administration of FlagT4v. Pigs were protected when challenged with CSFV starting at 2 days following intramuscular injection of FlagT4v, whereas intranasal administration induced complete protection when challenged at days 3 and 28 [101].

11. DURATION OF IMMUNITY

Duration of immunity for LAV vaccines varies from 10 months with oral administration [118] to lifelong CSF immunity with a single intramuscular vaccination [59, 78, 90]. E2 marker vaccines, however, induce a shorter immunity of approximately 6 to 13 months [59, 84, 86, 115, 117].

12. LIMITATIONS OF EXPERIMENTAL STUDIES

Extrapolation from experimental studies to the field situation must be done with care. For example, the R value can be affected by the density of animals and their interactions, as well as the infectivity and susceptibility of individual animals ([119] cited in [120]). Vaccine efficacy can vary due to concurrent diseases and other factors, and animals will be exposed to field viruses at different times after vaccination, rather than at a defined interval. Epidemics are also unpredictable, and experiments can never reproduce all possibilities.

13. FIELD EXPERIENCES WITH CSF VACCINATION

Summary

Vaccines that meet the standards for safety and efficacy and are administered correctly have the potential to decrease circulation of the virus, thereby reducing economic losses in different situations.

Countries have utilized a variety of approaches to control or eradicate CSFV. Several countries have utilized LAV vaccines in domestic swine including Brazil, Bulgaria, Israel, Korea, Mexico, Romania and the United States.

Bulgaria utilized LAV vaccine in an emergency vaccination protocol, including the vaccination of wild boars.

LAV vaccine was utilized for years in Romania and Brazil. In Romania, vaccine was mandatory from 1974 to 2001, then not allowed, but emergency vaccination was reinstated in 2006. In 2007, oral LAV vaccine contained in baits was also used to vaccinate the wild boar population. In Brazil, the country was divided into different areas and vaccine continues to be used in endemic areas.

Israel only utilized a small number of vaccine doses in 2010.

Various approaches have been tested in Germany to administer oral LAV vaccine in baits to feral swine.

Mexico utilized both the commercially available marker vaccine Porcilis Pesti manufactured by Intervet in 1998 and LAV vaccines in 2001 in an attempt to control spread of CSFV.

LAV vaccine was used successfully to eradicate CSFV in Korea by 2001; however, when the country re-broke with CSFV in April 2002, use of emergency CSF vaccination was utilized in areas surrounding the outbreaks while stamping-out was also conducted in the infected areas. In 2003, the Republic of Korea instituted a national vaccination policy.

Great Britain and the Netherlands both successfully eradicated CSFV without the use of vaccination, although the outbreaks vary greatly in the extent to which the countries were affected. In 2000, Great Britain culled 75,000 pigs to control disease spread while in 1997-1998 the Netherlands destroyed more than 11 million pigs to eradicate CSFV.

13.1 Brazil

From approximately 1980-1990, vaccination with the C-strain LAV vaccine was extensively utilized [121]. However, in 1992, a new plan was implemented as eradication appeared to be impossible with the current approach. The difficulty in eradicating CSFV from Brazil with the earlier program was mainly due to the large size of the country [121]. The new plan included subdividing Brazil into three areas. Area I was made up of the three southern states. This area was free of CSFV, and vaccination was prohibited. Area II included states with endemic CSFV. These states had a relatively large swine population, and vaccination was made mandatory. The remainder of the country comprised Area III. In Area III, raising swine was not viewed as significant, so vaccination was not made mandatory [122]. The swine industry stakeholders from each of the states in Area I created a private fund to cover expenses if herd depopulation was needed during an outbreak [122]. This plan was very successful, and by 1998, the use of CSF vaccine was prohibited in all of Brazil except when directed by the Ministry of Agriculture [123].

In 2001, regions in the south, southwest, central-west and the states of Bahia and Sergipe were declared CSFV free [121]. At that time, the country was divided into two regions - one region had been free of

CSFV since 1998 and in the second region, CSFV is endemic [121]. About 75% of Brazil's swine production occurs in the CSF Free zone [124]. Although Brazil was trying to eliminate the use of CSF vaccine, several States in the Northeast region (considered the CSF Infected zone) utilized live attenuated vaccines in 2001 to control CSF outbreaks [124]. During 2001, twelve CSF outbreaks occurred, zero in 2002 and four in 2003 all in the CSF Infected zone [124].

Although no outbreaks were reported in 2004, during 2006-2008, CSF outbreaks continued to occur outside of the area free of CSF. Outbreaks were resolved utilizing disinfection, quarantine and stamping-out [125]. In February 2009, Brazil notified the OIE of a CSF case in a modern swine facility outside of the area free of CSF [125]. The report stated that vaccine was not used as vaccine is prohibited in the infected area as well as throughout the country of Brazil. However, following additional outbreaks during April and May 2009, the Animal Health Department approved the use of vaccine for pigs in the State of Rio Grande do Norte [125]. During 2009, Brazil utilized an attenuated live vaccine to control confirmed CSF outbreaks in their area considered CSF endemic. Over 90,000 pigs received the vaccine [125]. Vaccine was not utilized in the area free of CSF, and remains prohibited in the rest of the country of Brazil.

13.2 Bulgaria

In March 2000, four month old pigs were diagnosed with CSF in eastern Bulgaria [40]. In 2006, Bulgaria received approval to utilize emergency vaccination to eradicate CSFV [10]. Backyard pigs tested positive in May 2008. A control program, including vaccination in wild boar, was implemented for all of Bulgaria in an effort to eradicate CSFV in the wild boar population [126]. In spite of utilizing vaccine, in September 2009, CSF was diagnosed in wild boar in northern Bulgaria close to the Romania border.

13.3 Germany

Between 1990-1998, 424 CSF outbreaks were reported in domestic pigs in Germany with additional cases diagnosed in wild boars [36]. Available information suggests direct or indirect contact with infected wild boars or swill feeding was responsible for a majority of outbreaks in domestic pigs.

In February 2002, the European Commission (2002/161/EC) [127] approved the use of CSF vaccine in feral pigs by oral immunization in specific areas of Germany. Those areas where vaccine was used were modified in October 2002 [128] and February 2003 [129]. Oral baits containing a LAV vaccine based on the 'C' strain were utilized to immunize wild boar [129].

13.4 Great Britain

During the last CSF outbreak in the United Kingdom in 2000, 16 farms were affected with about 75,000 pigs culled to control disease spread [130].

Article 19 of EU Directive 2001/89/EC [9] authorizes the use of CSF vaccine if needed to control disease spread when used in conjunction with other control measures such as stamping-out and disinfection. Therefore, according to the Classical Swine Fever Disease Control Strategy for Great Britain, "the policy is not to vaccinate against CSF, although it is available should the disease situation require it"[130]. If it is determined that CSF vaccine needs to be utilized to eradicate the disease in Great Britain, an emergency vaccination plan must be submitted to and approved by the European Commission [9]. Vaccine could then be acquired from the European Union bank [130].

13.5 Israel

According to the OIE website [131], CSF infection was confirmed in both domestic and wild animals in 2009. Domestic animals tested positive on a farm near the Lebanon border. Wild boars found dead in the area also tested positive for CSF antigen, therefore, the wild boars were suspected as a possible source of infection for the domestic herd. Fomites were also listed as a possible source. Vaccination, modified

stamping-out and disinfection were listed as measures to be taken to eradicate CSFV [132]. Israel did not report using any CSF vaccine to the OIE during 2009, but utilized 500 doses of CSF vaccine during 2010 [133].

13.6 Mexico

In 1996, Mexico was divided into three zones 1) the area free of CSF, 2) the eradication area, and 3) the control area. In the free and eradication areas, CSF vaccine was prohibited, whereas CSF vaccine was mandatory in the control area [134]. However, in 1998 a CSF outbreak occurred in the eradication area [134], an area free of CSFV since 1996. CSF infected pigs from the backyard pig population in the control area in Mexico were believed to be the source of the infection. Producers approached the government asking for approval of the commercially available marker vaccine Porcilis Pesti manufactured by Merck [134, 135]. The vaccine was registered for use in 1998, and vaccination with the marker vaccine was allowed in the eradication area to prevent spread of CSFV [135]. Martens et al. [135] studied the use of this vaccine in the field during this time. They concluded that the vaccine was useful in reducing clinical signs and limiting the spread of new outbreaks.

In August 1999, a CSF outbreak was reported in San Carlos, along the United States-Mexican border [136]. San Carlos is in the State of Tamaulipas which was thought to be CSF-free. The CSF infected pigs originated from a family production unit, which commonly includes a few head of free-ranging animals which may be fed swill [136]. The outbreak was eradicated using several control measures, some including quarantine, stamping-out and stop movement, but vaccine was not utilized [136].

However, by 2000, CSF outbreaks were occurring in both the eradication area and control areas in Mexico and CSF LAV vaccine was being used regularly to control these outbreaks [134]. In 2001, Mexico was then divided into just two areas with the northern-most states remaining CSF free while in the rest of the country CSF had become endemic. Infection and movement of backyard pigs was thought to be the main reason for CSFV spread in Mexico and the only way to eradicate CSFV from Mexico would be to focus on this population [134].

According to the OIE website [137], Mexico had 15 outbreaks from 2002-2004, two new outbreaks of CSF in 2005, no CSF cases in 2006-2008, 4 new outbreaks in 2009, and free of CSF during 2010-2011. In 2009, the 704 susceptible animals were destroyed.

13.7 Netherlands

The Netherlands had been free of CSFV for more than 10 years, until CSFV was detected in the Netherlands on February 4, 1997 in a pig dense area. By the time it was detected, it was estimated to have been in the country for at least 5-7 weeks [138]. During the outbreak which lasted from February 1997 to May 1998, more than 11 million pigs were destroyed and more than 13,000 farms involved [5]. At the time of the outbreak, vaccination for CSF was not allowed in the Netherlands unless special approval was granted for its use in an emergency vaccination program [9] in conjunction with other control measures. Only the Ministry of Agriculture can decide if vaccines will be utilized, which vaccines would be used and how they would be used within a program [139]. Only veterinarians can administer the CSF vaccine and only registered CSF vaccines may be used. Stamping-out and stop movement orders were the main tools used to eradicate CSFV from the Netherlands during this outbreak [8].

13.8 Republic of Korea

CSF was first reported in the Republic of Korea in 1908, but by 1947 CSFV had become endemic with many outbreaks to follow over the next several years [140]. In 1967, a tissue culture attenuated live vaccine, LOM-850 vaccine, was utilized in Korea which was responsible for a large decrease in the number of CSF cases [140]. In 1996, the country launched an effort to eradicate CSFV. The CSF

eradication campaign consisted of three stages. The goal of the first stage was to decrease the number of outbreaks, and the approach was to increase vaccine usage and culling of infected animals [74]. The second stage included mandatory vaccination and testing. In the third and final stage, vaccination would be prohibited as the country would move to CSF free status. The campaign was successful as the number of CSF outbreaks decreased until no cases were reported in 2000 and 2001. On December 1, 2001, CSF vaccination was prohibited and the OIE was notified as South Korea declared CSF-free status [74].

Korea's success was short lived, however. In April 2002, two CSF outbreaks were reported with several more cases to follow later in the year [74]. In December 2002, the use of emergency CSF vaccination was utilized in areas surrounding the outbreaks while stamping-out was also conducted in the infected areas. While the outbreaks appeared contained, 65 new CSF outbreaks again occurred in March and May 2003 [74]. A majority of these outbreaks were connected to the purchase of young breeding animals from a farm involved in the December 2002 outbreaks. Korea decided at that time to once again resume a national vaccination policy [74].

13.9 Romania

From 1974 to 2001, CSF vaccination with LAV vaccines in Romania was mandatory. During this time, only one CSF outbreak occurred in Romania, diagnosed in 2001 [141]. Starting January 1, 2002, vaccination against CSF was no longer allowed in western Romania. Following this ruling, the first CSF outbreak occurred in March 2002. During 2002, 38 cases were diagnosed [141]. Then over the next two years, the number of CSF cases remained fairly steady with 155 in 2003, and 182 in 2004. However, in 2005 and 2006 the number of CSF cases increased greatly with 1072 and 1393 cases respectively [141].

In December 2006, Romania received approval to reinstate emergency vaccination against CSF with the goal of CSF eradication [10]. During 2007 and 2008, the vaccination program included vaccination of domestic pigs in noncommercial holdings with LAV vaccine by injection and wild boar using baits, while a marker vaccine would be utilized by commercial pig herds [142]. The vaccination program was viewed as successful as virus spread and clinical signs had been reduced and Romania reported no CSF outbreaks during 2008 [142]. Commission Decision 2008/897/EC placed financial limits to the amount of funding provided for vaccines for 2009 [143]. Following this decision, changes were made to the 2009 emergency vaccination protocol. Pigs in commercial holdings would no longer be vaccinated, while domestic pigs in noncommercial holdings would continue to receive the LAV vaccine injections and the wild boar population would receive LAV vaccine in baits. A total of 4,098,478 pigs were vaccinated in nonprofessional holdings for CSF in 2009. A total of 252,236 baits were distributed in an attempt to vaccinate feral swine and 6862 were recovered because they were not consumed [144]. In 2010, Romania stopped vaccination of domestic pigs, but continued to vaccinate wild boars within 20km of other countries [142].

13.10 United States

Beginning in the late 1800s and 1900s, swine producers throughout the U.S. utilized a variety of serums and vaccines in an attempt to control CSF [1]. As safer vaccines became available in the 1950s, states began to prohibit the use of virulent hog cholera virus with 29 states prohibiting its use by June 1959 [1]. Eradication of CSFV was authorized on September 6, 1961 [1]. Federal funds began to support the program during the summer of 1962, although funding was not always available at the level needed to support the program over the years. During the early years of the eradication program, improvements were made to diagnostic procedures as well as establishing reporting systems and coordinating communications among all states. Each state reported their phase of progress from I to IV. The phases were established as follows: Phase I- Preparation; Phase II- Reduction of Incidence; Phase III- Elimination of Outbreaks; and Phase IV- Protection Against Reinfection [1]. By January 1, 1975, all states reported as Phase IV.

Although hog cholera vaccines were extensively utilized before the eradication program and during its early stages, as progress continued with diagnostic procedures and states reporting during the 1960s, the use of hog cholera vaccines were beginning to be phased out by 1969 and 1970 [1]. With objections to the phase out of CSF vaccine usage, unauthorized use of bovine virus diarrhea vaccine was being reported in swine. By 1969, eight states had prohibited the use of all CSF vaccines while 33 states reported prohibiting modified live virus CSF vaccines usage only [1]. Vaccine usage was addressed on the national level on May 24, 1969 when the USDA prohibited the interstate movement of CSF modified live virus vaccine after July 1, 1969 with the goal of eliminating the usage of all CSF vaccines by January 1, 1970.

Feral swine were infected in Florida in 1968 and 1969. Trapping, testing and removal of infected swine was successful and vaccine was not used to eliminate CSFV from the feral swine population [1].

With the elimination of CSF vaccine usage, additional measures were more aggressively utilized to eradicate the disease including quarantine and euthanasia of infected animals. Finally, in 1978, the U.S. was declared free of CSF [59]. At that time, the cost to eradicate CSF equaled more than \$140 million dollars, which would total more than \$540 million in 1999 [145].

14. STRATEGIES FOR VACCINE USE

Summary

In an eradication program, animals may be either “vaccinated-to-live” or “vaccinated-to-slaughter.” Both types of vaccination are expected to decrease virus transmission and decrease the short-term resources needed for carcass disposal, but will require the resources to implement, manage and maintain a vaccination, movement and permitting system for the vaccinates. All other factors being equal, vaccination-to-live would result in the most benefits for animal survival and domestic continuity of business. However, the detrimental effect on exports is likely to be greater.

Approaches to the application of CSF vaccination include prophylactic vaccination, emergency vaccination (which may be protective or suppressive), targeted vaccination, ring vaccination, barrier vaccination and blanket vaccination.

Because surveillance must be conducted to identify vaccinated animals that become infected, as well as to demonstrate the absence of virus transmission after the outbreak, the vaccination zone should be the smallest area necessary to control the outbreak. A variety of animal, virus and environmental factors must be considered in establishing an effective vaccination zone. Defining the size and shape of a vaccination zone in ring vaccination can be complex.

Consideration should be given to establishing a vaccination surveillance zone around the vaccination zone.

14.1 Vaccination-to-Live and Vaccination-to-Slaughter

In an eradication program, animals may be either “vaccinated-to-live” or “vaccinated-to-slaughter.” Animals that are “vaccinated-to-live” are allowed to live their normal lifespan unless they become infected. In contrast, animals that are “vaccinated-to-slaughter” are either slaughtered for human food consumption or killed and disposed of by some method. Both types of vaccination decrease the short-term resources required for carcass disposal, but will require resources to implement, manage and maintain a vaccination, movement and permitting system for the vaccinates. Both types of vaccination are also expected to suppress virus transmission. Vaccination-to-live could potentially decrease the number of animals that must be culled. All other factors being equal, vaccination-to-live would result in the most benefits for animal survival and domestic continuity of business. However, the detrimental effect on

exports is likely to be greater. According to Article 15.2.4 of the Terrestrial Animal Health Code, when a non-marker vaccine (e.g. LAV) is used, a country cannot declare CSF-free status until at least 3 months after the last case of CSF and after all vaccinated animals are slaughtered, or 12 months after the last case and after the last animal was vaccinated. If a marker vaccine is used, countries must wait at least 3 months after the last case if vaccinated animals are not slaughtered, or 12 months after the last case if no stamping-out policy was used. In reality it could be even longer, regardless of which vaccine is used, as use of a vaccination-to-live strategy may mean that vaccinated animals will continue to exist in breeding herds for years. [29]. If zones are set up in a country, it is possible that different zones could use a different vaccination strategy and have different waiting periods to regain free status.

14.2 Approaches to the Application of CSF Vaccination

In 2008, the NVS CSFCWG recommended the U.S. stockpile include CSF LAV vaccine to be used in infected and contact herds while the CSF E2 marker vaccines could be utilized in herds around the infected and contact herds to make a buffer to help prevent CSFV spread [59].

While several strategies can be used, EU member countries tend to utilize three different strategies:[59]

1. LAV CSF vaccines, particularly C strain, are used in endemic areas with feral swine and many small operations with backyard producers.
2. E2 marker vaccination programs are an option during a disease outbreak.
3. E2 marker vaccines and LAV are used in combination during a disease outbreak. Animals in the infected area are vaccinated with LAV vaccine as it provides protection more quickly and E2 vaccines are used in animals surrounding the area with a possible vaccination-to-live approach.

While E2 marker vaccines have been available in the past, the PORCILIS® PESTI vaccine is temporarily off the market due to technical issues. The Bayer vaccine is also not available at this time. However, according to the National Veterinary Stockpile Questions and Answers document [89], the NVS contains two vaccines. One is a LAV vaccine which can be administered either parenterally or orally. The second is a DIVA-compatible E2 antigen-based vaccine, which utilizes killed baculovirus vector technology. This vaccine would have to be administered parenterally only.

Under the subheadings below, different vaccination approaches are discussed. The NVS Questions and Answers document [89] includes two possible approaches. If the CSF outbreak is focal, using the inner ring vaccination program, the LAV vaccine could be injected into animals with the “vaccinate-to-kill” approach. The DIVA vaccine could be used in the outer “vaccinate-to-live” zone. The approach would be different if the CSF outbreak were widespread. In a widespread outbreak, the LAV vaccine may be administered to terminal market swine, and breeding stock injected with the DIVA vaccine.

14.2.1 Prophylactic Vaccination

Prophylactic (routine) vaccination is generally used only in endemic areas or regions at high risk for CSFV introduction, because it is a significant trade barrier for countries exporting animal products. LAV vaccines are often used.

14.2.2 Emergency Vaccination

Emergency vaccination (vaccination in the face of an outbreak) is usually conducted as reactive vaccination. In Romania in 2007, Commission Decision no. 2006/802/CE added the plan for emergency vaccination for all categories of pigs, in order to eradicate CSFV. During 2007 and 2008, the vaccination program included vaccination of domestic pigs in noncommercial holdings with LAV vaccine by injection and wild boar using baits, while a marker vaccine would be utilized by commercial pig herds [142]. The vaccination program was viewed as successful as virus spread and clinical signs had been reduced and Romania reported no CSF outbreaks during 2008 [142].

14.2.3 Protective Emergency Vaccination

Protective emergency vaccination, which is conducted among animals in uninfected areas, creates a zone of animals with reduced susceptibility around the infected area.

14.2.4 Suppressive (or “Damping Down”) Emergency Vaccination

Suppressive (or ‘damping down’) emergency vaccination is conducted in the infected area where the virus is already circulating. It is intended to reduce virus transmission, aid control efforts and prevent CSFV from spreading beyond the infected zone. Suppressive vaccination is likely to face a more severe virus challenge than protective vaccination: Infected animals may already be present on a farm in areas where this form of vaccination is used. In contrast, animals in uninfected areas (protective vaccination) are likely to be exposed to smaller amounts of virus in aerosols and on fomites.

14.2.5 Targeted Vaccination

Targeted vaccination attempts to protect specific groups of animals. Stamping out, as the sole eradication strategy, risks the destruction of rare species, rare breeds and high value genetic stock [146]. Targeted vaccination may be directed at uninfected animals of high value, which can include livestock with particularly valuable, rare or unusual genetic backgrounds, long-lived production animals, zoo animals or endangered species. Targeted vaccination can also be directed at uninfected areas where there is a high density of susceptible animals.

14.2.6 Ring Vaccination

Ring vaccination refers to a strategy of immunizing animals within a defined area around infected premises or infected zones. Its purpose is to reduce or prevent virus transmission from a focal outbreak to surrounding uninfected areas. Ring vaccination is most likely to be successful if foci of infection can be identified rapidly, before the virus can spread. It may not be appropriate in cases where the disease is widespread or contained in widely scattered foci, if the disease is difficult to identify, where there is a significant delay between infectivity and case confirmation, or where there is a significant delay between vaccine administration and the onset of protection.

In addition to stamping out infected herds and issuing a stop movement, immediate vaccination with the C-strain vaccine (or another LAV vaccine) may be conducted in a ring around an outbreak [78]. LAV vaccines induce a solid herd immunity 1–2 weeks earlier than E2 marker vaccines [78]. The program should include observation and surveillance of the vaccinated animals. If the vaccinated animals are not infected with the field CSFV strain, then the pigs can be slaughtered [78]. Whenever a LAV vaccine is used, export of pork and pork product restrictions needs to be considered.

14.2.7 Barrier Vaccination

Barrier vaccination is very similar in principle to ring vaccination; however, the vaccination zone is used to prevent the infection from spreading into the uninfected area from a neighboring country or region into the uninfected area, rather than to keep it from spreading outward from infected premises. Geographic and political features usually have an important influence on the shape and location of the vaccination zone.

14.2.8 Blanket Vaccination

Blanket (mass) vaccination can be conducted throughout an entire country or throughout an OIE-defined zone with a separate status. Countries are most likely to consider blanket vaccination when a disease becomes widespread. This form of vaccination can be carried out indefinitely in countries or zones defined as “CSF free with vaccination”; however, this designation affects trade status.

14.3 Establishing a Vaccination Zone

The vaccination zone should be the smallest area possible as vaccinated pigs may need to be destroyed in order to more quickly prove freedom from CSF [147]. Restrictions may need to be instituted to control the use of vaccine as well as pig movement when establishing a vaccination zone [130].

The size of vaccination zone may vary with the types of vaccines available, the density of domestic pigs in the area and if feral swine are present. For example, if the outbreak is in an area of high pig density, LAV vaccine may be used around the infected area while depopulation plans are being made[59]. The next step may be to vaccinate with E2 marker vaccine in an area around the original vaccination zone to act as a buffer.

In the U.S.:

- The **Containment Vaccination Zone** is an emergency vaccination zone within the CSF Control Area. Vaccination may be performed in the Infected Zone and/or the Buffer Zone.
- The **Protection Vaccination Zone** is an emergency vaccination zone outside the Control Area in the CSF-Free Area. Barrier vaccination is used in this zone to prevent CSFV from spreading into areas free of the virus.

More information on each of these strategies can be found in the APHIS Foreign Animal Disease Framework documents.

15. MODELING STUDIES AND VACCINATION

Summary

Models have limitations, but they may provide insights into the possible impacts of vaccination approaches in specific scenarios. Some models based on the 1997-98 outbreak in the Netherlands examined control strategies involving ring culling, ring vaccination utilizing various radii of 1 km, 2 km and 3km while another applied an economic evaluation. These models suggest that utilizing vaccination in a large radius may minimize the duration of the epidemic.

While models provide information as to what may happen during specific scenarios, they do have limitations. For example, mathematical models have been applied to assess the use of marker vaccines utilizing data from the 1997-1998 CSF outbreak in the Netherlands.

Backer et al. [148] utilized mathematical modeling to evaluate vaccination strategies utilizing data from the 1997-98 CSF outbreak in the Netherlands. The four control strategies included 1km ring culling, 1 km, 2 km and 3 km ring vaccination utilizing marker vaccine. The results indicated that 1 km ring culling had better results than 1 km vaccination while the 2 km and 3 km ring vaccination were more effective than culling or 1 km vaccination, or both at limiting the size and duration of the outbreaks[148]. The results may vary if U.S. data were utilized in the model as the size of U.S. operations and the densities differ from those in the Netherlands, however, the U.S. data also varies by region.

In 2009, Backer et al. [149] published a multilevel approach utilizing a large number of transmission experiments to parameterize the effect of vaccination on transmission between animals. Using the 2006 Dutch pig farming structure, the five control strategies compared included the EU required implementation of restriction zones and transport regulations, culling of detected infected herds and contact tracing (EU Council Directive 2001/89/EC); one preemptive ring culling strategy (in rings of 1 km radius around detected outbreaks); and three ring vaccination strategies (in rings of 1, 2 and 5 km radius) [149]. Findings indicated that a ring vaccination 2 km radius around an infected premises is as effective as ring culling in a 1 km radius [149].

The simulation results of the Backer et al. 2009 [149] study were utilized by Bergevoet et al. to devise an economic evaluation of the control strategies. Bergevoet et al. [150] developed a mathematical model describing the effects of marker vaccination and transmission of CSF virus between individual animals, pens and farms in the Netherlands [150].

While Bergevoet et al. [150] concluded that emergency vaccination can be an effective strategy when compared to pre-emptive culling to control CSF epidemics when a larger vaccination radius is used, Bergevoet pointed out that small outbreaks may occur more frequently on vaccinated farms. Therefore, frequency and type of diagnostics utilized needs to be determined with this in mind.

Information from the Bergevoet et al. [150] and Backer et al. [149] studies suggest that utilizing vaccination in a large radius may minimize the duration of the epidemic. Vaccination would address animal welfare concerns which arise when culling larger numbers of animals and would benefit the industry from an economic standpoint as vaccination would help reduce the duration of the outbreak. However, depending on the number of animals within the proposed area of ring vaccination, the number of vaccine doses available may be a limiting factor.

Paarlberg et al. [7] investigated two possible outcomes if the U.S. swine herd were infected with CSF. In this model, 11 million pigs are destroyed, export of live animals is halted, and domestic consumption falls by 1%. In the first scenario, grower/finisher pigs are more heavily affected whereas in the second scenario, the breeding herd is infected. Estimated losses range from \$2.6 to \$4.1 billion. This model did not include the use of vaccine as a tool to control the CSF outbreak.

In 2008, CSFCWG used another model, the quantitative Kemper-Trego (KT) decision model, to evaluate available vaccines and diagnostics [59]. The vaccine ideally needs to prevent transmission, be efficacious in all ages of animals, provide immunity for one year, prove safe in all pigs to be vaccinated, one dose administration, to be able to manufacture quickly to be able to provide when needed, possess an expiration date of at least 24 months, protect pigs in seven days or less, have an accompanying DIVA test, have a short withdrawal period and have a reasonable price [59]. Through this analysis, CSFCWG determined that while the commercially available CSF vaccines are safe and efficacious, they do need to be improved. When using serology, pigs vaccinated with LAV cannot be differentiated from animals infected with CSFV. Commercial recombinant marker vaccines, which are currently unavailable, do not induce protection earlier than 15 days post-vaccination [59].

16. MOVEMENT RESTRICTIONS AND VACCINATION

Movement restrictions may be utilized in combination with vaccination to limit the spread of CSFV. However, the use of vaccination without movement restrictions may be less beneficial unless the infection is already extensive.

Although vaccination was not utilized during the 1997-98 CSF outbreak in the Netherlands, animals were not allowed to be transported within a 10km radius of the infected farm [8]. Empty animal transporters were not even allowed movement within this zone. After a testing period of 7 days to determine CSF infection within the zone, the transport ban was limited to the movement of pigs and pig manure [8]. The extent of the transport ban would change depending on the number of infections occurring outside of the initial zone of infection.

In Mexico in the 1990s, pigs and pork products were not allowed movement from the endemic control area where CSF vaccine was mandatory into either the eradication area in which CSF had been eliminated and vaccine use was prohibited or the areas free of CSF [134]. However, in Mexico this was difficult to enforce as low market prices in the control areas encouraged smuggling live animals into the eradication

area. Vaccine was utilized in the control areas in Mexico; however, if vaccine was not administered correctly, these pigs could have served as a source of infection in the eradication area. Biosecurity is still a very important component to any CSF vaccine program. Even with CSF vaccine usage, CSF has spread when good biosecurity practices were not followed [134].

17. VACCINE SELECTION

In 2008, the National Veterinary Stockpile CSFCWG recommended the CSF LAV Strain C vaccine and the CSF E2 marker vaccine (Merck Intervet) to be the vaccines stockpiled while the long term goal is to develop second generation CSF vaccine that has the efficacy of CSF LAV vaccine strains with validated DIVA capabilities [59].

18. VACCINE ADMINISTRATION

LAV vaccines may be administered either orally or by injection. When administering to domestic pigs, the vaccine is given by injection whereas feral swine are administered vaccine through the use of baits. Injection is the only route to administer E2 marker vaccines.

When vaccines are administered to domestic pigs, many times animals are crowded to a tight pen and the vaccine is administered without individual animal restraint. When this occurs, not all animals may receive the correct dose as animals may move while the vaccine is being administered. Training vaccination teams would ensure more accurate vaccine administration [151].

Kaden et al. [76] studied the use of administering oral vaccination to wild boar in baits in field trials from 1993-1995. Animals initially received 2 doses approximately 14 days apart with booster doses every 6 months. While the overall rate of uptake of the baits was between 85-100%, less than 50% of the younger animals took the baits and became immunized. Rossi et al. [77] concluded that number of baits delivered per wild boar neither affected the proportion of immune animals nor the intensity of infection, which suggests that increasing the baiting distribution did not increase vaccination effectiveness.

Anytime vaccines are used in a manner that is not in accordance with the approved label directions, problems may occur. In Thailand, the C-strain vaccine was used in combination with a live gI-deleted PRV vaccine and administered as a single dose[152]. Pigs were protected against CSF if they were immunized with the combination PRV/CSF vaccine; however, they demonstrated a reduced CSF-specific cellular immune response compared to those pigs which were vaccinated with the CSF product only. More pathological changes were also documented in these pigs when compared to pigs receiving the CSF vaccine only [152].

19. MATERNAL ANTIBODIES

Maternal antibodies may complicate CSF control during an outbreak. Coggins [153] reported when pigs are not exposed themselves to CSFV, maternal antibodies will decline with approximately a 2 week half-life. Therefore, pigs with a high titer would not clear the antibodies until 12 to 14 weeks of age. Biront et al. [38] vaccinated and challenged piglets born from vaccinated and non-vaccinated dams. Virus was isolated in piglets with maternal antibodies, vaccinated at two weeks of age and challenged 1 week later. However, no virus was isolated in 23 of 25 pigs without maternal antibodies, vaccinated and challenged at the same time. While this study by Biront et al. and one conducted by Terpstra [154]both demonstrated that pigs with maternal antibodies may survive a CSF infection, Biront et al. suggests that these pigs may also shed CSFV for a limited time. The amount of maternal antibody may also affect the vaccination response. Vandeputte et al. [155] determined pigs with a higher maternal antibody titer when vaccinated had a stronger inhibition than those with a low level of maternal antibodies. Virus was detected for a greater length of time in animals vaccinated in the face of high maternal antibody versus their unvaccinated counterparts; whereas virus replication was prevented in vaccinated animals with low

maternal antibody levels [38]. When maternal antibodies are a concern, a general recommendation may include delaying the vaccination of young pigs until 6 weeks of age or older [78].

If immunizing pigs with an E2 marker vaccine, two doses may be needed to protect pigs if they have a low level of maternal antibodies. In Thailand, Damrongwatanapokin et al. [156] vaccinated pigs with a low level of maternal antibody using E2 marker vaccine. Following CSF challenge 14 days post vaccination, the pigs developed clinical signs of CSF infection and all died within 18 days post inoculation.

20. LIMITATIONS OF VACCINATION

Optimal protection of each individual animal is not usually possible during mass vaccination [157]. The level of immunity in each animal will be influenced by vaccine factors including effectiveness of vaccine administration (e.g., the maintenance of an effective cold chain and proper administration) and the animal's immune state such as the influence of maternal antibodies or immunosuppression (parasitism, poor nutrition, stress, etc.). Animals may also be exposed to the field strain before they have time to develop protective immunity.

20.1 Monitoring for Vaccination Coverage and Efficacy

Different diagnostic tests can be utilized depending on when the test is to be performed in relation to when the animal was vaccinated. For example, PCR would be most reliable in testing vaccine coverage if blood is tested within 14 days after MLV administration and tonsil tested within 42 days [111].

21. IDENTIFICATION OF VACCINATED ANIMALS

Vaccinated animals need to be permanently identified. Countries vary with how they identify animals. Recommendations in Australia included that all animals should be permanently identified in case a vaccination-to-kill policy is adopted in which all vaccinated animals would be destroyed [147]. In the Netherlands when use of the CSF vaccine was mandatory, animals were identified by ear tags [78].

In the U.S., many forms of identification are utilized for permanent identification such as ear tattoos and ear notches or semi-permanent ear tags. Which form would be utilized hasn't been determined. In the case of an introduction of foot and mouth disease, vaccinated animals must be permanently identified, using an official North American Foot and Mouth Disease Vaccine Bank pink metal ear tag with individual identification.

22. LOGISTICAL AND ECONOMIC CONSIDERATIONS IN THE DECISION TO VACCINATE

Summary

The technical feasibility of vaccination and funding for a vaccination campaign should be assessed before deciding to vaccinate. The assessment should include the availability of sufficient supplies of an effective and safe vaccine; the availability of DIVA tests (if applicable); the logistics of vaccine administration; and the resources needed for associated activities including individual animal identification, traceability, movement permitting and serosurveillance to prove freedom from disease. The swine density in the area of the outbreak will influence the use of vaccination. For example, a large number of vaccine doses would be needed if ring vaccination were to occur in a swine dense area.

With over 625,000 swine in trucks on the road each day, CSFV has the potential to be transmitted over several sites. A large number of sites affected will influence the decision whether or not to utilize CSF vaccine.

Disease transmission can be more difficult to control during the cold winter months as disinfecting vehicles, trucks and other fomites can be challenging. Vaccine may be needed to help reduce infectious dose even though strict biosecurity still needs to be attempted.

Feral swine are increasing in numbers across the U.S. The potential contact between feral and domestic swine endangers the health of the domestic herd. If feral swine become infected with CSFV, oral vaccination with a LAV vaccine may be beneficial.

The pros and cons of vaccination compared to pre-emptive culling should be considered. Considerations include the effects on trade and exports, market shocks, potential restrictions on marketing products from vaccinated animals, the types of stakeholders affected (e.g., small-scale operators with limited safety nets vs. large-scale operators), the extent of the outbreak and other factors such as the disruption of tourism or impacts on local economies.

Consideration should be given to whether genetically irreplaceable stock, endangered species or other unusually valuable animals can be successfully protected with biosecurity measures, and whether vaccination would be beneficial. Their degree of isolation from livestock should be part of this analysis.

Countries that eradicate CSFV by stamping out, without using vaccination, can declare to be CSF-free 3 months after the last case. If vaccination-to-kill is part of the eradication campaign, the country must wait until 3 months after all vaccinated animals have been slaughtered. If a vaccine is used in which infected animals can be distinguished from vaccinated animals and the test to be used is validated by OIE standards, the country again must wait until 3 months after the last case. If a country chooses to use vaccine in which vaccinated animals cannot be distinguished from infected animals, the country must wait 12 months after the last vaccination as long as no outbreaks are also reported during those 12 months.

22.1 Technical Feasibility of Vaccination

To conduct an effective vaccination campaign, an effective and safe vaccine must be available, and the vaccine supply (and DIVA testing, if utilized) must be sufficient to carry out the vaccination strategy in a timely manner. The vaccine and vaccination strategy should be expected to provide immunity quickly enough to stop or reduce virus transmission [12]. Consideration should also be given to whether animals would need to be vaccinated more than once (depending if LAV or E2 marker vaccine are utilized), and whether the duration of immunity from the vaccine is acceptable. If animals are infected in a swine dense area, are sufficient number of vaccination teams available to actually administer the vaccine and could this be done following biosecurity guidelines so as not to spread CSFV? Do laboratories have enough diagnostic capacity to perform DIVA testing if a marker vaccine is utilized [12]? Slaughter and disposal capacity also needs to be considered if a vaccination-slaughter program is implemented. Additional resources also need to be considered for associated activities including individual animal identification, traceability and movement permitting.

22.2 Epidemiological Considerations

Extreme weather conditions may play a role both in disease transmission and disease response efforts. During the 1997-1998 CSF outbreak in the Netherlands, transportation vehicles were believed to play a role in virus transmission as approximately 39 farms were believed to be infected before measures were taken to eliminate CSFV [51]. The outbreak occurred during the winter months at a time when the extreme cold may have affected people's ability to properly clean and disinfect the transport vehicles [51]. This possible breach in biosecurity could be a problem in the northern U.S., also, facilitating CSFV transmission during response efforts. Controlling disease spread while officials or vaccination teams leave a CSF positive site could pose a problem during the winter months.

The distance animals are transported can play a role in disease spread. In Europe, the introduction of a single common market has led to an increase in the distance pigs are transported [31]. This increased transportation distance in Europe can be correlated with the increase in the number of pigs currently moved daily in the U.S as well as the distance they are transported. Hundreds of thousands of pigs are being moved daily in the U.S. Conservative industry estimates place over 625,000 swine in trucks on the road each day [2]. Transportation could facilitate disease spread within the U.S. The distance animals are transported may influence the numbers of animals to receive the CSF vaccine.

The U.S. has many swine dense areas. If a herd or herds in one of these areas becomes infected with CSFV, a vaccination zone may include a large number of animals. The number of vaccine doses needed to vaccinate all the animals within the zone may itself be a limiting factor. Density of pig herds may be an important predictor of area spread. When analyzing the 1997-98 outbreak in the Netherlands, Benard et al. [158] determined a positive association between higher pig densities and local spread concerning disease transmission. This is important when preemptive slaughter is utilized to decrease pig densities and therefore, local spread.

The increased number of feral swine in many parts of the U.S. presents a disease threat to domestic swine. Contact between domestic and feral swine needs to be prevented. Feral swine have infected domestic swine in Germany [36] and Italy [159]. When CSFV has infected feral swine, oral immunization by using baits has been carried out during spring, summer and autumn [160]. During each season, baits are distributed twice at four week intervals [160]. Appropriate bait location and banning hunting of feral swine both need to be addressed if a vaccination program is to be successful in feral swine [160].

Other diseases circulating in the swine herd may influence the success of a CSF vaccination program. Suradhat [116] demonstrated when CSFV vaccinated pigs are co-infected with PRV when challenged with CSFV, fatal CSFV infection has resulted. In the United States, PRRSv has impacted production and could interfere with CSFV in our domestic swine. Suradhat et al. [116] investigated the possible interference of PRRSv with CSF vaccination and demonstrated when pigs are infected with PRRSv prior to vaccination with C-Strain vaccine, PRRSv infection may cause a vaccine failure.

22.3 Economic Viability of Vaccination

Economic viability plays an important role in the decision to vaccinate. There must be sufficient funding for the purchase of the vaccine, vaccine delivery and administration, and individual animal identification. In addition, funding must be provided for follow on traceability of the vaccinated animals and serosurveillance to prove freedom from disease.

The direct costs of vaccination include:

- Investment costs – e.g., vaccine development, vaccine availability and vaccine delivery infrastructure [161]
- Variable or recurrent costs including the cost of vaccines and delivery [161]
- Costs to identify vaccinated animals, permit their movement, and conduct serosurveillance to prove freedom from disease (in a vaccinate-to-live strategy)

There may also be some indirect costs from vaccination such as lost productivity caused by stress to animals, disruptions of agricultural routines, and adverse reactions to the vaccine [161].

The pros and cons of vaccination compared to pre-emptive culling should be considered. Culling herds that were never infected can cause economic losses without necessarily affecting disease spread.

However, blanket vaccination or inappropriately targeted vaccination is expensive, and there is an increased risk that infected animals will not be detected because clinical signs may be suppressed [162].

The overall impact of vaccination on international trade in livestock products, including longer term impacts on trade, is an important consideration for CSF. Vaccination is expected to be most beneficial when the outbreak ends sooner, or when vaccination allows the most stringent disease control measures to be carried out in a limited area [161]. It is also expected to be beneficial if it impacts a livestock sector in an area where there will be a limited effect on exports (e.g., zoning will be possible/practical). If the outbreak can be stopped with rapid culling, there is likely to be short-term distress but little long-term effect on livelihoods, especially if indemnity can be provided [161]. However, if culling is more widespread or the disease is out of control, vaccination may save livelihoods [161].

Vaccination is likely to be beneficial to livelihoods when it can:

- Provide effective disease control with little depopulation, especially if indemnity is not available for culled animals [161]
- Prevent national markets from being disrupted or rapidly restore them [161]
- Minimize other economically important factors such as the disruption of tourism or impacts on local economies [161]
- Reduce the time export markets are lost

Vaccination may be particularly beneficial to small-scale operators whose safety nets are limited [161]. If stamping-out is used, it is possible for culling to have a minimal effect on the national economy while having a significant effect on the livelihoods of the people who are directly affected, especially smallholders and small-scale traders who depend on regular cash flow from agriculture. Although indemnity may be available for animals that must be destroyed, it rarely covers the cost of lost production, time and cash flow [161]. The emotional impact of the destruction of apparently healthy animals should also be taken into consideration [161]. In the U.S., diseases have been controlled effectively in the past by culling infected and exposed animals, but there have been changes in agricultural practices, such as increased herd sizes, which may make the impact greater [93].

Consideration of market shocks should be part of the economic analysis. Market shocks can result from loss of consumer confidence (decreased demand), very severe culling or the closing of markets [161]. Unless consumers can be persuaded that products from vaccinated animals are safe, there may still be market shocks from consumer fear even if the disease itself is controlled by vaccination. Consideration should be given to whether meat and other products from vaccinated animals can be used, and whether they will need to be treated (because vaccination might mask the presence of virus) before they are allowed into markets. If export markets are affected by vaccination, domestic markets can be affected, because animal products that were once exported may be sold within the country, lowering prices [161]. Producers for domestic markets can also be affected by quarantines. If animals are larger than normal weight and/or are released into the market in a short period after quarantine is lifted, prices may be lower [161]. The cost of keeping and feeding animals through the quarantine period should also be taken into consideration.

During modeling of the 1997-1998 outbreak in the Netherlands, the epidemiological and economic calculations show that - if vaccination is chosen - vaccination within a radius of 2 to 5km is preferred to vaccination within a radius of 1km [150].

22.4 Vaccination of Genetically Irreplaceable Stock, Endangered Species or Other Unusually Valuable Animals

Consideration should be given to whether these animals can be successfully protected with biosecurity measures, and whether vaccination would be beneficial. Their degree of isolation from livestock should be part of this analysis.

22.5 Effect of Vaccination on Regaining OIE CSF-Free Status

According to the OIE, countries that eradicate CSFV by stamping-out, without using vaccination, can declare CSF-free status 3 months after the last case [29]. If vaccination-to-kill is part of the eradication campaign, the country must wait until 3 months after all vaccinated animals have been slaughtered. If a vaccine is used in which infected animals can be distinguished from vaccinated animals and the test to be used is validated by OIE standards, the country again must wait until 3 months after the last case. If a country chooses to use vaccine in which vaccinated animals cannot be distinguished from infected animals, the country must wait 12 months after the last vaccination as long as no outbreaks are also reported during those 12 months.

In 1996, Korea implemented a three stage CSF eradication program. While vaccination was a part of the program initially, CSF vaccination was prohibited during the final stage. Finally, on December 1, 2001, their CSF-free status was declared; although it was short lived as Korea re-broke with CSF in April 2002 [74].

CSF eradication programs may include the use of CSF vaccination for domestic swine, feral swine or both domestic and feral. Of course, the use of CSF vaccine in either of these populations will affect regaining OIE CSF-Free status. For example in 2010, Romania stopped vaccination of domestic pigs, but continued to vaccinate wild boars within 20km of other countries; therefore, with the use of CSF vaccine in feral pigs, Romania couldn't declare CSF-free status.

23. VACCINATION IN ZOOS AND SPECIAL COLLECTIONS

According to Article 5 of European Directive 2001/89/EC [9], in the European Union, if a CSF outbreak affects pigs kept for scientific purposes or if they are a rare breed in a laboratory, zoo, wildlife park or fenced area, officials may be exempt from killing these infected animals. Officials could also include these animals in an emergency vaccination plan request to the European Commission asking that these animals be vaccinated during an outbreak.

24. PUBLIC ACCEPTABILITY OF VACCINATION AS A COMPONENT OF CSF ERADICATION

Summary

Vaccines improve animal welfare or well-being as well as protecting animal health. Vaccines can be used to help improve animal welfare and productivity for the benefit of the producer as well as food safety and food security for the consumer. Attitudes toward CSF vaccination among the general public may be influenced by attitudes toward mass culling and animal welfare concerns, as well as by the acceptability of meat from CSF-vaccinated animals in markets. The public may be less likely to accept withholding CSF vaccine over concern of trade implications.

Classical swine fever virus poses no known risk of human infection for personnel handling the agent, handling infected animals, or carrying out diagnostic tests.

Vaccines are used regularly in livestock without adverse effects on human health. The CSF virus is highly species specific and under natural conditions it is capable of infecting only domestic pigs and wild boar.

Procedures have been established to inactivate CSFV in pork and pork products.

In a survey conducted in all EU countries, on the public perception of risk and particularly on food safety found that people were most concerned about factors such as pesticide residues, new viruses, bacterial contamination and unhygienic conditions outside the home. The report did not specifically address vaccination, but it suggests that consumers have a wide variety of concerns about food. Measures have been recommended to help minimize consumer concerns regarding food from animals vaccinated during an emergency.

In general, the use of vaccines improves animal and human health by preventing or controlling disease outbreaks. While some parents disagree with this statement, a majority of the public would agree that vaccinations are necessary as they take their children for routine vaccinations or they themselves receive the annual influenza vaccination. So, it would stand to reason that from a health standpoint, a majority of the public would understand that the use of vaccinations in the face of a disease outbreak would provide a great benefit.

One benefit, however, that sometimes is not recognized is when the use of vaccines improves animal welfare or well-being. When animals are in poor health, suffering from a disease that would have been prevented by vaccination, the welfare of the animals is a concern. Vaccines can be used to help improve animal welfare and productivity for the benefit of the producer as well as food safety and food security for the consumer [163]. Attitudes toward CSF vaccination among the general public may be influenced by attitudes on mass culling and animal welfare concerns, as well as by the acceptability of meat from CSF-vaccinated animals in markets. The public may be less likely to accept withholding CSF vaccine over concern of trade implications [164]. There has been intense public criticism when large numbers of apparently healthy animals were culled during some outbreaks, including the 2001 epizootics in the U.K. and the Netherlands. In the 1997-1998 CSF outbreak in the Netherlands, over 7 million head of weaned and slaughter weight pigs were killed for welfare reasons while over 2 million young pigs between 3 to 17 days of age were euthanized by lethal injection to ease the stress on the rendering system [8].

A survey was conducted in 2004 including member states of the European Union [165]. The goal of the survey was to better understand the view of those involved in the control strategies in countries having experienced outbreaks from FMD, CSF and avian influenza. During the outbreaks, members of the EU followed EU Directive 2001/89/EC in which vaccination is prohibited unless an emergency vaccination plan is submitted to and approved by the European Commission. Therefore, the control strategies utilized were mainly to quarantine infected herds, stop movement of animals in the area, and cull infected and suspect herds. According to Cohen et al. [165], the effect of stamping-out greatly affected people directly involved. Owners and workers described clinical signs relating to post-traumatic stress syndrome and experienced severe stress with a loss of self-esteem, a loss of self-confidence, and a significant economic loss.

A survey was conducted in the Netherlands to determine how the meat from vaccinated animals would be viewed by the consumer. How the product was presented played a large role in the mindset of the consumer. For example, even when meat was identified as coming from vaccinated animals, it was favored when described as 'exclusive', 'animal-friendly' and 'environmentally-friendly'. However, meat from vaccinated animals didn't perform as well due to concerns of flavor, convenience and quality. On the basis of this consumer survey, in the Netherlands it can be concluded that, consumers may continue to purchase meat from vaccinated animals depending on how it is presented to them [150].

24.1 Classical Swine Fever Disease as a Zoonosis

Classical swine fever virus poses no known risk of human infection for personnel handling the agent, handling infected animals, or carrying out diagnostic tests [47]. Accordingly, it has a low categorization in health and safety regulations [47].

24.2 The Use of Meat from Vaccinated and/or Potentially Infected Animals

Vaccines are used regularly in livestock without adverse effects on human health. The CSF virus is species specific and under natural conditions it is capable of infecting only domestic pigs and wild boar [166]. There is no evidence that it is capable of infecting humans. During the CSF outbreak in the U.K. in 2000, the U.K. Food Standards Agency stated that there weren't any food safety implications in their current outbreak [166].

If an individual animal tests negative with rRT-PCR in blood, it can be excluded as source of infectious fresh meat for a short period of time. Animals may register negative in the very early stages of infection or they may contract infection right after testing. When an animal is vaccinated with MLV then infected at least four days post vaccination, the risk of that carcass carrying infectious CSFV is very low [111]. Animals that are correctly vaccinated and test negative using rRT-PCR after time has passed for an immune response to develop are unlikely to have their fresh meat test positive at slaughter [111].

Modeling indicates an eradication strategy applying correct vaccine usage and compliance may lower the risk of infectious CSFV in fresh meat when compared to the conventional strategy of pre-emptive culling [111].

24.3 Procedures to Inactivate CSFV in Animal Products

In pork and pork products, CSFV survival varies depending how the product is stored and on the treatments used on processed meat [47]. CSFV survives the longest in frozen pork in which survival times of more than 4 years have been recorded [45, 47]. In chilled fresh pork, CSFV has survived up to 85 days [42-44, 47]. While little information is available on the survival of CSFV in pork stored at room temperature, artificially contaminated factory- processed abattoir waste held at 20°C for 3 weeks was inactivated within four days [47, 167].

Due to the varying survival times of CSFV in product, inactivation of CSFV needs to be accomplished by the OIE recommended methods. According to Article 15.2.21 of the OIE Terrestrial Animal Health Code [29], inactivation of CSFV in meat should be accomplished through the following:

- Heat treatment: Should occur with a F_0 value of 3.00 or greater in a hermetically sealed container; or at a temperature of 70°C or greater in the meat. F is the time needed to inactivate a given organism (in this case, CSFV) at a given temperature. It is a designation of the thermal death time.
- Natural fermentation and maturation: Treatment used should include either an available water (aw) value of not more than 0.93, or a pH value of not more than 6.0. Natural fermentation and maturation of hams should last at least 190 days and 140 days for loins.
- Dry cured pork meat: Bone-in Italian style hams should be cured with salt and dried for at least 313 days, and bone-in Spanish style pork meat for at least 252 days for Iberian hams, 140 days for Iberian shoulders, 126 days for Iberian loin, and 140 days for Serrano hams [29, 168].

Procedures have also been established for the inactivation of the CSF virus in skins and trophies [29].

24.4 Procedures for Marketing Animal Products After Emergency Vaccination

In general, there are increasing concerns among consumers about food safety and purity, and the understanding of the real risks in specific situations may be weak [169]. In 2005, the EU Directorate-

General for Health and Consumer Protection and the European Food Safety Authority (EFSA) commissioned a survey, conducted in all EU countries, on the public perception of risk and particularly on food safety ([170] reviewed in [169]). This study found that people were most concerned about factors such as pesticide residues, new viruses, bacterial contamination and unhygienic conditions outside the home. There were also concerns about animal welfare, genetically modified organisms, environmental pollutants, food additives and other issues. The report did not specifically address vaccination, but it suggests that consumers have a wide variety of concerns about food, with the most concern directed toward issues that are not under the person's control.

Measures that could be taken to minimize consumer concerns regarding the rejection of food from animals vaccinated during an emergency [169]:

- Develop a vaccination policy before an outbreak, and determine the conditions under which it would be used.
- Discuss the vaccination policy with all stakeholders. Remind stakeholders that vaccines are used routinely in livestock and poultry for endemic diseases.
- Obtain the support of the public for vaccination and other control policies.
- License vaccines before they will be needed. If a conditional license must be given to an emergency vaccine, consider its effect on consumer concerns. Provide safety information to all stakeholders about the use of such vaccines.
- Do not separately label products from animals vaccinated for CSF.
- Give unequivocal and authoritative assurance that vaccinated products are safe to eat. This should include statements from national and international independent bodies that consumers respect.
- Begin communication about CSF vaccines before an outbreak and continue to communicate during the outbreak.

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Authors:

- Pamela K. Zaabel, DVM
Veterinary Specialist
- Anna Rovid Spickler, DVM, PhD
Veterinary Specialist
- James A. Roth, DVM, PhD, DACVM
Director, CFSPH
Distinguished Professor, Veterinary Microbiology and Preventive Medicine

Assistance provided by:

- Janice P. Mogan, DVM
Veterinary Specialist
- Jessica Kennicker
Senior Dairy Science Student, Iowa State University

The following individuals reviewed or provided assistance with content development:

- Manuel V. Borca MV, PhD
Lead Scientist
Plum Island Animal Disease Center
USDA Agricultural Research Service
- Randall L. Crom, DVM
Senior Staff Veterinarian
Preparedness and Incident Coordination
Emergency Management and Diagnostics
USDA APHIS Veterinary Services
- Lawrence A. Elsken, DVM
Global Vaccine Manager
Center for Veterinary Biologics
USDA APHIS Veterinary Services
- Patricia Foley, DVM, PhD
Risk Manager
Policy, Evaluation, and Licensing
Center for Veterinary Biologics
USDA APHIS Veterinary Services

- Randall L. Levings, DVM, MS
Scientific Advisor
Emergency Management and Diagnostics
USDA APHIS Veterinary Services
- Gregory A. Mayr, PhD
Microbiologist
Diagnostic Services Section
Foreign Animal Disease Diagnostic Lab
USDA APHIS
- Guillermo Risatti, MV, MS, PhD
Associate Professor
Department of Pathobiology and Veterinary Science
College of Agriculture and Natural Resources
University of Connecticut

Glossary

Adjuvant

A substance added to vaccines to enhance the capacity to stimulate the production of antibodies or cell-mediated immune responses.

Animal Product

Blood or any of its components, bones, bristles, feathers, flesh, offal, skins, and any by product containing any of those components that originated from an animal or bird.

Biosecurity

A series of management practices designed to prevent the introduction of disease agents onto or prevents the spread from an animal production facility.

Buffer Zone

Zone that immediately surrounds an Infected Zone or a Contact Premises.

Cerebellar Hypoplasia

Underdevelopment of cerebellum, the region of the brain that has an important role in motor control.

Cold Chain

The system used to ensure that vaccines stay within an appropriate temperature range from manufacturer to the point of administration.

Containment Vaccination Zone

Emergency Vaccination Zone within the Control Area. This may be a secondary zone designation.

Control Area

Consists of an Infected Zone and a Buffer Zone.

Cull

To voluntarily remove from the herd and sell to a slaughter facility. Sometimes referred to as “market” cattle.

Detection of Infection in Vaccinated Animals (DIVA)

A type of vaccine that is marketed with a companion diagnostic kit to detect infection of a natural pathogen in animals vaccinated against that disease.

Ear Tags

Tags, usually plastic, put in animals’ ears to identify them. Every producer uses their own numbering system. They can easily be removed.

Efficacy

Specific ability or capacity of the biological product to effect the result for which it is offered when used under the conditions recommended by the manufacturer.

Endemic

Present in a population or geographical area at all times.

Epidemic

An (often suddenly) increased number of cases over a broad geographic area.

Euthanasia

Deliberate ending of an animal's life in a manner that causes minimal pain and distress.

Fomite

An inanimate object or material on which disease-producing agents may be conveyed (e.g. feces, bedding, clothes).

Free Area

Area not included in any Control Area.

Incubation Period

The period of time between infection and the development of clinical signs.

Infected Premises

Premises where a presumptive positive case or confirmed positive case exists based on laboratory results, compatible clinical signs, case definition, and international standards.

Infected Zone

Zone that immediately surrounds an Infected Premises.

Live Attenuated Vaccines (Modified Live Vaccines)

Vaccines that replicate themselves in the host but should produce no or only very mild clinical signs. They induce the animal to mount an immune response that will provide protection from severe disease by the natural pathogen.

Mortality

Death of an animal; dead animals can be referred to as mortalities.

National Veterinary Stockpile (NVS)

Established by Homeland Security Presidential Directive 9 and operational in 2006. Able to deploy large quantities of veterinary resources anywhere in the continental U.S. within 24 hours.

Outbreak

An increased number of cases (above what is expected) from a limited geographic area.

Potency

Relative strength of a biological product as determined by test methods or procedures as established by APHIS in Standard Requirements or in the approved Outline of Production for such product.

Prophylactic Vaccination

Taking measures to prevent disease via administration of vaccination.

Protection Vaccination Zone

Emergency Vaccination Zone outside the Control Area. This may be a secondary zone designation.

Purity

Quality of a biological product prepared to a final form relatively free of extraneous microorganisms and extraneous material (organic or inorganic) as determined by test methods or procedures established by APHIS in Standard Requirements or in the approved Outline of Production for such product, but free of extraneous microorganisms or material which in the opinion of the Administrator adversely affects the safety, potency, or efficacy of such product.

Quarantine

To place animals in strict isolation to prevent the spread of disease.

Rendering

A process of converting animal carcasses into a stable product that can be used for other purposes.

Reservoir

The environment in which a pathogen lives, grows, and multiplies. Can include humans, animals, and the physical environment. The reservoir is often, but not always, the source of infection.

Risk (Risk Pertaining to Infection)

The probability of becoming infected given that exposure to an infectious agent has occurred.

Sensitivity

The proportion of true positives that are detected by a diagnostic test.

Sentinel

A susceptible population, farm, or animal that is repeatedly sampled in order to assess health status over time; the 'sentinel' must be representative of the at-risk populations, farms, or animals.

Stamping-out

The killing of the animals which are affected and those suspected of being affected in the herd and, where appropriate, those in other herds which have been exposed to infection by direct animal to animal contact, or by indirect contact of a kind likely to cause the transmission of the causal pathogen.

Suppressive Vaccination

Emergency vaccination conducted both within and around infected zones. Suppressive vaccination can take place throughout a country or compartment; however, this strategy may require large quantities of vaccine and sufficient human resources.

Susceptible Animal

Any animal that can be infected with and replicate the disease pathogen of concern.

Targeted Vaccination

Vaccination of selected animals or populations (e.g., uninfected animals of high value including livestock with valuable or unusual genetic backgrounds, long-lived production animals, zoo animals, or endangered species). Can also be directed at uninfected areas where there is a high density of susceptible animals.

Tracing

Information gathering on recent movements (during a defined time period) of animals, personnel, vehicles, and fomites (both to and from affected farms) to identify potential spread of disease to other livestock premises and to detect a putative source of infection for the affected farm.

World Organization for Animal Health (OIE)

The intergovernmental organization created by the International Agreement of 25 January 1924, signed by 28 countries. In April 2011, the OIE totaled 178 Member Countries. OIE standards are recognized by the World Trade Organization as reference international sanitary rules. The purpose of the OIE is to guarantee the transparency of animal disease status world-wide.

Zoning

The practice of defining subpopulations of animals on a geographical basis, using natural, artificial, or legal boundaries, for the purpose of disease control (OIE).

Acronyms

AI

Artificial Insemination

APHIS

Animal and Plant Health Inspection Service; an agency of USDA

BVDV

Bovine Viral Diarrhea Virus

CLS

Chinese Lapinised Strain

CSFCWG

Classical Swine Fever Countermeasures Working Group

CSFV

Classical Swine Fever Virus

CVB

Center for Veterinary Biologics; a division of APHIS

DIVA

Detect Infection in Vaccinated Animals

DOI

Duration of Immunity

EFSA

European Food Safety Authority

ELISA

Enzyme-Linked Immunosorbent Assay

EU

European Union

FAT or FATST

Fluorescent Antibody Test

FAVN

Fluorescent Antibody Virus Neutralization Test

FMD

Foot and Mouth Disease

GPE

Guinea Pig Cell-Culture-Adapted

IBC

Institutional Biosafety Committee

KT

Kemper-Trego

LAV

Live Attenuated Vaccines

MLV

Modified Live Vaccines

NEPA

National Environmental Policy Act

NPLA

Neutralizing Peroxidase-Linked Assay

NVS

National Veterinary Stockpile

OIE

Office International des Epizooties', currently referred to as the World Organization for Animal Health

PCR

Polymerase Chain Reaction

PD₅₀

Protective Dose Fifty

PID

Porcine Infectious Dose

PK

Pig Kidney

PRRS

Porcine Reproductive and Respiratory Syndrome

PRV

Pseudorabies Virus

rRT-PCR

Real time Reverse Transcription Polymerase Chain Reaction

RT-PCR

Reverse Transcription Polymerase Chain Reaction

USAHA

United States Animal Health Association

USDA

United States Department of Agriculture

VNTs

Virus Neutralizing Tests