THESIS

EVALUATION OF STRATEGIES FOR ERADICATION OF AUJESZKY'S DISEASE (PSEUDORABIES) IN COMMERCIAL SWINE FARMS IN CHIANG-MAI AND LAMPOON PROVINCES, THAILAND

Submitted by

Naree Ketusing

Department of Clinical Sciences

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WE HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER OUR SUPERVISION BY NAREE KETUSING ENTITLED EVALUATION OF STRATEGIES FOR ERADICATION OF AUJESZKY'S DISEASE (PSEUDORABIES) IN COMMERCIAL SWINE FARMS IN CHIANG-MAI AND LAMPOON PROVINCES, THAILAND BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

Committee on Graduate Work

_____

Thomas Keefe

_____

Advisor: Mo Salman

_____

Co-Advisor: Francisco Olea-Popelka

_____

Department Head: Paul Lunn

ABSTRACT OF THESIS

EVALUATION OF STRATEGIES FOR ERADICATION OF AUJESZKY'S DISEASE (PSEUDORABIES) IN COMMERCIAL SWINE FARMS IN CHIANG-MAI AND LAMPOON PROVINCES, THAILAND

Several strategies for eradicating Aujeszky's disease (Pseudorabies) in Chiang-Mai and Lampoon Provinces, Thailand, were compared using a computer simulation model, the North American Animal Disease Spread Model (NAADSM). The duration of the outbreak, the number of infected herdss and the number destroyed herds were compared during these simulated outbreaks. Destruction, zoning for restricted movement and improved detection and vaccination strategies were studied.

Destruction was found to be the most effective method to eradicate Pseudorabies. Although zoning and ring vaccination did not influence this model, the recommendations from this study are to apply both destruction and three zone (3, 8 and 16 kilometers) restricted movements along with enhanced detection and a 16 vaccination ring.

Naree Ketusing
Department of Clinical Sciences
Colorado State University
Fort Collins, CO 80523
Summer 2010

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTODUCTION AND OBJECTIVE OF THESIS

Aujeszky's Disease Virus (ADV), also known as Pseudorabies virus (PRV), belongs to the subfamily Alphaherpesvirinae within the family Herpesviridae. This virus is responsible for causing severe economic losses to the swine industry worldwide. The disease was described in cattle in the United States as early as 1813 (Penseart and Kluge, 1989), but the etiology of ADV was first recognized as a nonbacterial agent in Hungary in 1902 (Aujeszky, 1902). Subsequently, ADV has emerged as an important disease in most areas of the world where pigs are raised. Clinical signs of ADV are variably characterized by central nervous system (CNS) signs in older pigs and reproductive failure in pregnant animals. Although pigs represent the only natural reservoir for ADV and serve as a source of infection for other species, most mammals, except horses and higher primates including human beings, are susceptible and show clinical signs of the disease with the potential to be fatal (Wittmann and Rziha, 1989).

In spite of ADV eradication efforts in several countries, outbreaks of Aujeszky's Disease (AD) are still reported in some countries. The evident increase in disease severity, prevalence, and worldwide distribution could be due to several possibilities. First, new viral strains have emerged; second, the disease may be aggravated by an interaction between ADV and other pathogens; third, animal movement and modern transportation may help spread the disease; and lastly, changes in swine management may provide a

suitable environment that makes it easy for the virus to maintain and spread within or among herds (Thanawongnuwech, 2002).

Control policies and eradication programs vary among countries. A control program is intended to reduce the prevalence of ADV-infected herds to a biologically and/or an economically justifiable level. An eradication program is endorsed with an initial aim of eliminating the virus from a specific area in order to reach the final goal of an ADV-free country. Many Asian countries choose to ignore the presence of ADV and have no official control policy. Thus, local veterinarians are responsible for implementing control programs with the pig producers. If no formal policy is in place, the end result could be the spread of ADV among swine herds, vaccine expenditures continuing for an indefinite time, economic losses due to reduced productivity, and fatalities in other domestic species living in proximity to the infected herds. Therefore, guidelines must be established to control the spread of ADV between herds and to reduce its prevalence within infected herds.

Since the first outbreak of ADV in Thailand in 1980, there is evidence that showed the virus was still circulating in the swine population. Currently, Thailand has not yet employed an eradication plan. Therefore, the objectives of this study were to evaluate the Pseudorabies virus (Aujeszky's Disease) eradication program in commercial swine operations and to estimate its effectiveness in the northern region of Thailand, specifically Chiang-mai and Lampoon Provinces, by using infectious disease modeling instead of experimental studies. Data sources are from retrospective studies of foot-and-mouth disease surveillance in these two areas.

The specific objectives of this study were to compare three eradication strategies—destruction strategy (destruction and no destruction of animals/herds infected), zoning or animal movement restriction strategy (no zoning, three and eight kilometers zoning, and three, eight, and 16 kilometers zoning), and vaccination strategy (no vaccination, vaccination within eight kilometers ring, and vaccination within 16 kilometers rings).

CHAPTER 2

REVIEW OF LITERATURE

Introduction

Pseudorabies, also known as Aujeszky's Disease (AD) or mad itch (Gustafson, 1986), is an important economic problem in the swine industry. The disease is characterized by three overlapping syndromes involving the CNS, respiratory system or reproductive system (Taylor, 1999) that vary among different age groups. Many parts of the world have Pseudorabies as an endemic disease; however, most of those countries have developed numerous programs for eradication.

Etiology

Pseudorabies is a viral disease, DNA herpesvirus-1. As a general rule, herpes viruses are composed of double-stranded, linear DNA genomes enclosed with an icosahedral capsid, and they often persist in a latent state in animals that have recovered from the disease (Pomeranze et al., 2005).

Although swine are the reservoir for this virus, it can affect other domestic animal species (cattle, sheep, goats, horses, dogs, cats), as well as wild animals (rats, mice, raccoons, opossums, rabbits, coyotes, several fur-bearing mammals and others), except higher primates and humans.

Viral characteristics

The virus is shed in the saliva and nasal secretions. It can be transmitted via direct contact, nose-to-nose or the fecal-oral route. Indirect

transmission via inhalation of aerosolized virus and transmission by fomites also commonly occurs.

Virus survival depends on environmental factors, such as humidity, temperature and pH. The virus can survive for seven hours in air with a relative humidity of 55% or greater and can spread up to two kilometers. Other studies have demonstrated that the virus can persist in nonchlorinated well water for up to seven hours, for two days in green grass, soil, and feces, for three days in contaminated feed, and for four days in straw bedding (Merial Ltd., 2008). In most instances, the virus probably does not survive more than two weeks outside the pig, except during cold weather when the virus may survive for up to 15 weeks. Because the virus is enveloped, it can be inactivated by drying, sunlight and high temperatures (≥ 37°C). Furthermore, it can be destroyed by many disinfectants, including orthophenyl phenol, quaternary ammonium compound, iodine compound and 5% sodium hydroxide.

Clinical Signs

Signs vary depending on the immune status and age of the pig, the viral strain, and the infectious dose. Younger swine infected with PRV typically show CNS signs while older swine more often show signs of respiratory disease.

For suckling pigs the incubation period of PRV is two to four days. Piglets have a loss of appetite, a fever, and are uninterested in their environment. Within 24 hours the piglets will dramatically develop signs of CNS infection including trembling, excessive salivation, incoordination, ataxia,

and seizures. They will die within 24 to 36 hours after showing CNS signs. The mortality rate for this group is extremely high, almost 100%.

Weaned pigs, aged three to nine weeks, tend to develop the same severe signs as described for suckling pigs. However, the mortality rate for weaned pigs is lower than for suckling pigs. Typically 50% of infected three to four week old animals die. Pigs five to ten weeks old develop lethargy, anorexia, and fever (41 to 42°C) within three to six days of infection. Infected animals often exhibit respiratory signs such as sneezing, nasal discharge, a severe cough, and difficulty breathing. Pigs with respiratory illness often lose body weight, leading to economic losses for commercial swine farms. Pigs will recover after five to ten days once the fever and anorexia resolve. Protection against secondary infection can reduce the mortality rate such that it rarely exceeds 10%.

In adult swine the typical signs of PRV infection involve the respiratory system, although some show CNS abnormalities. The morbidity is quite high (approaching 100% of infected animals), whereas the mortality is relatively low (1 to 2% of infected animals). Clinical signs appear in three to six days and include a febrile response (41 to 42°C), listless behavior, loss of appetite with accompanying weight loss, and mild-to-severe respiratory signs. These animals will typically exhibit rhinitis as evidenced by sneezing and nasal discharge. The respiratory illness may develop to pneumonia with a harsh cough and difficult breathing. Clinical signs are usually present for six to ten days followed by a rapid recovery.

Sows in the first trimester of pregnancy will usually reabsorb the fetuses *in utero*. If infection occurs within the second and third trimester, it can

lead to abortion, stillbirths, or weak piglets that die within 48 hours of birth. Some piglets may even be normal at birth, while others are weak and some are stillborn due to transplacental transmission of the PRV. The incidence of reproductive failure is low, being 20% or less of pregnant swine (Kluge et al., 1999).

Epidemiology

The first PRV outbreak reported in Asia was in China in the 1950s (Li and Guo, 1994). As time progressed the disease gained access to other Asian countries including Taiwan in 1971 (Lin et al., 1972), Malaysia in 1976 (Lee et al., 1979), Singapore in 1977 (Koh et al., 1979), Thailand in 1977 (Sunyasootcharee et al., 1978), Japan in 1981 (Fukusho, 1982), Philippines in 1985 (Marero, 1985), and South Korea in 1987 (Kim et al., 1988).

PRV may have spread to these Asian countries through the importation of PRV-infected breeding stock. The first outbreak in Japan was associated with the importation of sows from The Netherlands (Fukusho, 1982). Based on the results of the restriction endonuclease assay of the viral genome, PRVs isolated from Japan (Yamagata-S81 strain) and Thailand (NK strain) are similar to the virus found in central Europe (Nishimori et al., 1987; Yamada et al., 1992).

Movement of infected animals appears to be a major obstacle for disease control. Several outbreaks in Thailand were reported by local veterinarians and regional laboratories following the first outbreak in the centrally located Nakornpratom province (Sunyasootcharee et al., 1980;

Suksaithaichana et al., 1984). A similar scenario was observed in other Asian countries (Lee and Lin, 1975; Lee et al., 1979; Lou and Yang, 1997).

Several Asian countries have regions of high PRV prevalence (Wang, et al., 1996; Jasbir et al., 1998; Liao et al., 1999; Damrongwatanapokin et al., 2000), with the exception of Japan and South Korea (Lyoo et al., 1997) that have a low prevalence. In Japan the Pseudorabies incidence has been limited by an official control program, but persists in certain areas. The use of gE-deleted vaccines and differential enzyme-linked immunosorbent assay (ELISA) kits in Thailand has made it possible to determine PRV seroprevalence in that country's swine population since 1987 (Urairong et al., 1994). The PRV seroprevalence appeared to decline after more producers incorporated the attenuated gE-deleted vaccine into their vaccination program (Urairong et al., 1994). A recent report by Damrongwatanapokin et al. (2000) found that the estimated prevalence of PRV in Thailand was more than 40%, particularly in the breeding stock, within some high-density pig-farming areas; however, the prevalence of PRV infection in most fattening pig farms was lower than 30%. Based on year 2000 information from the Veterinary Diagnostic Laboratory at Chulalongkorn University in Thailand, more than 70% of swine herds that submitted sera for PRV gE ELISA had serological evidence of infection by a field PRV. A very high proportion of pigs with PRV become latently infected (Sabo, 1985); therefore, latently infected gilts entering the breeding pool may serve an important role in persistent herd infections. No existing PRV vaccine can completely prevent latency in the face of a superinfection, i.e., massive exposure with virulent virus. Thus reactivation of the infection in a latently infected animal might result in a high

proportion of a population becoming infected with field strain virus or a variant virulent virus without being detected.

Prevention and Control

Control and eradication programs are variable. The most precise program involves a no-vaccination strategy. In some cases, vaccination with differential vaccines is used and sometimes combined with the testing and slaughter of infected pigs. And, in some cases, there is no regulation of Pseudorabies. Unfortunately only a few Asian countries, including Japan and Taiwan, currently have official control policies (Fujita, 1994; Sung and Yang, 1994). In Taiwan, a program was initiated involving the use of hyperimmune serum, vaccination, and certain management procedures for the control of PRV; this program was established to reduce the number of fatalities and reproductive failure caused by PRV outbreaks (Hsu and Lee, 1984). Thailand has not yet implemented a control program but intends to do so in the near future.

Early efforts to control the disease include work in Malaysia on the use of a formalin-inactivated vaccine in pigs and sheep that, experimentally, produced satisfactory protection (Lee et al., 1979). However, oil-adjuvant inactivated vaccine did not work well in Singapore (Koh et al., 1979). The attenuated PRV vaccine developed for local use in China yielded satisfactory results in preventing the disease in pigs, sheep, and cattle (Li and Guo, 1994). In Japan, the gE-deletion vaccine was employed beginning in 1993 in Tohoku and PRV was eliminated from this area in 1997 (Asai et al., 1998). Vaccination has changed the disease status and tremendously reduced

serious outbreaks. Because of viral latency and the voluntary nature of vaccination and culling, PRV is able to persist even in herds that are regularly vaccinated. When regulations and controls are based on the misconception that PRV vaccinated pigs exposed to field virus will not become infected and will not spread the infection, widespread dissemination of the disease is possible. Sporadic PRV outbreaks have been reported in China regardless of prophylactic measures (Lou and Yang, 1997; Xu et al., 1997; Tong and Chen, 1999). Efficient vaccination programs rely on an understanding of the limitations of the vaccine and strict controls on the movement of infected and exposed pigs, regardless of their vaccination status. Since vaccination is voluntary at the farmer's expense, and since there is no financial aid in the case of the outbreak, PRV outbreaks are usually not reported. This situation makes control programs impossible in some countries.

Epidemiological Modeling

As we move through the 21st century, the use of epidemiological modeling is increasing dramatically. Models are built to explain and predict patterns of disease and to see what is likely to happen if various control strategies are adopted. The most efficient disease control program can be generated by these precise models. Accurate models also lead to a better understanding of the life cycle of infectious agents (Thrushfield, 2005).

Several studies report the strategies and criteria for controlling and eradicating other infectious diseases, and the following are some examples that use modeling as a tool. Schoenbaum and Disney (2003) used a stochastic model to simulate outbreaks of foot-and-mouth disease (FMD) and

to recommend a mitigation strategy in the United States. A similar study was performed in Japan by Tsutsui et al. (2003) in following an outbreak in 2000. In addition, Wongsathapornchai et al. (2008) used a compartment model (the SLIRV model) in 2008 to evaluate control of FMD in southern Thailand. Stochastic modeling has also been used to evaluate the effectiveness of control measures for Johne's disease in dairy herds (Lu et al., 2010). In The Netherlands a computer simulation model was used to support policy making in the control of Pseudorabies (Buijtels et al., 1997). Researchers used modeling to aid in making disease import decisions regarding risky animal (Disney et al., 2003).

An epidemiological model can also be used to evaluate national surveillance programs and improve surveillance for infected and uninfected countries. For example, Pratley et al. (2007) used the BSurvE model to evaluate the national surveillance programs for bovine spongiform encephalopathy in an unspecified European country. The use of simulation modeling can save money and time. It was a valuable aid in interpreting the serological test in a survey study of Newcastle Disease (ND) in Switzerland and resulted in easier decision making regarding ND control and surveillance there and in other countries (Gohm et al., 1999). Sometimes models are employed to examine retrospective data in order to clarify historical epidemiological or risk analysis for the spread of disease. Examples of retrospective or historical modeling of emerging zoonoses include model analysis of Ebola outbreaks in Congo and Uganda (Chowell et al., 2004) and model analysis of the spread of bovine viral diarrhea in beef herds (Smith et al., 2010).

Modeling can aid the decision making process relative to control or eradication of animal disease, predicting disease incidence or prevalence, testing epidemiological hypotheses, monitoring health programs and to manipulate society or influence people (Salman, 2009). Models built to simulate an outbreak have the distinct advantage of being relatively inexpensive compared to actual disease outbreaks. They can be used to determine how a system might respond to different events or interventions and provide an alternative experimental approach. Models may be used to assess disease behavior under a variety of conditions and to compare the efficacy of different disease control strategies (Reeves, 2009). Also, models attempt to mimic processes that occur within a system. They emphasize realism rather than mathematical rigor (Miller, 1976). However, the models also have their limitations. It is impossible to create a fully accurate model, although more reliable data will result in a more precise model. There are some characteristics and components of disease or even of host behavior which are still unknown. Models are not able to predict precisely the term of the epidemic or which animals will be infected, but a model may provide confidence intervals for epidemic behavior and establish the risk of infection (Keeling and Rohani, 2008). Although most pathogens have several hosts, most modeling studies are limited to examining one host and one pathogen (Keush et al., 2009).

CHAPTER 3

EVALUATION OF STRATEGIES FOR ERADICATION OF AUJESZKY'S DISEASE (PSEUDORABIES) IN COMMERCIAL SWINE FARMS IN CHIANG-MAI AND LAMPOON PROVINCES, THAILAND

INTRODUCTION

Aujeszky's disease (AD), also known as Pseudorabies, is a major economic threat to swine producers all over the world. This is a viral disease, and the clinical signs vary with the age of the animal at the time of infection. The Pseudorabies virus (PRV) belongs to the Alphaherpesvirinae subfamily of the Herpesviridae family of viruses (Mettenleiter, 2000). In piglets, Pseudorabies infection can result in a disorder of the central nervous system. In weaners and fatteners the respiratory system is primarily affected, but the nervous system may also be involved. When boars and sows are infected, AD may result in disorders of the reproductive system. Swine are known to be a reservoir of the Pseudorabies virus and serve as a source of infection for most mammals with the exception of primates and humans (Pejsak and Truszcyński, 2006).

The first description of Pseudorabies in the USA was made as early as 1813, and cattle were reported to have severe itching; this gave rise to *mad itch* as a name for the disease. In 1902 Aladar Aujeszky isolated this virus from a dog, ox, and cat and demonstrated that it caused the same disease in swine (Beran, 2002). In Asia the first report of a PRV outbreak occurred in China in the 1950s (Li and Guo, 1994). Later the disease was introduced into

other Asian countries, including Thailand in 1977 (Sunyasootcharee et al., 1978).

PRV can be found throughout the world, especially in regions with dense swine populations including South America, Asia and Europe. There have been no reports of PRV in Norway, Finland or Malta. The countries of Germany, Austria, Sweden, Denmark, The United Kingdom, Canada and New Zealand have eradicated the disease from their domestic swine populations. The United States domestic swine population has been free from PRV since 2004. In the countries that are considered free from the PRV, vaccination is not allowed. PRV is still circulating, however, in the wild boar or feral swine populations in the United States, Germany, Poland, France, Italy and other places (Lipowski and Pejsak, 2002).

As mentioned above, PRV was first diagnosed in Thailand in 1977 and still continues to circulate in the swine population in that country. There is a desire to eradicate PRV in Thailand. The Thai government through the Department of Livestock Development is considering a plan to review available control strategies, and to compare and evaluate which strategies would be suitable for Thailand; this would be accomplished utilizing a computer simulation model, The North American Animal Disease Spread Model.

The North American Animal Disease Spread Model (NAADSM) was created to simulate the spread and control of animal diseases in a population of susceptible livestock herds. The characteristics of NAADSM are represented at the herd base level rather than at the individual animal level. The disease model is a state transition model from susceptible to infected and

immune state (Figure 1). Random stochastic processes are used in each simulated outbreak, and the results include a range of possible outcomes from each simulation. In a scenario each herd is assigned a particular latitude and longitude, and the disease development is shown in daily time steps. Furthermore, NAADSM also includes a cost-accounting component that is useful for estimating costs related to simulated outbreaks. Therefore NAADSM is a suitable model for evaluating a PRV eradication program in commercial swine farms; estimating the effectiveness of a PRV eradication program in the northern region of Thailand, in Chiang-mai and Lampoon Provinces; estimating the number of vaccine doses needed in the event of a Pseudorabies virus outbreak in Chiang-Mai and Lampoon Provinces; and estimating the cost to the government for implementing such eradication strategies (Further study).

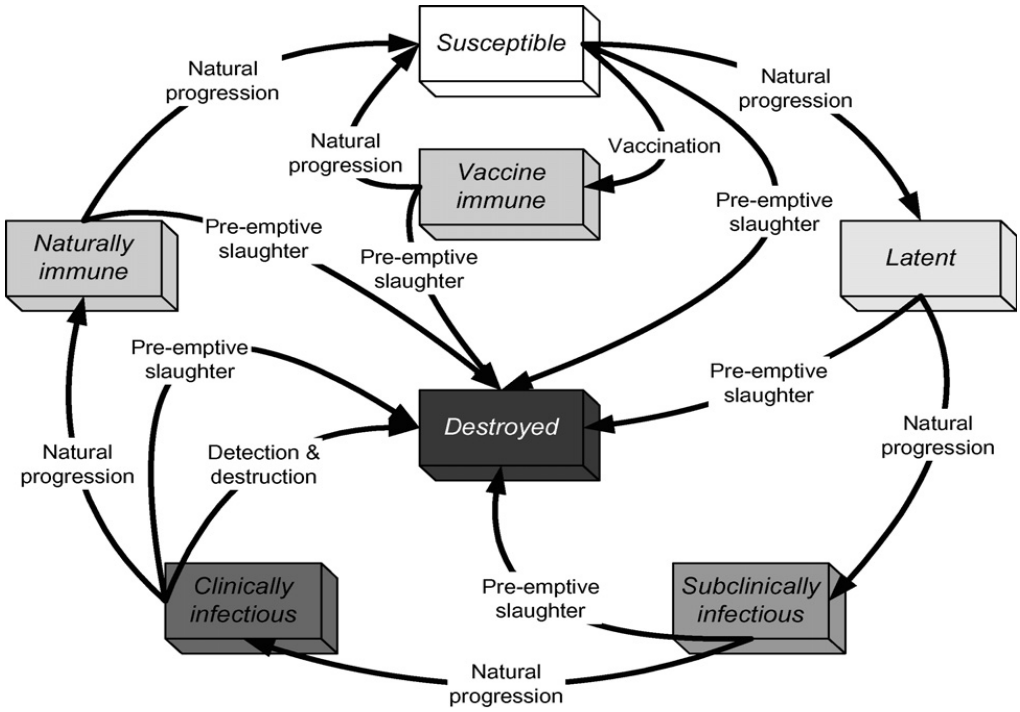

Figure 1. Illustration of the state transition model as simulated by NAADSM. When disease occurs within a unit, it moves from one disease state to another. The interruption of this cycle may occur upon the implementation of disease control mechanisms (Harvey et al., 2007).

MATERIALS AND METHODS

Area, study population

This study was conducted in the northern region of Thailand, in Chiang-Mai and Lampoon Provinces (Figure 2). This area was selected because of available detailed data. The study included finishing, farrow-to-finish, and parent stock swine farms.

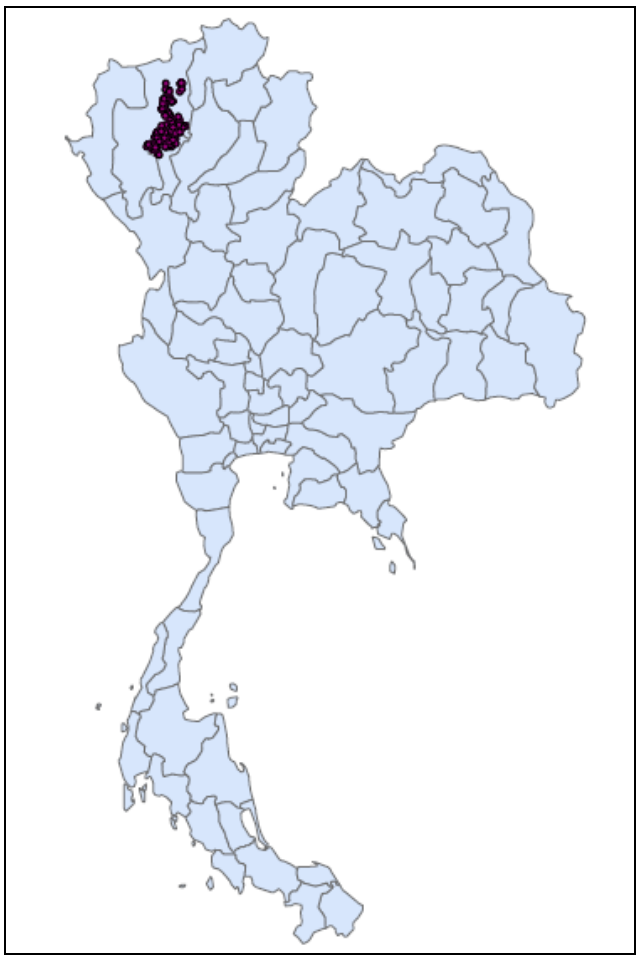

Figure 2. Map of Thailand showing the area, within Chiang-Mai and Lampoon Provinces covered by the current study.

Source of the data

Geographical coordinates for commercial swine farms were collected by a research team conducting the Study of Prototype of Foot and Mouth Disease Free Area in the Chiang Mai - Lampoon Zone and Nan Provinces

(Rojanasathein et al., 2004). Herds were geocoded with a Global Positioning system (GPS, Garmin® GPS72) in the World Geodetic System 1984. The research team also provided information on the type of herd (finishing farm, farrow-to-finish farm and parent stock farm) and census data. Any duplicate data were deleted, and the data were combined if they had the same coordinates but a different owner. Farm size was classified by the total number of pigs: small (<500), medium (500 to 5000), and large (≥5000).

Factors included in the analysis

This study was conducted under the implicit assumptions that (1) all susceptible swine were equally susceptible, (2) all infected swine were equally infected and spread the virus throughout the herd, and (3) all PRV-infected swine eventually showed clinical signs. Since there have been no previous studies of PRV characteristics in Thailand, disease parameters may vary from those seen in other countries.

Model structure

In this study we used The North American Animal Disease Spread Model (NAADSM) version 3.1.23. The model is focused on between-herd spread, and the herd is used as the modeling unit. To control variables among herds, herds were subdivided into three different herd types: parent stock, farrow-to-finish, and finishing farm.

MODEL PARAMETERS

1. Disease parameter

NAADSM is a state spatial model and a herd based model. We assigned one state to each simulated herd: susceptible, latent, subclinical infectious, clinical infectious, naturally immune, vaccine immune or dead. While running the model the herds change among these states. **Table 1** shows the definition of the disease transition states. The model of each scenario started with one latent herd and the rest were susceptible. A latently infected herd was selected from the central and more densely populated area. This central location was selected to provide susceptible herds in all directions for secondary spread of PRV.

Table 1: Definitions of disease transition states used in this model.

Transition (health) state of the herd	Definition of the health state
Susceptible	All animals in the herd are not infected and are able to contract the infection.
Latent	Period between exposure and infectious. Some animals in the herd are infected during the time before they shed the virus.
Subclinical infectious	Some animals in the herd are infected and are shedding the virus but exhibit no clinical signs.
Clinical infectious	Some animals in the herd are infected, shedding the virus and having visible clinical signs.
Naturally immune	Animals in the herd have recently recovered from the infection and the herd is not susceptible.
Vaccine immune	Animals in the herd have vaccine-induced active immunity toward the disease and the herd is not susceptible.
Dead	All animals in the herd were slaughtered via a stamping-out program to control the disease.

The disease characteristics and time periods in transition states of PRV were modeled based on historical outbreaks, literature reviews and expert opinions. Probability density functions were needed to describe the duration of each state on a herd level basis **(Table 2)**. Using risk analysis software for Excel (@RISK version 4.5) we selected the best probability density function by fitting disease characteristics, based on expert opinion, with the study population. For each production type, the latent period was assumed to follow a log-logistic distribution. The value of alpha, beta and gamma varies by the type of production. The farrow-to-finish production values were -0.36, 2.29 and 2.00, respectively. The finishing production values were -0.42, 2.32 and 2.15, and the parent stock production values were -0.32, 2.20 and 2.02, respectively. The subclinical infectious period for the farrow-to-finish and finishing production type were assumed to follow Gaussian (Normal) distributions with a mean and standard deviation of 5.41 and 0.88 days and 14.43 and 1.19 days, respectively. Parent stock was assumed to follow a triangular distribution with minimum, most likely, and maximum of 2.96, 5.00 and 8.04 days. The clinical infection period was assumed to follow log-logistic distribution for all production types with various values for alpha, beta and gamma. The farrow-to-finish production type had values of 24.85, 22.49 and 2.25, while finishing had 27.07, 104.19 and 2.18, and the values for parent stock were 13.59, 42.72 and 4.75. We assumed that every vaccinated herd remained immune for the whole year covering the time period according to a lognormal distribution (mean and standard deviation of 300 and 60 days). Examples of the probability density functions which were used for the disease parameters are shown in APPENDIX A.

Table 2: Probability density function used for each disease state and production type. Distributions parameters are listed for Log-logistic (gamma, alpha, beta), Gaussian (mean, standard deviation), Triangular (minimum, mode, maximum) and Lognormal (mean, standard deviation).

Disease state	Production type	Value/distribution used
Latent	Farrow-to-finish	Log-logistic (-0.36, 2.29, 2.00)
	Finishing	Log-logistic (-0.42, 2.32, 2.15)
	Parent stock	Log-logistic (-0.32, 2.20, 2.02)
Subclinical Infectious	Farrow-to-finish	Gaussian (5.41, 0.88)
	Finishing	Gaussian (14.31, 1.19)
	Parent stock	Triangular (2.96, 5.00, 8.04)
Clinical Infectious	Farrow-to-finish	Log-logistic (24.85, 22.49, 2.25)
	Finishing	Log-logistic (27.07, 104.19, 2.18)
	Parent stock	Log-logistic (13.59, 42.72, 4.75)
Immune	All production	Lognormal (300, 60)

2. Spread option—contact spread and airborne spread

2.1 Contact spread

The spread option in this model simulated three simultaneous spread mechanisms: direct contact, indirect contact and airborne spread. Spread of infection by direct contact was based on simulated contact or movements of animals among infected and susceptible herds. Indirect contact was based on simulated contact or movements of people, equipment and vehicles. The movement directions were random. Transmission via direct contact, indirect contact and airborne spread can occur if the infected unit is subclinically infectious or clinically infectious. The disease can spread between different production types.

The contact rate is the average number of shipping or outgoing contacts per day from a unit. Normally contact rates are specified independently for each pairing of production type; however, in this model we assumed the contact rate for each pairing was the same and used contact

rates of 0.03 (direct) and 2.1 (indirect). Thus, 0.03 indicates that the average number of movements or contacts between herds would occur three times in a period of 100 days, and the indirect contact rate means that the average number of shipments would be twice (2.1) per day. We used a probability of infection transfer of 0.2 (direct) and 0.01 (indirect) (P. Katie, personal communication, January 13, 2010); this is the probability that if a contact occurs, it will be adequate for transferring the infection.

The movement directions were random, and the distances of movement were based on two probability density functions, one for direct contact and the other for indirect contact. The distance distributions for direct and indirect contact were assumed to each be a triangular density with a minimum, most likely, and maximum of 0, 40, 190 days for direct contact and 0.5, 25 and 60 days for indirect contact (P. Katie, personal communication, January 13, 2010).

2.2 Airborne spread

An airborne spread or local area spread was simulated based on proximity to infected farms. The input parameters included in an airborne spread option are wind direction, rate of spread, probability of infection at 1km from the source and the maximum distance of spread. In this study, wind spread was assumed to be random (0-360 degrees). The rate of disease transfer (based on expert opinion) declined exponentially from the source, and the probability of spread per day at 1 km distance was set at 0.5.

3. Control strategy–detection, tracing and zoning

3.1 Detection

This model can detect only clinically infectious herds. The detection of infectious herds was based on two probabilities as input parameters, the probability of observing signs and the probability of reporting signs. The overall probability of detection was equal to the product of these two probabilities. Probability describing detection is given as a time dependence function. It is assumed to be 100% specific, with no false positive cases and the detected units are automatically quarantined the same day of detection.

The probability of observing clinical signs represents the probability that the farmer or the veterinarian would report suspicious signs of PRV to regulatory authorities given that infection had been present in the herd for a certain number of days. This probability of observing signs may be set individually by production type. For the farrow-to-finish and parent stock production types, it was assumed that signs would worsen over 60 days, and that probability would be linear with 1% at day 0, 50% at day 14 and 90% at day 60. For the finishing production type the assumption was that signs would worsen over 60 days, and that probability of observing and reporting for this production type would be linear with 0% at day 0, 15% at day 7 and reaching up to 85% at day 60.

The probability of reporting an observed clinical sign represents the probability that the herd would be reported to animal health authorities based on the awareness of farmers and veterinarians of a recent outbreak of PRV. We assumed that this probability was the same for all production types. Time dependence function starts at 88% probability at day 0 and 99% at day 8-14.

3.2 Tracing

In this model, we conducted trace-forward (trace-out) investigation for all production types. The tracing occurred immediately and only one step forward. If a recipient of contact was successfully traced, it was automatically quarantined and may also have been preemptively destroyed. Assuming traces were the same for all production types, the trace direct contacts were simulated at 60 days before detection with 98% probability of trace success and trace indirect contacts were simulated 14 days before detection with 80% probability of trace success.

3.3 Zoning (animal movement restriction)

Zoning (animal movement restriction) involved a circular zone created to restrict movement and enhance detection in a surveillance area. Different strategies for zoning were studied and added after the destruction strategy. The first strategy was no zoning; in this case there was no movement restriction and no enhanced detection. Other strategies included a zoning radius of three kilometers, eight kilometers and 16 kilometers.

The effect of a *three kilometer zone radius* for all production types was to alter the direct movement rate (i.e.,100% at day 0, dramatically decreased to 0% at day 2, and maintained at 0% until day 14), the indirect movement rate (i.e.,100% at day 0, decreased to 20% at day 3-4, and progressed linearly to 25% of day 14), and the probability of detection (i.e., multiplied for the probability of observing clinical signs by 2).

The effect of an *eight kilometer zone radius* for all production types was to alter the direct movement rate (i.e., 100% at day 0, decreased to 25% at

day 3-4, and decreased to 1% at day 7), the indirect movement rate (i.e., 100% at day 0, decreased to 50% at day 3-4, and decreased to 25% day 7) and the probability of detection (i.e., multiplied for the probability of observing clinical signs by 1).

The effect of a *16 kilometer zone radius* for all production types was to alter the probability of detection (i.e. multiplied for the probability of observing clinical signs by 1).

6. Eradication strategies—destruction and vaccination

6.1 Destruction

The model simulated the destruction of herds detected with PRV for all production types. A delay of two days before implementing the destruction program was assumed. The destruction capacity was assumed to be up to five units per day at day 14. Priorities for destruction were based on detection, number of days holding (the greater the number of holding days, the higher the priority) and production type (parent stock, farrow-to-finish then finishing only). All detected herds were assumed to be destroyed.

6.2 Vaccination

Vaccination campaigns were simulated in this model for all production types. Assuming two diseased units of any production type must be detected before the vaccination program begins, a 14-day delay in unit immunity followed vaccination. Capacity to vaccinate herds was assumed to be up to 100 herds per day at day 14 with the vaccination ring having a radius of up to 16 km. The vaccination priorities were based on reason for vaccination (ring

size), production type (parent stock, farrow-to-finish and finish only) and days holding. As a limitation of NAADSM version 3.1.23, the vaccine would be 100% effective in bringing complete immunity to the entire vaccinated herd.

7. *Scenarios and output*

Different scenarios were studied in the same demographic population of herds, rate of disease spread and disease detection except vaccination and zoning strategies. One thousand iterations of each scenario were modeled.

This study compared destruction with no destruction strategies, then added zoning (by comparing no zone, three and eight kilometers, and three, eight and 16 kilometers) and finally added vaccination (by comparing no vaccination, vaccination 8 kilometers, and vaccination 16 kilometers).

Output varied with the primary items of interest including the number of herds and animals infected, number of herds detected, number of herds and animals vaccinated, and duration of outbreaks in days. When destruction and vaccinations were complete, the outbreak was considered over with no more latent or infectious herds.

RESULTS

The following results were based on 1000 simulated iterations (or outbreaks) of each scenario. The 95th percentile of all possible outcomes produced by the simulation model was used for summarizing output parameters, unless otherwise specifically noted. The strategy initially compared was the population-destroy strategy **(Table 3)**. When destruction was included in the model, the duration of the outbreak was 165 days. In contrast, when the strategy was excluded in the model, the disease becomes

endemic (the outbreak was greater than 30,000 days). The total number of herds and animals infected decreased by 99% if the model contained the population-destroy strategy.

Table 3: Mean, standard deviation (SD) and the 95 percentile (p95) for the duration of outbreak (days), total number of herds infected, and total number animals infected over the outbreak (1000 scenarios) by different destruction strategies (no destroy and destroy).

Output summary		Scenario	
		No destroy	**Destroy**
Duration of outbreak (days)	Mean	>20000	96
	SD	>10000	51
	p95	>30000	165
Total number of herds infected over the outbreak	Mean	14313	194
	SD	2499	17
	p95	15418	213
Total number of animals infected over the outbreak	Mean	13297183	177117
	SD	2171056	19451
	p95	14306444	199702

The comparisons of zoning strategies are summarized in **Table 4**. When considering zoning as it was described in the materials and methods, the duration of the outbreak varied from 176 to 181 days (approximately six months) depending on the scenario. In each of these scenarios, the first day of detection for an infected herd was day 20. Disease detection was a hundred percent in all scenarios since the model assumed a hundred percent specificity of detection.

When comparing the scenario that included zones of three kilometers and eight kilometers with the no-zone (no movement restriction) scenario, the length of the outbreak was increased by one day. Approximately 1300 fewer animals (with approximately 1% of the total infected animals) and seven fewer herds (with approximately 3% of the total infected herds) became infected. The total number of detected and destroyed animals and the total number of

detected and destroyed herds was decreased 1% and 3%, respectively, when the zoning was added.

Table 4: Mean, standard deviation (SD), and the 95 percentile (p95) of duration of outbreak (days), the first day of detection, total number of herds and animals infected, detected and destroyed over the outbreak (1000 scenarios) by different zoning or animal movement restriction strategies (no zoning, three and eight kilometers zoning, and three, eight, and 16 kilometers zoning).

Output summary		Scenario		
		No zone	**3 and 8 Kilometers**	**3, 8 and 16 kilometers**
Duration of outbreak (day)	Mean	117	112	114
	SD	43	51	58
	p95	176	177	181
Day of 1st detection of infected herd	Mean	16	16	16
	SD	3	3	3
	p95	20	20	20
Total number of herds infected over the outbreak	Mean	221	206	203
	SD	5	13	16
	P95	226	219	218
Total number of animals infected over the outbreak	Mean	200241	189359	185702
	SD	4201	14961	17496
	p95	202401	201147	200949
Total number of herds detected by clinical signs over the outbreak	Mean	221	206	203
	SD	5	13	16
	p95	226	219	218
Total number of herds destroyed over the outbreak	Mean	221	206	203
	SD	5	13	16
	p95	226	219	218
Total number of animals destroyed over the outbreak	Mean	200241	189359	185702
	SD	4201	14961	17496
	p95	202401	201147	200949

On the other hand, when including zoning of three kilometers, eight kilometers and 16 kilometers, the duration of the outbreak was increased by five days based on the 95% percentile of the no-zone scenario. There were 1500 fewer animals (with approximately 1% of the total infected animals) and eight fewer herds (with approximately 4% of the total infected herds) that became infected when the zoning was added. The total number of detected and destroyed animals and the total number of detected and destroyed herds with zoning were, respectively, 1% and 4% less than the total number of destroyed animals in the no-zone scenario. In view of vaccination, by comparing the eight kilometer and 16 kilometer vaccination ring with no vaccination (**Table 5**), the duration of outbreak was decreased by 16 days (6%) for both the eight kilometer ring and the 16 kilometer ring. Approximately 2% fewer herds became infected when the vaccination ring was eight kilometers and 16 kilometers. The total number of destroyed herds was decreased by 3% with the eight kilometer vaccination ring and 4% with the 16 kilometer vaccination ring. The total number of vaccinated herds in the eight kilometer vaccination ring was 420. When the ring size was increased to 16 kilometers the total number of vaccinated herds increased by 6%.

Table 5: Mean, standard deviation (SD), and the 95 percentile (p95) of duration of outbreak (days), total number of herds and animals infected, destroyed, and vaccinated over the outbreak (1000 scenarios) by different vaccination strategies (no vaccination, vaccination within eight kilometers ring and vaccination within 16 kilometers ring).

Output summary		Scenario		
		No vac	**8Km**	**16Km**
Duration of outbreak	Mean	114	99	96
	SD	58	77	51
	p95	181	165	165
Total number of herds infected over the outbreak	Mean	203	194	194
	SD	16	17	17
	p95	218	214	213
Total number of animals infected over the outbreak	Mean	185702	177125	177117
	SD	17496	19629	19451
	p95	200949	199993	199702
Total number of herds destroyed over the outbreak	Mean	203	189	188
	SD	16	18	18
	p95	218	211	209
Total number of animals destroyed over the outbreak	Mean	185702	173922	172422
	SD	17496	19891	19995
	p95	200949	198464	198184
Total number of herds vaccinated	Mean		380	402
	SD		30	30
	p95		420	447
Total number of animals vaccinated	Mean		323776	348898
	SD		34725	33998
	p95		374206	400036

DISCUSSION

Simulation models are limited in that they cannot predict the future nor do they represent a real-time outbreak; instead they should be used to aid decision making, planning, identifying potential results and evaluating strategies based on available data. The results in this study represent an outbreak in commercial swine farms in Chiang-Mai and Lampoon Provinces

only and do not refer to the national or regional level. The accuracy of data affects the usefulness of the disease spread model. Our data were obtained since 2004 and was the most current and accurate data available for this study. The population data could certainly be modified if more current information became available.

The model used in this study, North American Animal Disease Spread Model (NAADSM) version 3.1.23, has its own limitations. This model was developed for foot and mouth disease and may not accurately reflect the properties of pseudorabies virus (PRV). The latency, a major characteristic of herpesvirus, was difficult to confine in this model. Additionally, in this study the model assumes the movements are random, and this may not be appropriate in the swine industry, especially when animals move within a production system.

The disease parameters were not specific for the viral strain in Thailand but were instead based on viral properties reported in the scientific literature. It is reasonable that a new viral strain with different properties could appear, and the results may deviate from this study. Generally, vaccines are not 100% effective; however, this model assumed 100% effectiveness of vaccination. Vaccination only prevented the appearance of clinical signs but did not prevent viral infection. The efficiency of vaccination refers to its ability to protect the animals from showing clinical signs. Since the NAADSM version 3.1.23 does not allow for adjustment of the vaccine effectiveness, the actual duration of outbreak (days), as well as the total number of animals and herds infected and destroyed, may differ from this study. Alternative control measures may be necessary. The immune status of commercial swine in this

model was considered to be naïve, and this also may have affected the results.

Destruction (destroy strategy) of infected herds is an action common to many countries as they attempt to eradicate PRV. We compared two strategies, with and without destruction. Destruction appeared to be the most beneficial of all the approaches toward eradicating PRV infection; the duration of the outbreak (days) decreased dramatically from over 30,000 days (7 years) to 165 days (less than one year), and total number of herds and animals infected decreased by 99% when the destruction strategy was added.

The zoning (animal movement restriction) strategy was added after the destruction strategy and was implemented to restrict movement and enhance detection in a surveillance area. There did not seem to be any relevant difference between the three zone scenarios examined in this study as the duration of outbreak increased one to five days when zoning was applied. However, if we applied the 3, 8 and 16 kilometer zones, this appeared to relieve the infection and decrease the number of herds that had to be destroyed.

Ring vaccination was also studied as a tool to control and eradicate PRV. The model applied a vaccination strategy after the implementation of destruction and zoning (animal movement restriction) strategies. Both eight kilometer and 16 kilometer ring vaccination decreased the 95^{th} percentile duration of outbreaks from 181 days to 165 days. The 16 kilometer ring seemed more effective in alleviating the outbreak and reduced the infection and destruction rates more than the eight kilometer ring.

CONCLUSION

It is apparent from this study that the destruction strategy has the greatest impact in eradicating Pseudorabies virus (PRV). Zoning (animal movement restriction) and ring vaccination after the destruction strategy were not shown to be significant influences to this model based on the duration of outbreak (days), and the total number of animals and herds infected, detected, and destroyed. However, the duration of outbreak, number of infections and herds destroyed declined when zoning and vaccination were implemented. Therefore, until further study is completed the recommendations from this study are to apply a destroy strategy and three-zone (3, 8 and 16 kilometers) movement restriction, as well as enhanced detection with a 16 kilometer vaccination ring to eradicate PRV in Chiang-Mai and Lampoon Provinces.

FURTHER STUDY

Determination of the most cost-effective choice of both zone and vaccination rings is recommended for future research. Evaluation of other strategies for eradicating Pseudorabies virus (PRV) is also recommended for future study.

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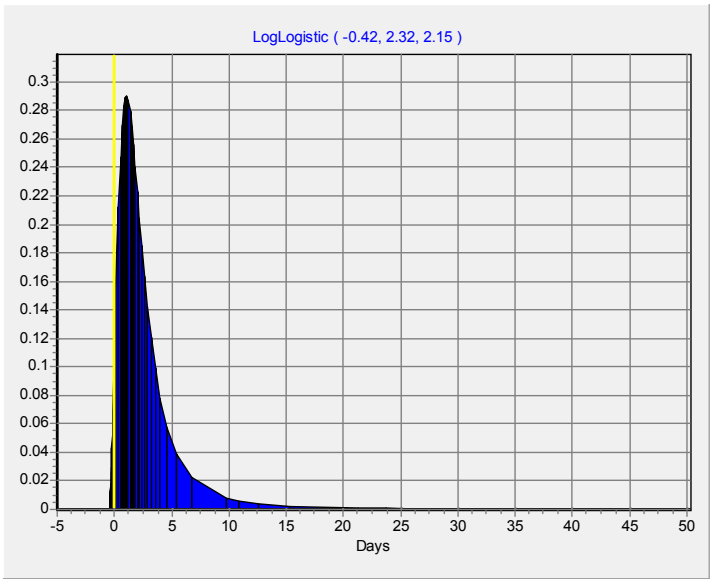
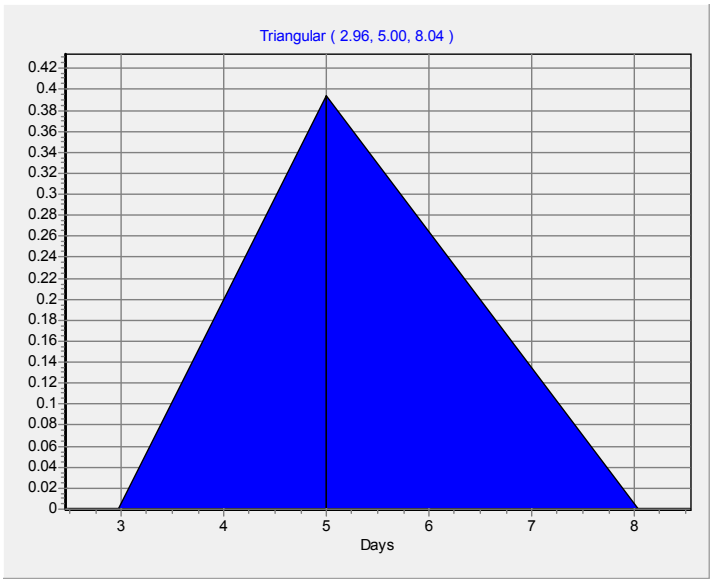
APPENDIX

Examples of the probability density function used for disease parameter of Pseudorabies

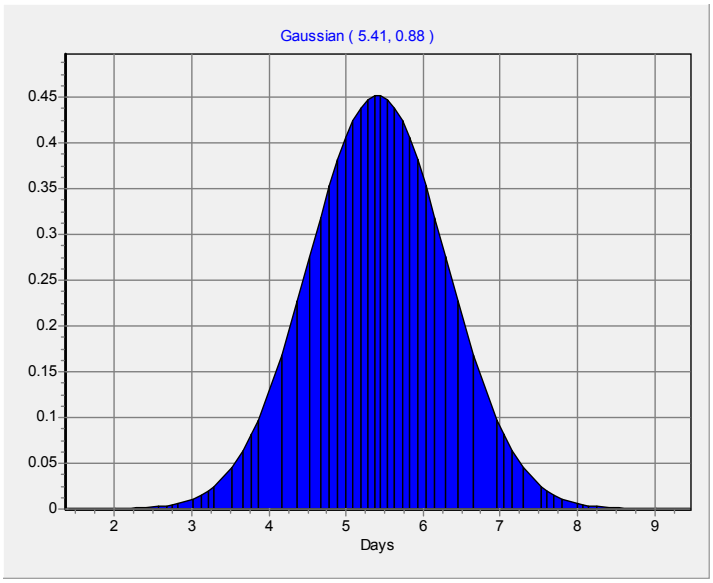
Example 1: Log-logistic function described the disease state (latent period) of finishing production type.



Example 2: Triangular function described the disease state (subclinical infectious period) of parent stock production type.



Example 3: Gaussian function described the disease state (subclinical infectious period) of farrow-to-finish production type.



Example 4: Lognormal function described the disease state (immune period) of all production types.