

DISSERTATION

CONTROL OF FOOT AND MOUTH DISEASE FOR THE
MALAYSIA-THAILAND-MYANMAR
PENINSULA CAMPAIGN:
USES OF QUANTITATIVE RISK ASSESSMENT AND
EPIDEMIOLOGICAL MODELING

Submitted by

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In partial fulfillment of the requirements

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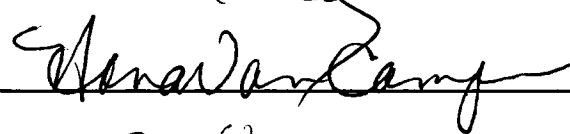
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April 17, 2006

WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY KACHEN WONGSATHAPORNCHAI ENTITLED CONTROL OF FMD FOR THE MALAYSIA-THAILAND-MYANMAR PENINSULAR CAMPAIGN: USES OF RISK ASSESSMENT AND EPIDEMIOLOGICAL MODELING BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

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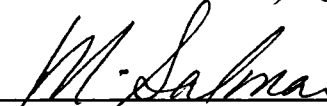








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ABSTRACT OF DISSERTATION
CONTROL OF FOOT AND MOUTH DISEASE FOR THE
MALAYSIA-THAILAND-MYANMAR (MTM)
PENINSULA CAMPAIGN:
USES OF QUANTITATIVE RISK ASSESSMENT AND
EPIDEMIOLOGICAL MODELING

Livestock industries in the countries of South East Asia (SEA) have suffered from the presence of foot and mouth disease (FMD). Realizing that FMD is transboundary, SEA countries have formed a regional collaborative organization utilizing a progressive zoning approach to assist in the FMD eradication. A campaign involving three countries, including Malaysia, Myanmar, and Thailand, called MTM, has been initiated. To assist the campaign in achieving its ultimate goal, the MTM Tri-state Commission identified the necessity of the risk analysis study. Hence, a quantitative risk assessment (QRA) study was conducted in the MTM peninsula to assess the likelihood of an introduction to FMD through importation of livestock. Patterns of livestock movement were ascertained through reviewing the relevant governmental records, and by interviewing farmers, traders and local officers when the records did not exist. Movement regulations were reviewed and the information was used to construct QRA scenario trees. QRA processes began by identifying model parameters and their values. The parameters were probabilities of livestock having FMD and of FMD infection undetected during import

processes. Given current import regulations, the study determined the probability of a livestock accepted for import having FMD. The sensitivity analysis was carried out to determine the effects that each parameter had on the model. The model simulations were run in @Risk[®] for Excel[®] software using a stochastic approach. The simulations yielded the most-likely prevalence at 8%. On average, each animal in a quarantine station would have 2.7% chance of having an unapparent form of FMD infection; hence will not be identified as infected. The findings showed that the average probability of an accepted livestock carrying FMD was 2.9%, and the risk was as high as 11%.

A compartmental epidemiological model was developed to assess the impacts of the introduction of FMD and FMD control programs in Southern Thailand. The values for the model parameters were ascertained by reviews of literatures and records retrieved from Department of Livestock Development (DLD). Outbreak data was gathered from reports submitted to DLD and from the database of the Southeast Asia Foot and Mouth Disease (SEAFMD) Regional Coordinating Unit (RCU). The value for the transmission rate was acknowledged by comparing observed to expected outbreak data using least square method. Stochastic simulations were also run in the @Risk for Excel[®] software. The sensitivity analysis for annual cumulative incidence (ACI) was performed; and the effects of vaccination (ϵ), stamping-out policy (κ), and sensitivity of the screening processes during quarantine (p_S) were examined. The significances of the parameters used in the sensitivity analysis were evaluated using a partial rank correlation coefficient method. The results showed that all parameters revealed negative correlations with ACI, but only p_S was considered significant (p-value < 0.0001). This suggested that prevention of the introduction of FMD was more important than dealing with the disease once it enters the areas.

Further analyses for the alternative control options were carried out. Five scenarios were created to imitate different FMD control strategies in Southern Thailand. The baseline scenario (BS) was constructed emulating current control strategy used in the south, and was used as the comparison point for all other subsequent scenarios. Eradication Scenario (ES) I was created for the investigation of improved sensitivity during the disease screening process, i.e. assimilation of NSP test during the quarantine. Having created much debate in recent years, the impact of mass vaccination was examined in the ES II, where 80% vaccination coverage was assumed to be implemented randomly in the MTM zones in Thailand. ES III evaluated an integrated use of NSP test and vaccines; and ES IV investigated an addition of the implementation of the stamping-out policy to the ES III. Approximately thirty-five thousands cases were expected from the BS. About 30% and 85% reduction of ACI from the BS were observed for the ES I and ES II, respectively. ES III resulted in the 96% ACI reduction; and slightly more drop in the ACI (98%) was seen in the ES IV. The results from the analyses suggested that the vaccination had more impact on the ACI than the use of NSP test. It was indicative that the use of NSP test reduced the ACI during the peak season, where the vaccination diminished the underlying incidence of FMD. The model indicated that the best mitigation strategy was the integrated and strategic use of control techniques.

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This dissertation is composed of series of interrelated, ground-breaking studies using epidemiological approaches that, so far, have not before been prevailed in the Southeast Asian region. One of the major challenges and limitations for such innovative composition was the availability of reliable and relevant data. Collection of required data was time-consuming and involved many organizations and individuals, both at the national and regional levels. Several national institutions within the MTM member countries have contributed appreciably to the completion of the studies, including the Department of Veterinary Services of Malaysia, the Department of Livestock Development of Thailand, and the Livestock Breeding and Veterinary Department of Myanmar. Many veterinarians from local veterinary offices and laboratories within these departments have also provided valuable assistances in terms of personal inputs and data gatherings. On a regional level, I am very much obliged to the SEAFMD Member Countries and the FMD Regional Reference Laboratory at Pakchong (RRL) for the assistance and technical guidance. Particularly, I would like to thank the SEAFMD Regional Coordinating Unit of the OIE (RCU). The RCU has provided me with the place to work and with the support for my travels during the data collection phase. Lots of data used in these studies also derived from the RCU comprehensive, yet improvable database.

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Chapter 1

1.1 Introduction

Foot and mouth disease (foot-and-mouth disease or FMD) is a viral disease in cloven-hoofed animals. FMD is one of the most important diseases in livestock because it constrains animal productivity and international trade of animals and animal products. Many FMD-endemic countries are struggling to control this disease. In FMD-free countries, FMD posts a great risk as an emerging disease and always results in tremendous economic loss when FMD reappears. Controlling and eventually eradicating FMD is one of the top priorities for FMD-endemic areas, whereas preventing a new introduction is a major concern for FMD-free countries.

There are various approaches in preventing, controlling, and eradicating FMD. Slaughtering of infected and those in close contact with infected animals, or so called stamping-out, is generally employed to rapidly control an FMD outbreak in an area previously free from FMD. Examples of practical uses for stamping-out policy were revealed in the FMD outbreaks that reemerged in the United Kingdom and South Korea in 2001. Stamping-out sometimes is incorporated with other controlling methods, such as vaccination and movement restriction. Uses of stamping-out in combination with vaccination were demonstrated during the reemerging outbreaks in Argentina in 2003. In FMD-endemic areas, control of FMD often relies on the use of vaccine. However, it has

been well documented that vaccines are not 100 percent effective against FMD virus (FMDV). Many have recommended that, to effectively control or even eradicate FMD, animal movement management is a must. This became a major obstacle in many situations, especially for developing countries and countries in transition because managing the movement of animal is not always an easy task. When there is no single method to counter FMD, dealing with the disease requires strategic approaches that combine and “optimize” various measures and must be suitable for the situations under consideration.

Testing for FMD infection is not particularly difficult; however, there exist practical constraints and limitations. Antigen diagnosis is a conclusive evidence for FMD infection. Nonetheless, acquiring field sample that is ideal for antigen detection is exceptionally challenging and requires experience in sample collection and transportation. In addition, antigen detection, is typically not suitable for screening purposes. Serological tests for antibody to FMDV, on the other hand, are recommended to be used as screening tests. The tests for antibody, however, pose another major limitation. Most of the serological tests for antibody to FMDV are unable to differentiate between naturally-infected animals and animals that have acquired immunity from vaccination. Until recently, the introduction of antibody test to non-structural proteins (NSP) can, in theory, solve the loophole in serological tests for FMD antibody. Applications of NSP test for variety of situations, nevertheless, have not been well understood, and researches are being carried out throughout the world. Despite all ambiguities, NSP test has been widely used by veterinary officers in many, if not all, circumstances.

FMD is a global concern, but outbreak areas occur mostly in Asian, African, and South American continents. FMD is endemic in most parts of Southeast Asia (SEA), with the exception of Brunei, Singapore, Indonesia, and parts of the Philippines and Malaysia. Only 3 known serotypes circulate within SEA, with serotype O being predominant. Serotype A, however, has become a major concern since 2003, especially in the mainland of SEA.

FMD is a transboundary disease, which means the disease is spread regardless of predefined boundaries. Therefore, dealing with the disease often requires collaborative efforts between regions or, sometimes, countries. The Malaysia-Thailand-Myanmar Peninsula Campaign for FMD Freedom was initiated by the Office International des Epizooties (OIE), an international organization responsible for regulating animal health and related issues. The campaign aims to encourage international cooperation to systematically establish, to the OIE standards, FMD-free areas.

There are several mitigation strategies to contest with FMD. The decisions on which strategy to use cannot be solely instinctive. Also, different organizations may choose to employ approaches they see fit for their own situations. Harmonization of different approaches is suggested for a collaborative working environment. There are needs for well-constructed plans that can provide scientifically-based recommendations for the *best* mitigation measures that will maximize the use of existing resources, itemize the required complementary studies, and optimize pros and cons for the strategies employed. To achieve these objectives, there is a crucial demand for a risk analysis.

Risk analysis is a systematic process that maximizes the use of current knowledge and information to make sound recommendations to groups or persons responsible for

making decisions. Risk analysis has gained global acceptance and has been largely utilized in many situations, especially for trade purposes. In many circumstances, risk analysis is also exploited to assist in making crucial decisions pertaining to control and eradication of diseases.

In our study, we demonstrate the practical use of risk assessment — a critically preceding step in the risk analysis processes — together with mathematical disease modeling in assisting the FMD control efforts in the MTM areas. We begin with a review of relevant literature to provide the basic knowledge of the disease. The background information of the FMD situation in the MTM areas was highlighted. In addition, fundamental applications and limitations of risk assessment and mathematical modeling have been elaborated. This dissertation consists of three self-explanatory and interrelated manuscripts that have been submitted to scientific journals. Each manuscript, therefore, serves as a separate chapter of this dissertation. Results and discussions for the manuscripts are provided exclusively and separately in the respective chapters.

1.2 Review of Literature and Justification for Research

1.2.1 Foot and Mouth Disease Virus

It is particularly important to understand the biology of FMD and of the virus causing the disease. Knowledge of the virus will set the fundamental understanding of how various antigenicities play different roles in causing the disease, factors determining antigenic variations of the virus, differences in disease appearances, the viral infectivity, pathogenicity, virulence, and etcetera.

FMDV belongs to the genus *Aphthovirus* of the family *Picornaviridae*. The virus has played a historically important role in virology and has always caught virologists' attentions since its first discovery as a filterable virus in 1897 (Grubman and Baxt, 2004). It is imperative to appreciate some of the FMD viral properties with respect to the FMD characteristics and to difficulties in control and eradication of the disease.

The FMDV complete virion has a diameter of 23 nm (21-25 nm) and its molecular weight is 8.5×10^6 Da (Ferrer-Orta and Fita, 2004), 69% being protein. The capsid consists of 32 capsomeres in the form of an icosahedron, which surrounds the RNA genome. The single-stranded RNA molecule of the ether- and chloroform-resistant complete virion consist of 8450 (8000-8500) bases and has a sedimentation coefficient of 35 S. The ribonucleic acid (RNA) is the infectious unit because it is positive in polarity and acts as a messenger. The virion is composed of 60 identical copies of the structural polypeptides VP1, VP2, VP3, and VP4. The capsid protein VP1 induces the production of neutralizing antibodies in cattle and pigs; the same can be accomplished with chemically broken down fragments of VP1. It is thought that wide variation in the protein VP1 is responsible for genetic differences between serotypes. The VP1 - VP3 proteins form the surface structure of the viral capsid and VP4 protein mediates between RNA and other proteins. The receptor binding amino acid (ligands) are located superficially on flexible, sequence-variable structures protruding from the surface of the virion. These protrusion structures enhance the ability of the virus to bind to the host cell. Six types of FMDV non-structural proteins (NSP), which are mainly enzymes, have been identified, namely 3A, 3B, 3C, 2B, 2C, and 3D (Figure 1.1). The importance of these proteins lie largely in the differentiation of vaccinated from naturally infected animals.

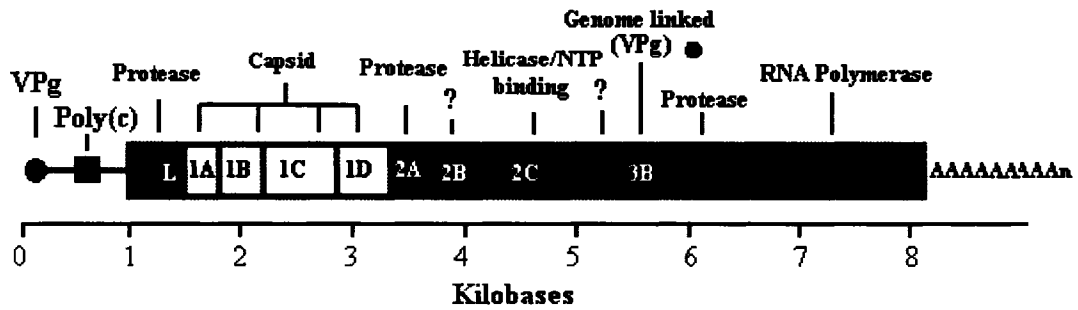


Figure 1.1: Aphthovirus genome map

FMD viral RNA is an infectious unit, meaning that the viral RNA contains all the information required to initiate the infection and the infection cycle can occur without the requisite of viral proteins. The entire viral replication that takes place in the cytoplasm of the cells results in the disruption of nearly all of the host macromolecular synthesis and only allows the production of viral RNA and viral proteins. The replication process occurs in two main stages; first, the initial synthesis of negative stranded RNA using the positive strand template, then many positive-sense infectious RNAs are produced from the negative strands. The infectious RNAs are then “packaged” (organized) by the structural proteins to produce new viral particles. The viral RNA encodes 15 proteins that are involved in the replication process of the FMDV, including the two forms of the Leader (L) protein and three different copies of VPg (3B). The readers are encouraged to read Graham and Martinez-Salas (2004) for the detailed information on the functions of these proteins and the regulation of their synthesis.

Regarding their functions and structures, the antigenic components of FMD virus stimulate antibodies within the infected animal differently. The immunizing component of the complete virion produces type-specific antibodies. These type-specific antibodies can be regarded as 7 serological differences, or serotypes, including serotype O, A, C, SAT1, SAT 2, SAT 3, and Asia I. Within these serotypes, there are 61 subtypes, and,

within these subtypes, numerous strains with different antigenic properties can be distinguished. The FMD types O, A, and C exist all over the world, while outbreaks of the SAT (South African Territories, named because of their geographic occurrences) types are mainly restricted to Africa, and those of the Asia-I type to Asia.

The FMD virus is relatively resistant in the environment; it survives 5-10 weeks in protected places during cool weather, especially in tissues or other organic matter, a pH not below 6.5 being prerequisite. While after drying up, the FMD virus can survive from one week to months in and on inanimate material, lower temperatures result in an even longer survival period. The virus can remain viable for years at -20°C. In the dirt of sheds, it remains viable for 14 days, in animal refuse for 39 days, in manure for 6 days, on the surface of manure during summer for 28 days, and in winter for 67 days. The virus can survive in feed for 15 weeks, on cattle hair for 4 weeks and in wastewater for up to 103 days.

1.2.2 Foot and Mouth Disease

Infection of FMDV is characterized by vesicular lesions on hairless areas of the skin, particularly on the mucous membrane of the mouth, muzzle, snout, udder, and feet. The lesions on the feet are localized in the interdigital space (space between the toes) and the coronary band (delineation between the hoof and skin).

After the incubation period, the first clinical symptom occurs when the animals salivate. The mucosa of the oral cavity becomes reddened. The oral lesions typically become complicated with secondary infection by opportunistic bacteria. Typical signs caused by these lesions are salivation, smacking of the lips, and grinding of the teeth. Simultaneously or later, erosions of the interdigital space appear at the bulbs of the heel

and around the coronet as well as on the udder. The animals become lame and show disinclination to stand. In an immunologically naïve population, if the disease takes a favorable course, a severe myocarditis (called “tiger-heart”) may appear especially in young animals, which may die suddenly without premonitory signs. In most outbreaks, the morbidity is high and the mortality is low except in young animals that become malnourished from inadequate nursing due to oral lesions combined with the teat lesions of their mothers.

Susceptible animals generally acquire infection through the respiratory route, which is where the initial viral replication occurs. Respiratory mucosa and lymphoid tissues of the pharynx are the preferential sites for the virus to replicate. Following the initial replication at lymphatic tissues, a primary viremia takes place whereby the FMDV reaches other organs and tissues, resulting in further replication.

In cattle and sheep, viral replication occurs initially in the mucosa and the lymphoid tissues of the pharynx, followed by an initial viremia and the occurrence of further replication. The predilection sites for FMD virus infection are squamous epithelium cells and areas of persistent local irritation or friction. The incubation period varies depending on what type of animal is infected. The incubation period in cattle is approximately 5-7 days, 1-6 days in small ruminants, and 2-12 days in pigs.

Infected cattle show initial signs of fever, which last about one to two days. Following the initial pyrexia, mouth lesions are often observed, including development of vesicles on the tongue, hard palate, lips, gum and muzzle. Vesicular lesions are also seen on the dental pad, coronary band and interdigital space, and udder and teats (Kitching, 2002). Pigs often develop clinical lesions around the coronary bands of the feet. In pigs,

other clinical signs, such as fever and vesicular lesions on the snout and tongue, are less common (Kitching and Alexandersen, 2002). Temperature increase in infected pigs is inconsistent and sometimes a temperature drop is recorded in severely affected pigs. In young pigs, mortality is observed without development of clinical symptoms due to the cardiac condition known as tiger heart syndrome. Vesicular lesions in small ruminants are not always apparent. Hughes et al. (2002) reported that approximately 25% of infected sheep did not develop vesicles, and about 20% developed only a single observable lesion. Classical lesions of FMD are not easily observed in small ruminants. General symptoms in infected sheep and goats include fever and lameness, which neither of them are the indication for FMD infection. Loss of production may be seen in lactating animals. Young lambs and kids, like infection in other species, may also suffer from heart failure.

An important characteristic of FMD is the persistent infection, known as the carrier state. The persistent infection is defined as the recovery of FMDV 28 days post-infection from samples taken from oesophago-pharyngeal (OP) region. Carriers are most certainly a natural reservoir of FMD virus in enzootic areas and a potential source of antigenically mutated virus variants because variations of the virus with subsequent selection of virus mutants occur continuously in the animal during the carrier state. Persistence of FMDV is often found in cattle recovered from natural infection. So far, there is no evidence that pigs can become carriers for FMD. Infection in pigs is cleared within 3-4 weeks and FMDV cannot be recovered from the OP region (the area where FMDV is found in convalescent cattle) of pigs recovering from FMD infection. A study

by Mezencio et al. (1999) reported the presence of FMD viral RNA in the blood of a convalescent pig; however, its epidemiological significance is unclear.

1.2.2.1 The Host

The impact of the FMD infection on livestock is defined by strains of FMDV, species of hosts, conditions of the animals, and other environmental factors. In this section, we will attempt to describe the relevance of host species and conditions that influence the FMD infection. Almost all domesticated, cloven-hoofed livestock can be infected with FMDV. In domesticated animals, FMD can be observed in cattle, buffalo, sheep, goats, pigs and camelids. Some species of wildlife animals are also susceptible to FMDV; examples are 22 members of the Bovidae, 10 Cervidae, 4 Suidae, 1 Tayasuidae and 4 Camelidae. There are many other species that are recorded to have been infected with FMDV as described by Hedger (1980) and Thomson et al. (2003). Despite the variety of host ranges, only FMD infections in some species of livestock have received public attention and have been extensively studied, including cattle and swine.

Infection with FMDV stimulates the early antibody response of the Immunoglobulin (Ig) M class. The IgM can be detected from about 4 days and reaches the peak levels in 7 to 14 days following the infection. This early IgM will neutralize and precipitate both homologous and heterologous virus. At about 10 to 14 days after infection, another class of Ig, IgG, arises and reaches its peak at about 28 days. Besides the neutralization and precipitation properties, this IgG class will also fix complement and is much more specific to different types of FMDV than those belonging to the IgM class. The IgA class antibody can be detected early after the infection in upper

respiratory secretions. Its role in the protection against the systemic infection is, however, considered irrelevant.

In cattle, the initial route of infection is usually the respiratory tract by aerosolized virus. Only about 10-25 fifty-percent tissue culture infective dose (TCID₅₀) is needed to trigger infection in cattle (Donaldson et al., 1987). Swine, on the other hand, are more tolerant to aerosol infection than cattle. At least 800 (Alexandersen et al., 2002) and up to 6,000 (Alexandersen and Donaldson, 2002) TCID₅₀ may be required to cause infection in pigs. Although pigs are less susceptible to airborne FMD infection, infectious pigs produce much more aerosol virus than that produced by ruminants (Donaldson and Alexandersen, 2002). A study by Alexandersen and Donaldson (2002) reported that an adult pig secreted around 10⁶ TCID₅₀ per 24 hours; there are small variations depending on virus strains, individual pig variation, and other environmental conditions. Hence, pigs are known to be the amplifying hosts for the aerosolized form of FMDV because of their ability to generate large amounts of virus.

Pigs are more susceptible than cattle to infection via ingestion of infectious materials. Viral infectious units required to infect cattle are about 100 times more than those required to infect pigs (Donaldson et al., 1987) via the oral route. Thus, initial acquisition of FMD in swine generally results from consuming materials contaminated with viable FMDV. Other routes of transmission for swine normally occur after the disease has already been established in the herd.

Susceptibility of small ruminants, sheep and goats in particular, to FMDV infection varies depending upon breeds of the animal and strains of the virus. In general, sheep and goats are highly susceptible to infection by aerosolized FMDV. Similar to

other ruminants, the report documented that as little as 20 TCID₅₀ sufficed to cause infection in sheep (Gibson and Donaldson, 1986). Considering air uptake, small ruminants are less likely to become infected by airborne virus than cattle. However, small ruminants are not major producers of aerosolized FMDV; and an infected sheep is unlikely to transmit virus over distances greater than 100 meters (Sorensen et al., 2000). Thus, the infection in small ruminants most often occurs by direct contact with infected animals or by mechanical transmission of the virus through fomites. The morbidity in small ruminants also appears to be lower than in cattle. Kitching and Hughes (2002) revealed the empirical evidence of the recent FMD outbreaks in the UK. The authors demonstrated that a much lower numbers of sheep were affected as compared to cattle in the same premises. The authors speculated that this was due to low transmission rate of FMD in sheep (Hughes, 2001).

The significance of FMD in wildlife adheres to the potential that the infected wildlife can spread the disease to domesticated animals. In addition, the presence of FMD in wildlife can hamper international trade of livestock and livestock products. However, FMD in wildlife species has not been well studied in any detail. Only extrapolation from what is known to occur in domesticated species is currently accepted to also occur in wildlife. In general, shedding of the virus occurs at high levels in oronasal secretions 1 to 3 days prior to, and 7 to 14 days after observance of the lesions (Thomson et al., 2003). Spread of FMD from wildlife to domesticated animals normally takes place where there is commingling between species, and usually occurs by direct or mechanical transmission. Evidences suggested that transmission over long distances by aerosolized virus rarely happened (Thomson et al., 2003). Because so little is known, for

now, we limit our discussion regarding FMD in wildlife and their significance in maintaining the disease.

1.2.2.2 Global Distribution of FMD

FMD is the disease of global concerns. FMD is observed in many parts of the world, especially in the continent of Asia, Africa, and less so in South America¹. In 2000, FMD was officially reported in fifty-nine countries. In Europe, the disease was observed in Greece. In Asia, FMD was alphabetically reported from Armenia, Azerbaijan, Bangladesh, Cambodia, China, Georgia, Iran, Iraq, Japan, Kazakhstan, Kyrgyzstan, Laos, Mongolia, Nepal, Pakistan, Philippines, Republic of Korea, Russia, Taiwan, Tajikistan, Thailand, Turkey, Turkmenistan, and Vietnam. In the countries of Africa, Egypt, Kenya, Malawi, Mauritania, Namibia, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe reported the outbreaks of FMD. For South America, countries that reported the outbreaks of FMD were Brazil, Bolivia, Colombia, Ecuador, Peru, Uruguay, and Venezuela. In 2001, the dramatic episodes of FMD occurred when the disease spread to the countries that were previously FMD-free. The reemergence of FMD occurred in Western Europe (the United Kingdom, the Netherlands, France, and Ireland) and South America (Argentina). The outbreaks in the UK resulted in the catastrophic events to the livestock industries in the country, and millions of livestock were culled to control the epidemics².

¹ Geographical Distribution of List A Disease, Office international des Epizooties, http://www.oie.int/eng/info/en_presdistribgeo.htm, viewed October 23, 2005.

² Handistatus II, Office international des Epizooties, <http://www.oie.int/hs2/report.asp?lang=en>, viewed January 11, 2003



Figure 1.2: Global distribution of FMD from 1992-2002³.

As of September of 2004, 62 countries reported outbreaks of FMD between 2003 to September 2004. Countries in North America, Western Europe, and Australia were free from FMD without the use of vaccination, as declared by the OIE. There were also some countries in the endemic continents that were declared free of FMD, such as Japan, Indonesia, and Chile. Other countries were also successful with the regionalization process to develop the OIE-approved FMD free regions. These regions included southern Brazil, southern Philippines, southern Argentina, and eastern island of Malaysia etcetera. FMDV serotype O was dominating and was reported in 44 countries (71%), followed by serotype A (27%). Outbreaks of FMDV serotype Asia 1 and C were reported to the OIE by 4 countries in South Asia and 3 countries in Africa, respectively. FMDV serotype SAT 1, SAT 2, and SAT3 were limited to only in the countries of South Africa⁴.

³ Nick Knowles, World Reference Laboratory for FMD,
<http://www.iah.bbsrc.ac.uk/virus/picornaviridae/aphthovirus>, viewed October 24, 2005

⁴ Valarcher, J., Knowles, N., Fernandez, R., Davies, P., Midgley, R., Hutchings, G., Newman, B., Statham, B., Ferris, N., and Paton, D. FMD Global Update 2003-2004. FAO World Reference Laboratory for FMD.



Figure 1.3: Global distribution of FMD in 2004¹

1.2.3 Regional Status and Approach to Control and Eradicate FMD in the MTM Areas

Concerns over FMD as one of the major transboundary diseases prompted the countries in South East Asia (SEA) to establish a regional collaboration. In 1990, the Regional Coordinating Unit was established by the OIE as the first regional effort to coordinate FMD control activities in the countries of SEA. The group of the countries in SEA involved in the regional FMD campaign, later called South East Asia Foot and Mouth Disease (SEAFMD) Campaign, includes Cambodia, Indonesia, Lao People's Democratic Republic (PDR), Malaysia, Myanmar, the Philippines, Thailand, and Vietnam. In late 1999, the OIE conducted a review of the Campaign. Eight main components to the program were identified. During this process it was identified that the

Presentations from the Open Session of the EUFMD Research Group, 12-15 October 2004, Chania, Greece. <http://www.iah.bbsrc.ac.uk/virus/Picornaviridae/Aphthovirus/WRLFMD/EUFMD-Crete/Valarcher.ppt>, viewed March 12, 2005.

establishment of a disease free region to OIE-recognized standards is an effective way to progressively increase the control and eradication of FMD. Individual ASEAN countries have been successful in establishing disease free zones (e.g., Indonesia and zones within the Philippines and Malaysia). It was also necessary to demonstrate progress with a regionalization approach involving more than one country in the mainland Southeast Asia. A collaborative effort between three countries in the mainland of SEA was initiated. The three countries include Malaysia, Myanmar, and Thailand (called MTM). An area of the MTM peninsula was selected as a potential free zone for FMD because:

- *There are natural advantages that favor FMD Control and Eradication;*
- *there is a relatively high chance of success;*
- *this is a good tripartite example of the need for international cooperation and there are benefits to all three participating countries. These include the ability to increase trade, reduced impact of FMD, reduced costs of control and the spin off benefits for the control of other important diseases (Edwards, 2004).*

Within the MTM areas, “zones” of different status have been established. The MTM member countries agreed during the first Tri-state Commission Meeting to delineate project zoning as stated in the Minimum Standards of Definitions and Rules (SDRs) (submitted to the Tri-state Commission in 2002 and revised in 2003) (Turton, 2002; Turton, 2003). The details for the zoning recommendations are as the following:

Infected Zone (IZ):

Thailand: The IZ in Thailand includes the provinces north of the Prachuap Kirikhan province in the BZ.

Myanmar: The IZ in Myanmar involves areas north of the Tanintharyi division.

Buffer Zone (BZ):

Thailand: Prachuap Kirikhan province of Region 7 serves as the BZ for Thailand.

Myanmar: The BZ will include Tanintharyi division from Thayetchung south to the control zone. This involves all of Myeik district, including Palaw, Myeik, Tanintharyi and Myeik Kyunsu township of Dawei district.

Control Zone (CZ):

Thailand: The CZ in Thailand consists of Region 8 and 9, from Chumpon southward to the Thai-Malaysian border.

Myanmar: The CZ includes Kawthaung District in Tanintharyi Division, which comprises Kawthuang and Bokpyin townships.

Malaysia: The CZ includes the whole State of Perlis and Kedah; districts of Seberang Perai Utara, Seberang Perai Tengah and Seberang Perai Selatan of Penang state; districts of Hulu Perak in the Perak state; districts of Tumpat, Parsir Mas, Kota Bharu, Bachok, Kuala Kerai, and Pasir Putih of Kelantan state; and district of Besut in the Terengganu state.

Eradication Zone (EZ):

Malaysia: The EZ includes southern Malaysia, starting from south of the CZ.

Further details on the zoning standards and standards for zone progressions are elaborated in the SDRs.

In the next sections, we review the histories and current situations of FMD within the respective MTM countries. FMD control, prevention, and eradication efforts, if exist, are described.

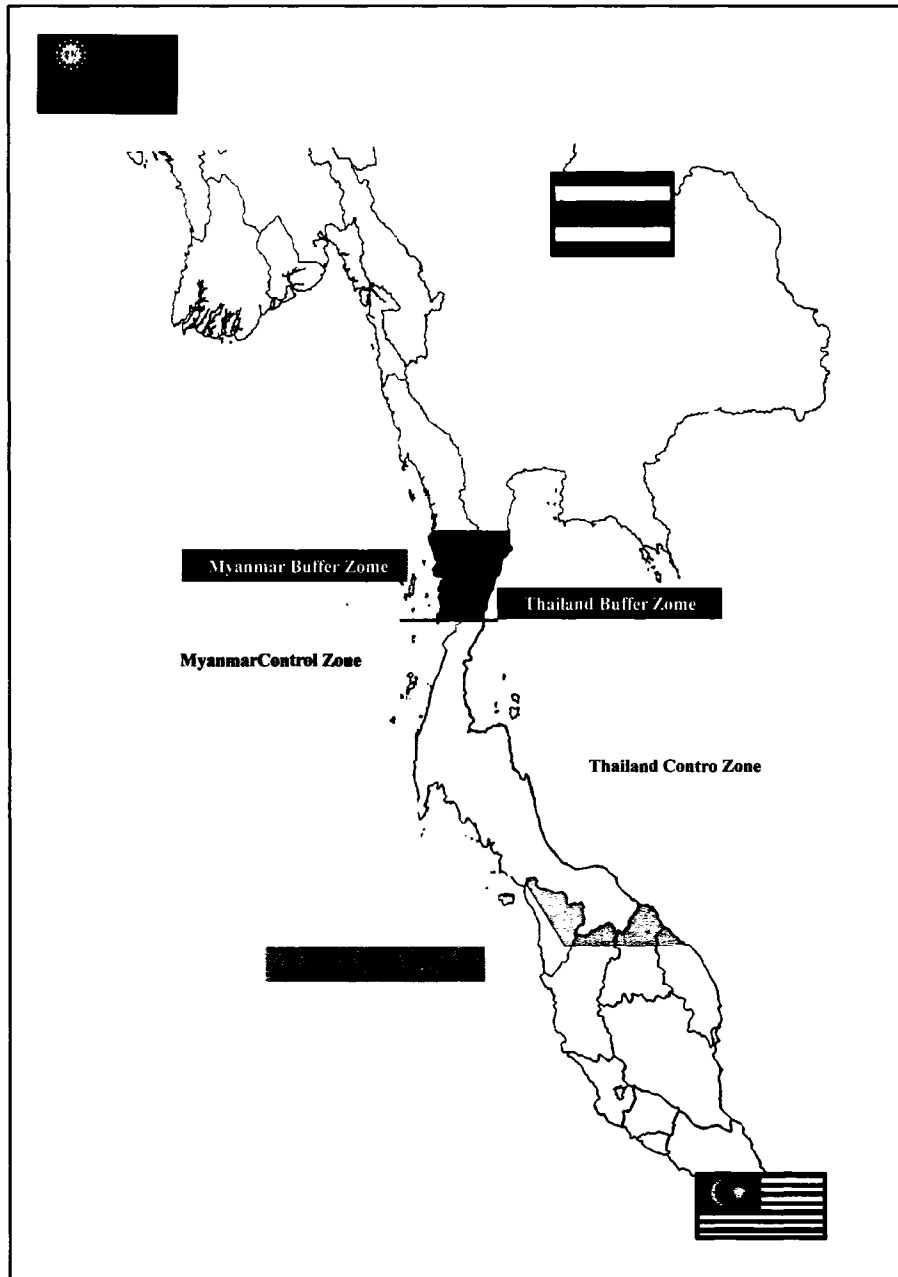


Figure 1.4: MTM Buffer Zone and Control Zone in Malaysia, Myanmar, and Thailand.

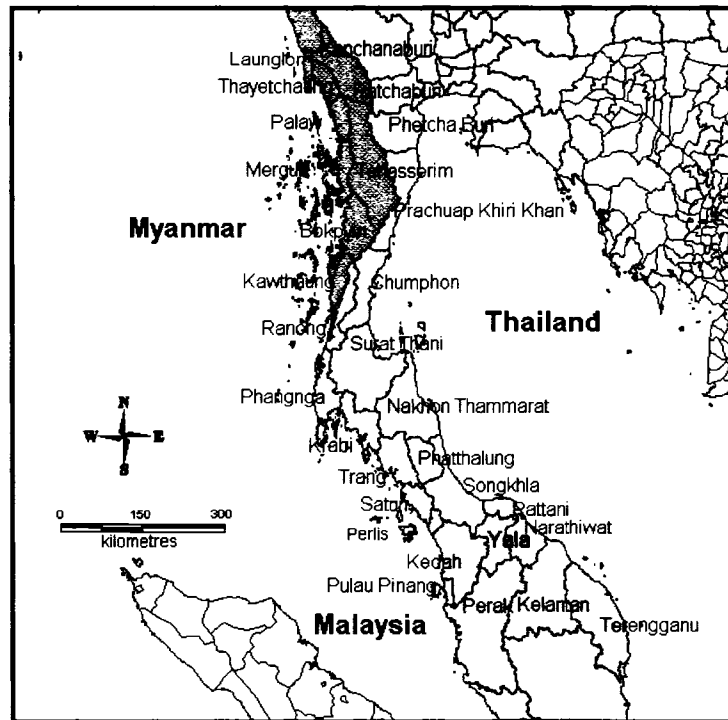


Figure 1.5: Divisions, States, and Provinces in the MTM zones

1.2.3.1 FMD in Malaysia

Malaysia has a human population of about 24 million⁵ living in a country with a land area of about 328,550 square kilometers. The country is located in Southeastern Asia, with Peninsula Malaysia accounting for 40% of the country's landmass, where the remainder covering the northern one-third of the island of Borneo. Sabah and Sarawak are the two states of Malaysia on the island of Borneo. These two states have achieved FMD-free status without the use of vaccines as approved by the OIE in 2004. Peninsula Malaysia's neighbors are Thailand and Singapore. Sabah and Sarawak border Kalimantan (the Indonesian part of Borneo) and Sarawak surrounds Brunei. The domestic livestock population of Peninsula Malaysia by state for 2001 is shown in Table 1.1.

⁵ Malaysian Department of Statistics website, <http://www.statistics.gov.my/English/framesetKeystats.htm>, viewed 19 June 2003.

District	Beef	Dairy	Buffalo	Total
Kota Bharu	13,308	32	253	13,593
Pasir Mas	19,585	22	2,660	22,267
Tumpat	6,023	0	469	6,492
Machang	11,197	25	1,685	12,907
Tanah Merah	14,366	160	903	15,429
Jeli	3,000	0	82	3,082
Perlis	4,361	113	148	4,622
Besut (Terengganu)	18,039	100	461	18,600
Selama (Perak)	4,502	220	2,067	6,789
Hulu Perak (Perak)	6,344	17	801	7,162
Kota Setar (Kedah)	4,360	108	56	4,524
Kubang Pasu (Kedah)	9,851	113	2,010	11,974
Pdg terap (Kedah)	9,818	441	2,066	12,325
Sik (Kedah)	4,623	161	901	5,685
Baling (Kedah)	7,640	291	631	8,562
Total	137,017	1,803	15,193	154,013

Table 1.1: Domestic livestock population of Peninsula Malaysia in 2001⁶

There has been virtually no increase in the cattle population of Peninsula Malaysia in the last ten years. There is an active program to increase numbers of native beef animals by natural breeding and reducing the rate of turnoff to slaughter. This is occurring at the same time that demand for meat is increasing. This has lead to increasing numbers of live bovine animals and products being imported into Malaysia.

⁶ Department of Veterinary Services, Malaysia - Last Updated on September-2002 sourced from <http://agrolink.moa.my/jph/dvs/statistics/stban1.html>, viewed 19 June 2003.

The livestock production system in the CZ ranges from extensive in the states of Kedah and Kelantan to more intensive in some parts of the western part of the zone. In Kelantan, most farmers are small-scale livestock owners with two to four heads of livestock. There are some larger herds with between 20 and 50 animals, but these are relatively rare. Cattle and buffalo tend to graze together in communal areas but are tied up during the harvesting season. Vaccination and surveillance activities are carried out despite some difficulties.

Malaysia has a well-resourced animal health service with staff working within State and Federal systems. The Federal Department of Veterinary Services (DVS) has responsibility for the prevention, control and eradication of livestock diseases of economic and public health importance. However, state services assist in the delivery of programs. FMD affects the economic performance of animal industries in Malaysia, and resources are allocated to the control and eradication of this disease. Indeed, the FMD program is funded by the government through the annual development and operating budget allocation.

In the MTM peninsula, the movement of FMD-susceptible livestock tends to be from Myanmar to Thailand and from Thailand to Malaysia. There is very little illegal movement of livestock from the BZ or CZ of Myanmar direct to Malaysia. Malaysia has an increasing demand for livestock (mostly cattle and buffalo), and although most come from Australia, about 7,000 to 10,000 head have been legally imported per year from Thailand and Myanmar in recent years before the ban in September 2003. In addition, it is estimated that more than 200 head per week (i.e., more than 10,000 per year) move illegally from Thailand into Kelantan state of Malaysia (Dr. Naheed bin Mhd. Hussein,

Malaysia DVS, personal communication, March 2004). There is some illegal movement into other border states, but the vast majority is into Kelantan state. These numbers indicate that about half of the movements of susceptible livestock into Malaysia move legally.

Most of the FMD outbreaks in Malaysia in recent years occurred in CZ. However, eight outbreaks of FMDV serotype O in cattle were reported in the proposed EZ in 2003⁷. The outbreaks in the EZ were attributable to illegal movement of cattle from the adjacent CZ in Malaysia.

1.2.3.2 FMD in Myanmar

Myanmar has a population of about 51 million living in a country with an area of about 676,586 square kilometres⁸. The country extends about 2000 km from the north to the south and about 900 km from west to east. Myanmar shares borders with Bangladesh and India in the northwest, China in the northeast and Laos and Thailand in the east.

Current government policy is to maintain the cattle and buffalo populations so that draft power levels may be sustained and thereby decrease reliance on fossil fuels for agricultural activity. Considerable trading of cattle and buffalo takes place via the extensive market system that operates in Myanmar. Most trading is for draft purposes although some animals are purchased at markets for slaughter. Myanmar does not import livestock, and usually less than 10,000 cattle would be legally exported in any year. Illegal movement of cattle and buffalo from Myanmar to other countries is extensive. It

⁷ OIE Regional Coordination Unit, OIE SEAFMD Annual and Monthly Outbreak Reports.
<http://www.seafmd-rcu.oie.int/tabindex.htm>, viewed February 24, 2004

⁸ Government of Myanmar 2003, Salient points of livestock sector report.

is estimated that between 100,000 to 300,000 cattle and buffalo leave Myanmar to other countries each year.

In the BZ, there are four townships, namely Myeik, Kyunsu, Palaw and Tanintharyi. Each township has some veterinary staff, and there are good relationships between animal health staffs and local authorities. There are two townships in the CZ, namely Bokpyin and Kawthaung. There are 37 village tracts in the CZ and three veterinary staffs. The BZ and CZ constitute the southern part of the Division of Tanintharyi. The livestock production system in the BZ and CZ is mostly extensive. Villages are often scattered and this makes vaccination and surveillance activities more difficult. Farmers live in villages, and most farms are small scale with four to five animals each. Villages have about 64 households. Animals are grazed communally, and a village tract is a common grazing area used by two to ten villages. Farmers often buy animals before the planting season. The animals are used during this period and then sold again. Animal movements therefore tend to peak just before the monsoon and then after soil preparation has been completed.

Movement of animals (mostly cattle) to Thailand tends to be mainly via routes to the north of the BZ, although there is some limited movement of animals to Thailand direct from the BZ. The major routes seem to be to the BZ of Thailand via the roads to Bang Saphan in the south of the BZ of Thailand and Rai Suan Khwan closer to Prachupkhirikhan in the BZ. The area comprising the BZ and CZ within Myanmar is relatively isolated and there is little movement of livestock from the rest of Myanmar into this area. There is only one major road from Dawai to Myeik and there are mountain ranges to the east (see Figure 1.6).

Zone	Township	Buffalo	Cattle	Sheep and goats	Pigs
BZ	Myeik	16,453	18,548	3,511	15,470
	Myeik Kyunsu	7,250	5,450	1,007	6,100
	Palaw	12,640	12,112	604	14,620
	Tanintharyi	24,270	14,383	4,135	14,360
	Total	60,613	50,493	9,257	50,550
CZ	Bokpyin	7,000	1,587	1,217	5,120
	Kawthoung	4,015	5,367	1,740	2,700
	Total	11,015	6,954	2,957	7,820
Grand total		71,628	57,447	12,214	58,370

Table 1.2: FMD susceptible livestock populations in the BZ and CZ of Myanmar 2002

In the last four years, FMDV has been diagnosed in thirteen of the fourteen districts. Generally, FMD was more common in the monsoon period and was rarely reported in the dry season. Animal movement including movements through the market system and via cattle traders, was recorded as being responsible for most outbreaks. Type O was responsible for most outbreaks. There were two cases of Asia 1 in 2001–02 and a single type A outbreak detected in 1999. This type A outbreak occurred in the Taninthayi division and was the last clinical outbreak detected in the BZ. FMDV has not been detected in the CZ for many years. Active sero-surveillance for antibody to NSP has been carried out yearly in the MTM areas since 2000, and the results showed the evidences of the low prevalence or the absence of infection. Edwards and Wongsathapornchai⁹

⁹ Edwards, J. and Wongsathapornchai, K., 2004. Report to the Director General of the LBVD, Myanmar, regarding the mission to the MTM zones in April 2004.

investigated the presence of FMD and livestock movement patterns in the MTM zones in Myanmar in 2004. Their findings were also in agreement with the surveillance, which concluded that the prevalence of FMD in the MTM areas in Myanmar was extremely low to nil.

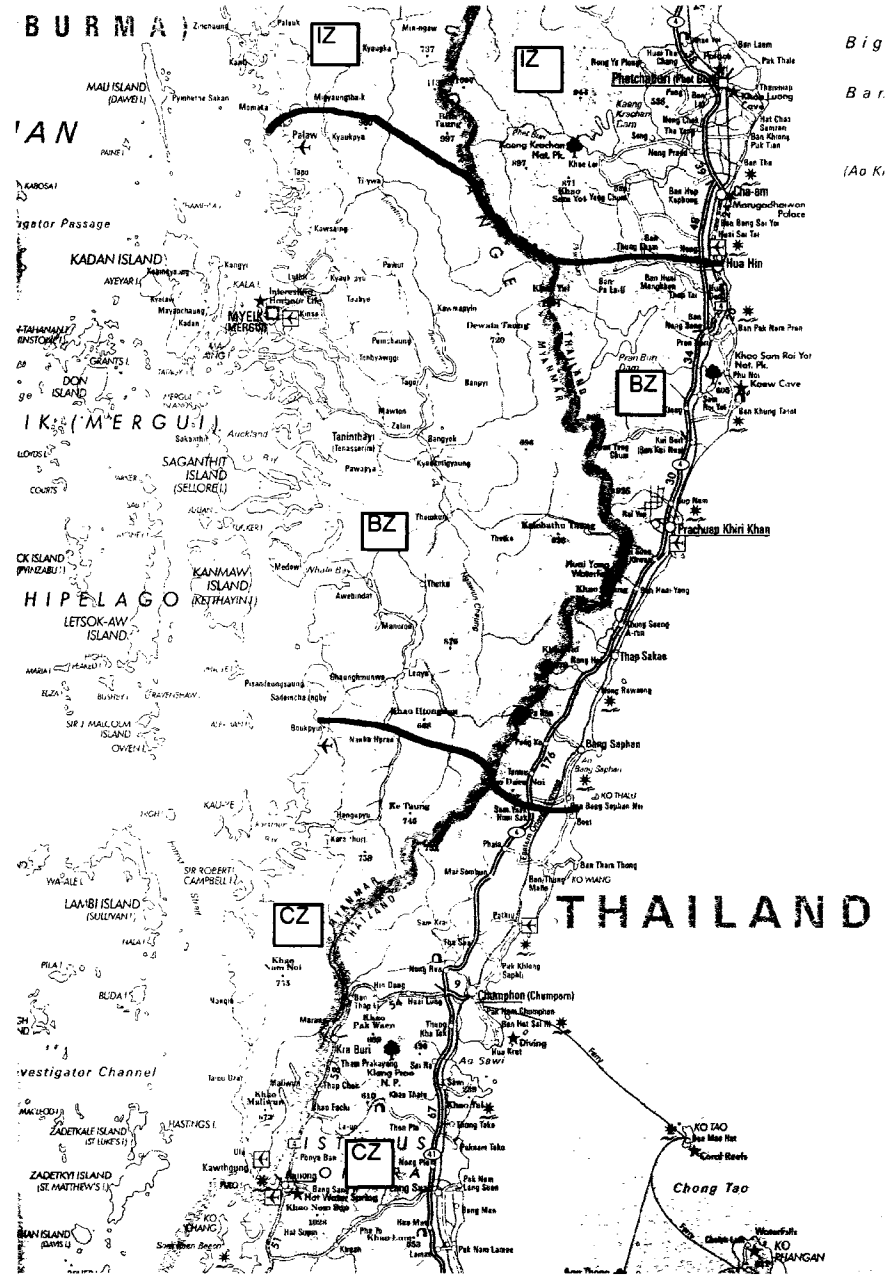


Figure 1.6: BZ and CZ of Myanmar and Thailand showing the three main crossing points (●) at the border between the BZ areas

Regarding livestock movement, the Tanintharyi Division is mountainous and roads are narrow and difficult to traverse particularly in the wet season. Livestock transport is difficult and slow. There are very few movements south from Mon state as all cattle movements above the border with Tanintharyi Division move to Thailand in the area around Three Pagoda Pass. There are regular but small movements of pigs by truck and boat for slaughter to locations as far south as Myeik. In the Tanintharyi Division, there are four main places where cattle and buffalo move into Thailand, including Maw Htaung point in the BZ to the east of Tanintharyi Township, and Kawthaung to the southeast of the CZ. The other two of these places are in Dawei District, which is situated in the area north of the BZ. In the BZ, most movements of cattle, buffalo and pigs move towards Myeik from north and west of the Tanintharyi Township and there are very few movements from the north of Myeik. Movements of cattle and buffalo to Maw Htaung are almost entirely from the Tanintharyi Township. There are very few movements south from the buffer zone into the Kawthaung District.

Outbreaks in Myanmar have generally been controlled with ring vaccination and movement controls. Monovalent Type 'O' and Asia 1 FMD vaccine is produced by the FMD laboratory of the Livestock Breeding and Veterinary Department (LBVD). However, it was recommended by the Tri-state Commission that the locally produced monovalent vaccine should not be used in the MTM zones due to concerns over the purity of the vaccine production. Thailand has donated Thai-produced trivalent vaccines to Myanmar to use during FMD emergencies. However, no vaccine has been used in the CZ or BZ since about 2000.

1.2.3.3 FMD in Thailand

Thailand has a population of about 61 million¹⁰ living in a country with an area of about 514,000 square kilometers¹¹. The country extends about 2,200 kilometers from the north to the south and about 1,700 kilometers from the west to the east at its widest. Thailand shares borders with Myanmar in the west and the north; Lao PDR and Cambodia in the north and the east and Malaysia in the south. The border with Malaysia is about 506 km long and the border with Myanmar is about 1,800 kilometers long.

Livestock raising (excluding ducks and poultry) in Thailand tends to be classified into intensive and extensive. Intensive livestock production systems include commercial farms in the dairy, beef and pig fattening class. The extensive production systems include the smaller farms with lower levels of input. In these cases, livestock production often complements cropping activities. Large ruminants are important as sources of draft power although buffalo numbers have decreased dramatically in Thailand in the last ten years. Cattle and buffalo are now being promoted to raise more for supplementary income and for meat production. There has been a government initiative to increase sheep and goat productions in southern Thailand to meet a demand for meat from these animals in Moslem areas of southern Thailand and Malaysia.

The BZ in Thailand is the Prachuapkirikhan province of region 7. It consists of eight districts, 48 subdistricts and 404 villages. The CZ includes regions 8 and 9. Within region 8 are the provinces of Suratthani, Chumpon, Nakhonsithammarat, Ranong, Krabi, Phangnga and Phuket. Region 9 contains the provinces of Songkhla, Phattalung, Trang, Yala, Narathiwat, Pattani and Satun (see Figure 1.4 and 1.5). The BZ and CZ constitute

¹⁰ http://www.nso.go.th/syb/syb2002_e/poptab_e.pdf, viewed 1 August 2003.

¹¹ <http://www.sawadee.com/thailand/statistics/>, viewed 1 August 2003.

the southern part of Thailand. The livestock production system in the BZ and CZ for all stock except pigs is mostly extensive. The susceptible animal populations in the CZ and BZ are listed in table 1.3.

Zone	Province	Dairy	Beef	Buffalo	Goats	Sheep	Pigs
BZ	Prachuapkirikhan	22,089	78,723	2,561	5,629	180	80,512
CZ	Chumpon	2,004	26,542	5,355	1,586	3	62,436
Region 8	Krabi	-	17,034	1,844	7,890	15	28,386
	Nakhonsithammarat	1,020	130,234	4,664	5,565	1,025	175,010
	Phuket	51	1,624	3,059	5,327	63	38,648
	Phangnga	197	6,752	6,106	4,332	69	37,436
	Ranong	27	3,062	1,281	1,922	8	29,734
	Suratthani	502	47,848	3,368	2,046	790	82,642
	Total		3,801	233,096	25,677	28,668	1,973
Region 9	Narathiwat	28	62,136	6,036	14,683	3,931	10,949
	Pattani	-	57,859	725	13,850	11,080	11,186
	Phattalung	3,769	67,143	2,403	5,555	163	117,670
	Satun	10	20,716	1,108	12,907	75	9,602
	Songkhla	180	84,030	2,961	13,338	1,578	143,439
	Trang	10	44,063	615	9,399	3	60,210
	Yala	103	37,314	2,602	15,879	7,901	19,600
Total		4,100	373,261	16,450	85,611	24,731	372,656
Grand total		7,901	606,357	42,127	114,279	26,704	826,948

Table 1.3: FMD susceptible livestock populations in the BZ and CZ of Thailand 2002

Animal movement (mostly cattle and buffalo) to Thailand occurs from all neighboring countries to some degree. In the context of the MTM, more animals move

into the MTM from within Thailand north of the BZ than are introduced from Myanmar (see Figure 1.7). From Myanmar, the major route into Thailand north of the BZ boundary is via the Three Pagoda pass from the Kayin district of Myanmar. Movements directly from Myanmar into the Thailand BZ seem to be via the roads to Bang Saphan in the south and Rai Suan Khwan closer to Prachupkhirikhan in the BZ (refer to Figure 1.6).

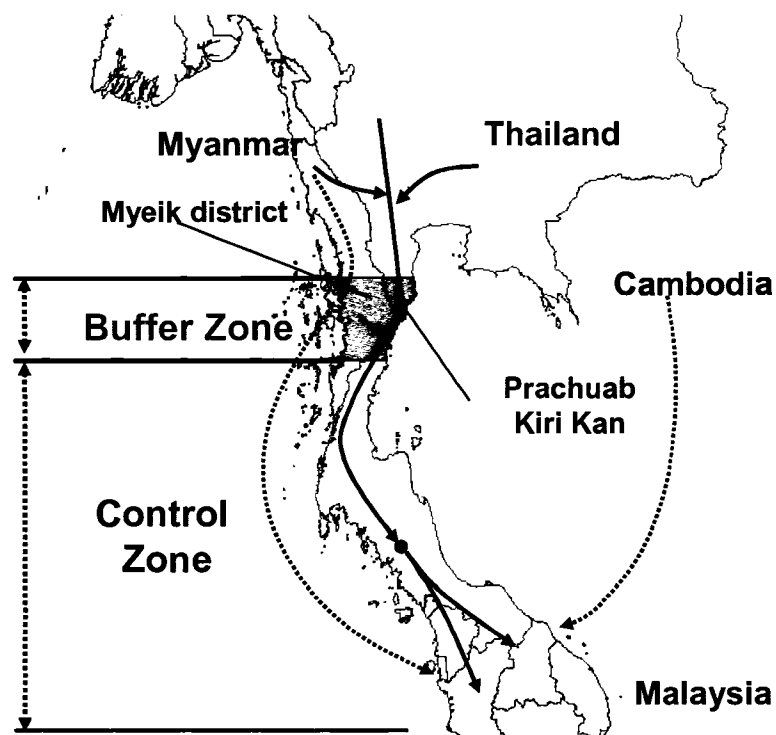


Figure 1.7: Movement of livestock in the MTM zones

Thailand is affected by many animal diseases that constrain the productivity of different livestock species. Among these diseases, FMD of cattle and buffalo is considered to be very damaging. In accordance with the OIE classification, FMD has serious socioeconomic or public health consequences and its control is crucial to the enhancement of trade within and outside the country. There have been attempts in

controlling, or favorably eradicating, FMD since the FMD type A15 was firstly confirmed in 1953. The Department of Livestock Development (DLD) of the Royal Thai Government started disease control measures, primarily aimed at FMD, in 1958 (Chaisrisongkram, 1994). These measures initially comprised strict control of animal movement, a vaccination program, animal quarantine, sanitary control, outbreak investigation, field surveillance and slaughtering of sick animals. Unfortunately, the goal of FMD control was not realized due mainly to the shortage of veterinary infrastructure at that time and the geographical location of the country. Thailand is positioned in the central of Southeast Asia and shares long boundaries with many countries, with Myanmar in the northwest and west, Laos in the northeast, Cambodia in the east and Malaysia in the south. These shared boundaries pose the difficulty to the government in controlling the spread of FMD due to animal migration across borders into Thai territory. The DLD therefore plans a five-year strategic project, the Foot-and-Mouth Disease Prevention and Eradication Project, started on January 1991 (Chaisrisongkram, 1994). The strategy was aimed to decrease the incidence of FMD in the country and to promote the FMD-free status of Regions 2, 8, and 9 (Region 8 and 9 in the south, and Region 2 in the east). The project emphasized animal movement control, vaccination, and new epidemiological techniques, such as health surveillance and an outbreak reporting system. The overall strategies were fairly successful. National annual incidence was sharply decreased from 0.09% in 1992 to approximately 0.04% in 1996 (Perry et al., 1999). Nevertheless, the objective of establishing FMD-free status in Regions 2, 8 and 9 was not accomplished. The achievement of the project was attributable to the success in vaccination performance, not the epidemiological approaches. The control of animal movement

within, or even outside, of the country had not been well implemented. The sporadic occurrences of FMD along the borders and in the presumed FMD-free regions due to animal migrations were the reflective occasions of the failure of movement control operation. The movements of animals from production areas (North and Northeast) into consumption areas (Central) and further down to the Southern Area and Malaysian Territory have been considered traditional as well as the passages in which animals are transported from neighboring countries into Thai territory (Perry et al., 1999).

In 2004, Suseno and Wongsathapornchai carried out a preliminary report of the outbreak of FMD in the MTM zone in Thailand using OIE-RCU outbreak database¹². The report found that the majority of the outbreaks in the MTM area in Thailand occurred in cattle. The morbidity was fairly high but the mortality was low. Dominating serotype was reported to be FMDV serotype O, until the recent change in 2003 when the outbreaks caused by FMDV serotype A became significantly increased. In 2001 – 2002, all of the outbreaks reported occurred in CZ. Six FMD outbreaks were reported in BZ of Thailand in 2003, which mostly affected cattle.

1.2.4 Risk Assessment

The importance of risk assessment in animals and animal products has been highlighted with the global adoption of the concept of the Sanitary and Phytosanitary (SPS) Agreement (Zepeda et al., 2001). The SPS Agreement encourages the World Trade Organization (WTO) Member Countries to base their import/export decisions on internationally accepted standards and guidelines (Sheesley and Greifer, 1996). In this

¹² OIE Regional Coordination Unit, OIE SEAFMD Annual and Monthly Outbreak Reports.
<http://www.seafmd-rcu.oie.int/tabindex.htm>, viewed February 24, 2004

context, the countries are obligated to recognize Office International des Epizooties (OIE) as the relevant organization for trades of animals and animal products, and to consider the implementation of risk assessment as stated in the OIE guidelines (Walton, 2000; OIE, 2005).

Risk assessment is a systematic process utilized for the assessment of the likelihood of an introduction of a pathogen leading to a disease, the likelihood of the insemination of the pathogen, and the subsequent impacts. According to this definition, the risk assessment processes are categorized into four interrelated steps, including release assessment, exposure assessment, consequent assessment, and risk estimation (OIE, 2005).

The release assessment step describes the potential sources of the pathogens whether they can be released or introduced into an environment accessible to live animals or animal products. The release assessment identifies the biological pathways necessary for the introduction of the agent, and identifies the activities leading to the release of the virus into the environment. The release assessment also describes the probabilities of the release of the pathogenic agent according to each specific set of conditions with respect to amounts and timing, and how these attributes may change as a result of various actions or events. Exposure assessment describes the relevant pathways and conditions that lead to the exposure of susceptible animals to the pathogen released from a given release pathway identified in the release assessment step. Exposure assessment may include an evaluation of amount and duration of exposures through various media, routes of exposure, characteristics of animals being exposed, and other conditions that may affect consequences (Covello and Merkhofer, 1993). Consequence assessment describes the potential adverse outcomes to animal health and productivities. The consequence

assessment also takes into consideration the relevant ecological and socio-economic condition resulting from the exposure pathway. Risk estimation is the process of integrating the result from release, exposure and consequence assessments. The outcome of the risk estimation step is the objective measures of the risks associated with a specific adverse condition.

Risk assessment is normally carried out to facilitate trades between trading parties. Though the steps composing the risk assessment processes are clearly outlined and distinguished, often the risk assessment is inferred to only the beginning step — release assessment — in the process chain. In other words, normal perception lends itself to only concern with the likelihood of the introduction of the pathogenic agent from the source of the animals or products into the respective destination; but the likelihood of the insemination and the subsequent impact of such introduction are often taken for granted for trade purposes. We looked at the risk assessment study by Jones et al. (2004) as an example. Jones et al. conducted a study to quantitatively evaluate the risk of importation of cattle infected with brucellosis into the UK. The study concluded that there were substantial levels of risks of brucellosis introduction, conditional on the import regulations implemented at the time. There were practical uses of the study, where the results had led to the introduction of post-calving testing on all imported cattle. Yet, the study did not extend to cover the aspects of exposure and consequence assessments. Another example was the study of the risk of Bovine Spongiform Encephalopathies (BSE) introduction into Japan (Sugiura et al., 2003; Sugiura, 2004). The study assessed the risk using historical import information; and again only the risk of introduction was considered. The risk assessment framework for importation of FMD vaccinated animals

(Sutmoller and Casas Olascoaga, 2003) also focuses only on assessment of the introduction of the risk, without mentioning the subsequent steps in the risk assessment processes. Examples are also seen from other risk assessment studies of similar extent (Heng et al., 1993; White et al., 1996; Yu et al., 1997; Moutou et al., 2001; de Vos et al., 2003;).

It is important to understand that introduction of a pathogenic agent does not necessarily always result in infection. In fact, only a fraction of the agent is able to establish themselves in the hosts. While the aforementioned studies have neglected the assessment of the risks after they were introduced, we will now demonstrate a couple of examples where the exposure and consequences assessments are also taken into consideration in the analyses. Similar to previous examples, Hartnett et al. (2003) investigated the risk of FMD introduction in the UK. Taking the steps further, the study also calculated the probability that the introduction resulting in the FMD infection in UK livestock. Results from the Hartnett study showed that the probability of contamination, on average, was estimated at 95 kilograms per year. In spite of the annual introduction of FMD virus, the model estimated that infection in UK livestock occurred only once in every 130 years. Another instance, a comprehensive risk assessment model for human infection with the cestode *Taenia saginata* by Van Der Logt et al. (1997) was carried out to provide the quantitatively probabilistic assessment of the risk of the microorganism in New Zealand. The model evaluated the probability of contamination of the cestode in beef for export and domestic consumption, as well as the likelihood of human exposure to such contamination. The study demonstrated that only a percentage of the exposure,

estimated by Beta distribution, would cause the disease in human. Hence, the probability of infection (consequence) resulting from such exposure was further calculated.

As demonstrated in the above examples, we bare in mind the importance of acknowledging the likelihood of exposure and the impact following the introduction of the risk. Therefore, in our study, we carried out the processes to analyze the probability of the release of FMD virus into the environment in the MTM areas. In addition, we assessed the likelihood of the exposure of the introduced virus to the susceptible animals, as well as the consequences resulting from the preceding release and exposure steps.

1.2.5 Mathematical Disease Modeling

This section is devoted to provide fundamental knowledge about disease modeling. Different types of disease modeling and their practical applications will be reviewed. Then, the authors will narrow the focus to modeling of FMD. Existing works on FMD modeling will be discussed for their benefits and limitations (Section 1.2.5.1).

The history of modeling in relation to the study of infectious disease was initiated back in the early 20th century. This early development provides a key contribution to the fundamental understanding of the epidemiology and assists in designing control programs for major infectious diseases. The examples of the recent applications of mathematical modeling in human diseases include the study on human immunodeficiency virus (HIV) infection (Blower and Dowlatabadi, 1994; Garnett, G.P., 1998; Coutinho et al., 2001; Velasco-Hernandez et al., 2002), severe acute respiratory syndrome (SARS) (Chowell et al., 2004; Chowell et al., 2004; Donnelly et al., 2004), and tuberculosis (Blower et al., 1995; Sanchez and Blower, 1997). In recent years, there have also been applications of mathematical modeling to animal diseases. Examples are the study on bovine

spongiform encephalitis (BSE) (Anderson et al., 1996), classical swine fever (Stegeman et al., 1999), scrapie (Matthews et al., 2001), pseudorabies (van Nes, 2001), bovine viral diarrhea (Cherry et al., 1998), and various wildlife diseases (Hudson et al., 2002). These studies have demonstrated the beneficial uses of various types of mathematical and epidemiological models to assist in and to evaluate the effectiveness of the control and eradication programs of the infectious diseases.

Extrapolations of model results to field applications usually suffer from general model limitations. The first limitation is the gap between data required for mathematical models and data that are available. This limitation was stressed by Solomon and Isham (2000) in their paper titled “Disease surveillance and data collection issues in epidemic modeling.” A particular example on the study of HIV/AIDS in Cambodia was given. The problem arose with the massive under-reporting of HIV/AIDS cases due to uncontrollable factors including logistical difficulties—such as lack of basic infrastructure, ethical considerations, and financial feasibility. The HIV/AIDS model was knowingly built on this difficulty with the major attempt to mathematically solve the problem. The modeling study on equine influenza 1 by Glass et al. (2002) also suffered from the similar problem. The number of horses reported to have been infected with equine influenza 1 did not allow the estimation of a realistic value of the transmission parameter, leading to the assumption of potentially under-reported cases. To deal with the problem, the researchers had to re-examine the size of the epidemic from the expected morbidity rate. This problem may be viewed as the lack of knowledge in the estimation of parameter values and/or conditions surrounding them. This is sometimes referred to as the levels of uncertainties in the model. Several studies in recent years have

demonstrated that this problem could be partly dealt with using the concepts of probability distributions and stochastic approach. The stochastic sampling techniques are elaborated in several excellent textbooks (Murray, 2002; Vose, 2003; Murray, 2004; Tempo, 2005). The techniques however are still dependent upon the knowledge of the distribution values, such as a minimum and maximum, standard deviation, variance, and alpha and beta, which are not always available. This recurrent lack of knowledge apparently causes a loop in the modeling problem.

Another generally known limitation in building a model for infectious agents is the assumption of mass action principle (MAP) (i.e., homogeneous mixing or homogeneity) in the population. Several aspects of MAP are considered as the sensible points of model development. For instance, the principle assumes that susceptible and infectious individuals mix in a homogeneous (i.e., random) manner. In practice, the randomness rarely occurs between individuals in the population. There are usually the aspects of spatial (space) and temporal (age) dependencies involved in the exposure processes. Anderson and May (1991) described the tendencies for non-homogeneous mixing in their book, "Infectious Diseases of Human: Dynamics and Control." Using the examples from the studies on measles in England and Wales (Grenfell and Anderson, 1985), Anderson and May highlighted the dependency of the force of infection upon age. Their report quantitatively illustrated that the rate at which susceptible individuals got infection (i.e., force of infection) depended predictably on the age at which the infection was acquired. Another major debility in MAP is that it assumes that all individuals in the population behave in a homogeneous pattern with respect to the infection. For example, if exposed, all individuals have the same probability of becoming infected; they possess

the same probability of transmitting the infection to other susceptible individuals; they respond to the infection in exactly the same way; and they react similarly to any control programs being implemented. Without doubt, this homogeneity assumption is not biologically plausible. Mathematically speaking, there is variability in any individuals. An example of this variation is given in the study of SARS epidemic (Donnelly et al., 2004). Donnelly summarized the incubation periods for SARS and found that the incubation periods reported varied between 1 to 20 days. These variations in the incubation periods reflected the non-homogeneity in the way the individuals responded to the infection, depending on the conditions in which the individual were become infected, such as time and place. Scientists have perceived this limitation in the disease modeling, and attempts have been made to resolve it. In the modeling study of the SARS epidemic by Chowell et al. (2003), the susceptible population was stratified into two distinct susceptible classes—most and less susceptible—because previous reports suggested the heterogeneity in susceptibility due to age-dependent or “unknown” genetic factors. The study of tuberculosis by Blower et al. (1995) found that a portion of infected individuals were not able to transmit the disease. Blower’s model attempted to manage this heterogeneous transmission characteristic by subdividing the infected population into two transmission classes according to their transmission ability. Despite the attempts, it is not possible to account for all the heterogeneity inherited in the biology of disease transmission. In Blower’s study, for instance, the model could not explain tuberculosis reinfection in some individuals, especially those that were immuno-compromised.

Despite suffering from the abovementioned limitations, uses of mathematical models have been widely accepted as the important tools in planning for control and

prevention of infectious diseases, both in human and animals. The study of bovine viral diarrhea (BVD) virus control utilized mathematical modeling techniques to demonstrate the importance of persistently infected animals in maintaining the disease (Cherry et al., 1997). A pertinent conclusion was also drawn from the study regarding the minimum level of herd immunity required to put out the infection. Van Nes (2001) showed the application of mathematical model to aid in the design of the eradication program for pseudorabies virus from the Netherlands swine population. Different strategies were suggested with the aim to lower the reproductive ratio to below a threshold value of one. For mathematical models in human, the model of SARS epidemics (Chowell et al., 2003; Chowell et al., 2004; Donnelly et al., 2004) is a good example. The researchers were able to provide tangible results to support the significance of the isolation of diagnosed cases in controlling the spread of the disease. The modeling technique was also one of the vital instruments in assessing and designing the global control program for lymphatic filariasis (Michael et al., 2004). The model was used to assess the overall effectiveness of the current control practices. More importantly, results from Michael et al. study provided critical decision-support framework for the global filariasis-control program.

Above are just a few examples of the advantages of using mathematical model in epidemiology. There are, of course, many other examples revealing the benefit of the model which are not outlined here. With the advanced knowledge in disease biology and dramatic improvements in computer hardware and mathematical software, it has become relatively more feasible and efficient to carry out modeling studies than studies with experimental settings in many circumstances.

1.2.5.1 Foot and Mouth Disease Modeling

Several applications of mathematical modeling are beneficial for the study of the transmission of FMD infection. Epidemiology of FMD is fairly complex, which makes it very difficult, on the basis of practical experience alone, to develop a quantitative understanding of the epidemiological process, or to predict the impact of control measures, or to generalize from one situation to others. Below, we show how transmission modeling can play a very important role in providing information leading to potential resolutions for the abovementioned constraints.

The modeling approach is often utilized for a specific FMD outbreak, aiming to evaluate alternative mitigation strategies, oftentimes referred to as “what-if” scenarios. Because of the availability of exceptional data for modeling studies, the studies of the recent FMD outbreak in Great Britain in 2001 (Ferguson et al., 2001^a; Ferguson et al., 2001^b; Keeling et al., 2001; Morris et al., 2001; Woolhouse et al., 2001) were the excellent examples for the demonstration of the “what-if” scenarios. During the 2001 UK epidemic, Ferguson et al. (2001^a) conducted the modeling study to assess the impacts of control strategies. The study assessed the potential impacts of control strategies being implemented, such as slaughtering of animals on infected premises (IPs) and premises identified as having had dangerous contacts (DCs) with IPs and movement restrictions. Alternative control strategies, such as vaccination, were also evaluated. The study suggested that achieving the goal of slaughtering on all farms within 24 hours of case reporting without waiting for laboratory confirmation could significantly slow the epidemic; though not necessarily extinguish the epidemic (R_0 was still estimated to be more than unity). The study also showed that ring vaccination, despite being both

potentially and equally effective, needed to be more extensive than comparable stamping-out policies, thereby making vaccination less appealing in terms of cost-beneficial outcomes. The recommendations made from the study by Ferguson et al. were used extensively to inform decisions regarding control policies, such as more rapid destruction of animals on affected farms. Another study by Ferguson et al. (2001^b) was carried out particularly on the 2001 epidemic of FMD in UK. The second study (2001^b) was the elaborated version of the former study (2001^a) in terms of the comparisons between different control schemes. In the second Ferguson study (2001^b), the comparisons of intervention-adjusted basic reproduction number, effective reproduction number, and average daily transmission (rate) coefficient from different control scenarios were made. The study concluded that the control strategies implemented during the 2001 UK epidemic was not necessarily the best; and if the most efficient control measures had been rigorously applied earlier, the epidemic situation would have been substantially improved. In both studies (Ferguson et al., 2001^a and 2001^b), the transmission capability of FMD was shown to be inherently correlated with distances between infected and susceptible premises. Hence, Keeling et al. (2001) conducted a modeling study using data from the 2001 UK epidemic taking into consideration spatio-temporal patterns of the spread. Conclusions similar to the former studies were drawn, reinforcing the pertinence of culling of IPs and DCs and rapid response to the outbreak in controlling the epidemic. Like the former studies, Keeling's research concluded that vaccination was not an optimal choice from an economic perspective. A different model was constructed by Morris et al. (2001) using the same epidemic data. The focus of this study was the prediction of outbreak foci using a spatio-temporal model developed by the researchers.

The Morris study was also in agreement with the pre-emptive slaughtering policy (slaughter of animals on DCs) and the prohibition of vaccine usages, as suggested by the other studies. However, only a slight increase in epidemic size was observed with delay in the slaughter of animals. We intended to also give an example of the modeling study in areas other than the UK. Woolhouse et al. (1996) conducted a study to evaluate the efficiency of vaccination to prevent outbreaks of FMD in Saudi Arabia. The study utilized the simple *SLIR* model (Susceptible, *S*; Latent infection, *L*; Infectious, *I*; and Recovered, *R*). Using the model, the researchers were able to disprove the use of vaccine as an effective control for FMD outbreaks due to vaccine efficacies. These are just a few examples to demonstrate an application of disease modeling to the episode of the FMD outbreak. There are also many other examples, which are not elaborated here (Durand and Mahul, 2000; Howard and Donnelly, 2000; Kao, 2002; Bouma et al., 2003; Perez et al., 2004), revealing the significant contribution of modeling approaches to the control of FMD.

Mathematical models can also assist epidemiologists in answering some vital questions in the transmission processes of FMD, which otherwise would not be feasible to study in experimental settings. We used the study of atmospheric spread of FMD virus as an example. Study of the wind-borne spread of FMD virus has posed a difficulty in designed experimentation. Most of the studies in the late 1960s were based upon observations of the spread patterns and theoretical speculations known as the Lee Wave Hypothesis, particularly owing to the 1967-1968 FMD epidemic in the UK (Henderson, 1968; Hurst, 1968; Tinline, 1969; Wright, 1969). The role of wind and weather as the factors of the transmission of FMD during the epidemic was unquestionable. Relying on

only observation data, however, allowed neither the quantifications of the factors nor their relative contributions to other causes in the transmission of the FMD. The attempt to introduce the mathematical approach in the 1967-8 UK epidemic was initiated by Hugh-Jones and Wright (1970). Hugh-Jones and Wright used the estimated values of the daily 'rate of spread,' the formula of which was introduced by the authors. The study graphically related the daily rate of spread of disease to the weather patterns (i.e., wind speed, precipitation duration) and found the possibility of high correlation among the two. The results from the Hugh-Jones and Wright study, however, were not sufficient to untangle the importance of weather from other factors in the spread of FMD virus during the outbreak. Another example of a modeling study to ascertain the airborne spread of FMD was done by Sorensen et al. (2000). Apart from the conventional school of mathematical disease modeling, the Sorensen study introduced computer simulation software for atmospheric data, called Rimpuff, to deal with the complexity of the transmission. The variability of epidemiological parameters (e.g., the rate of excretion and survival of the virus, minimum infectious dose, and species differences) and the atmospheric data were studied using the integrated approach of the conventional and the Rimpuff models. Using data from outbreaks of FMD in France and the UK in 1981 and from Denmark and the former German Democratic Republic (GDR) in 1982 to validate the model, the researchers concluded that the integrated Rimpuff model was useful for assisting decision makers during an FMD emergency. Nevertheless, the model was only limited to the simulation of atmospheric spread of the FMD virus. Failure to account for other means of FMD transmission was the major weakness of the model in the study of FMD transmission processes. There have been many other studies using traditional,

mathematical disease modeling (Gloster et al., 1981; Donaldson et al., 1982) and alternative simulation modeling (Casal et al., 1997) to assess the importance of windborne spread of FMD, most of which has proven to be very useful for decision making process during emergencies despite certain limitations. However, none of the abovementioned models claimed to be accurate, but rather depended upon the accuracy and availability of data used in the analyses.

Another major application of disease modeling, which has been extensively studied in recent years, was the evaluation of the capacity and control options to deal with the reemerged FMD outbreak. There have been many examples of such reintroduction of FMD in previously disease-free countries, such as the outbreaks of FMD in Taiwan in 1997 (Dunn and Donaldson, 1997; Cheng, 2002), 2000 in Japan (Sugiura et al., 2001; Sakamoto and Yoshida, 2002), 2000 in the Republic of Korea (Joo et al., 2002), and 2001 in European community (Sobrino and Domingo, 2001), and other areas around the globe (Kitching, 1999). Hence, it has always been of great concern to FMD-free areas/countries that the outbreak of FMD would reappear despite the strongest efforts to prevent the introduction. Certainly, it is not practical to conduct an experimental study of large outbreaks of FMD in the areas where they are free of the disease. Mathematical disease modeling has played a vital role in the simulation of the outbreaks without risk of spreading the disease, and has helped in planning of control programs during FMD emergencies. The earliest modeling work was the study done by Miller (1976). Miller developed a simple SIR model to simulate the hypothetical outbreak of FMD in the United States. Though the model was under much debate in terms of its practical uses and the extrapolation of the results to the real epidemic, it demonstrated many strong

potentials to predict the outcome of FMD controls and preventions. In 2003¹, Bates et al. constructed a Reed-Frost epidemic model simulating an theoretical epidemic of FMD in California, United States. The simulation was more complex than the Miller model with an integration of a spatial component. With more advanced computerized software, yet, the calculation step was much simplified, which was the major improvement from the modeling study in the 1970s. The epidemiological model allowed examination of the impacts of artificial FMD outbreak in California, while the spatial stochastic modeling allowed identification of newly infected herds following infection of an index herd. The model compared several control options and made suggestions for the appropriate strategies to deal with the disease should it enter the area (Bates, 2003²). In the same year, Schoenbaum and Disney (2003) developed an epidemiological model to simulate a hypothetical country-wide outbreak of FMD in the United States. The main interest was put into developing an emergency response program for FMD and other animal diseases with similar characteristics. This model also incorporated economic aspects of FMD outbreaks, such as direct cost of the outbreaks, government cost of control and eradication, and impact of FMD to product markets. Again, different control options were evaluated, including vaccination and slaughter strategies, as well as control of animal movement. The study concluded that “the choice of best mitigation strategy depended on herd demographics and the rate of contact among herds” (Schoenbaum and Disney, 2003). Although the aforementioned models revealed many potential benefits, all of them suffered from a general constraint. The model accuracy was generally not validated. Because the models were constructed to simulate FMD outbreaks in the areas where they were free of FMD, experimentation of FMD outbreak for validation purpose

was considered to be too costly or too dangerous. Attempts to conduct the validation process have been made in other areas where there were outbreaks of FMD using the developed models. Yet, mathematical modeling is still regarded as a valuable tool for emergency preparedness despite the limitation.

1.3 Objective

This study attempts to utilize modeling approaches in epidemiology to assist in the evaluation of FMD situation and control strategies used in the MTM zones. The objectives of this study are;

- 1) To assess the likelihood of FMD involving in the terrestrial movement of livestock from areas outside of the MTM zones into the MTM zones;
- 2) To examine factors related to terrestrial movement of livestock that contributed to the outbreaks of FMD in the particular area of the MTM;
- 3) To assess the impacts of the FMD introduction and the current FMD control strategy being implemented in the MTM zones;
- 4) To evaluate the alternative control options that would ultimately assist in eradication FMD from the MTM zones.

Chapter 2

Assessment of the likelihood of foot and mouth disease introduction through importation of live animals into the Malaysia-Thailand-Myanmar peninsula

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2.1 Introduction

Foot-and-mouth disease (FMD) is a highly contagious disease of cloven-hoofed animals. The disease has tremendous impacts on susceptible livestock in terms of

production loss and economic disruptions due to trade restrictions. The virus is easily transmitted by both direct (contact with infected animal or secretion) and indirect (through living and non-living objects) means. The disease is characterized by vesicular eruptions of the epithelium of the mouth and feet, where it inherits the name “foot-and-mouth disease.” Epithelial eruptions can also be observed on the teats and udder.

FMD is endemic in most of the countries in Southeast Asia, with the exceptions of Indonesia and parts of Malaysia and the Philippines. There have been continuing efforts to eradicate the disease from the region. A key ongoing effort has been coordinated by the Regional Coordination Unit (RCU) of the Office International des Epizooties (OIE) through the Southeast Asia Foot and Mouth Disease (SEAFMD) Campaign. The Campaign involves eight countries in the region, including Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Thailand, and Vietnam. The OIE review on the SEAFMD Campaign in 1999 identified the importance of the establishment of a disease free area to accelerate the eradication of FMD in the Southeast Asian region. To facilitate the recommendation, the five-year program developed in 2001 includes Malaysia Peninsula and parts of Thailand and Myanmar, known as Malaysia-Thailand-Myanmar Peninsula (MTM) Campaign. An area of MTM peninsula was selected as a potential FMD free area in the region due to its natural advantages and current FMD situation that favour FMD control and eradication. The MTM countries also have developed a good tripartite example of international co-operation.

Within the MTM Campaign, zones are clearly defined areas that are declared by legislative or administrative action of the respective countries to facilitate movements within zones and to enable the control, eradication and exclusion of FMD. The zone

statuses for the MTM Campaign include buffer zone (BZ), control zone (CZ), and eradication zone (EZ). In summary, MTM zones include areas in mainland Southeast Asia from Prachuab Khiri Khan Province in Thailand and Myeik District, Tanintharyi Division in Myanmar (latitude 12° 30'") south to the most southern tip of mainland Malaysia. Details on the zone demarcations, definitions, and requirements for progression of zone status are explicitly documented in the Minimum Standard Definitions and Rules (SDRs) by Turton (2003).

Various programs have been designed to help assure the achievement of the MTM Campaign's objectives. One of the important programs is the prevention of the introduction of the disease whilst ongoing eradication efforts are carried out in the MTM areas. In this paper, a quantitative risk assessment model was developed. The main purpose was to evaluate the risk of FMD introduction resulting from terrestrial movement of live animals from areas outside of the MTM zones.

2.2 Materials and Methods

Risk assessment is a complex system, which consists of several analytical processes. The general processes for conducting a risk assessment were clearly outlined in the Terrestrial Animal Health Code (²OIE, 2004) and Handbook on Import Risk Analysis for Animals and Animal Products (³OIE, 2004). Following the OIE guidelines, the risk assessment process began with a hazard identification step. The risk scenario trees were developed and were used as the study framework.

2.2.1 Hazard Identification

The review of literature and existing information indicated that cattle movement was the most crucial source of the spread of FMD. For instance among 207 reported outbreaks of FMD in the MTM peninsula from January 2001 to February 2002, more than half (58%) were attributable to the movement of livestock, both legal and illegal (OIE-RCU, 2004). MTM member countries were also aware of the significance of animal movement and have made the recommendation that “Illegal movements are believed to increase the spread of disease (FMD). It is recommended that MTM member countries move to a policy of controlled legal movements to reduce the spread of disease” (OIE-RCU¹, 2002). This study thus considered assessing the risk of FMD introduction into MTM Peninsula associated with terrestrial movement of livestock.

It was of interest to the RCU and the MTM countries as to whether swine should be a major concern to the campaign (OIE-RCU¹, 2002; OIE-RCU², 2002). There were scientific evidences suggesting a minor role of swine as a direct cause of FMD virus in the region (Chamnanpood et al., 1995; Cleland et al., 1996). Normal swine management practices in Thailand and Malaysia somewhat reduced the chance of swine being exposed to the virus. Swine were not fed with raw meat, offal, bone marrow or unpasteurized milk and were also commonly housed in individual pens, separated from other species of livestock. There were small numbers of swine moving to the MTM areas as a result of lesser demand in the Muslim communities. Though a report from Myanmar suggested numbers of swine which were grazed extensively (OIE-RCU², 2002), there was only one report of FMD outbreak in a swine population from the period of 2000 to 2003 (OIE-RCU, 2004). Swine also do not develop persistent infection with FMDV; thus, it is less

likely for swine to become a candidate for a carrier (Alexandersen et al., 2002; Suttmoller and Casas Olascoaga, 2002). Due to insignificant role of swine in the epidemic of FMD, the term 'livestock' in this study will refer only to dairy cattle, beef cattle, and buffalo.

2.2.2 Study Framework and Risk Scenario Trees

Development of risk scenario trees was identified to be a pertinent part in assessing risk of disease introduction (Miller et al., 1993; OIE, 2004). Import/export policies and procedures have to be examined preceding scenario tree development. Inquiries for import/export regulations were made to the relevant institutions within the respective MTM countries. The information was then utilized to construct a risk scenario diagram. In addition, the local villagers and traders in the MTM zones were interviewed for other possible routes of livestock trafficking that might not necessarily bind to the aforementioned movement regulations. These 'other' routes of movement were also taken into consideration, and additional scenario trees were created.

The framework for a complete risk assessment model is illustrated in Figure 2.1. The model involves a movement permit issuance and a subsequent period of quarantine. This diagram mimics movements of livestock from IZ to MTM zones within Thai territories. Application of this diagram also extends to some trans-boundary movements from Myanmar into Thailand where there are inspection and quarantine only when the animals reach Thai borders.

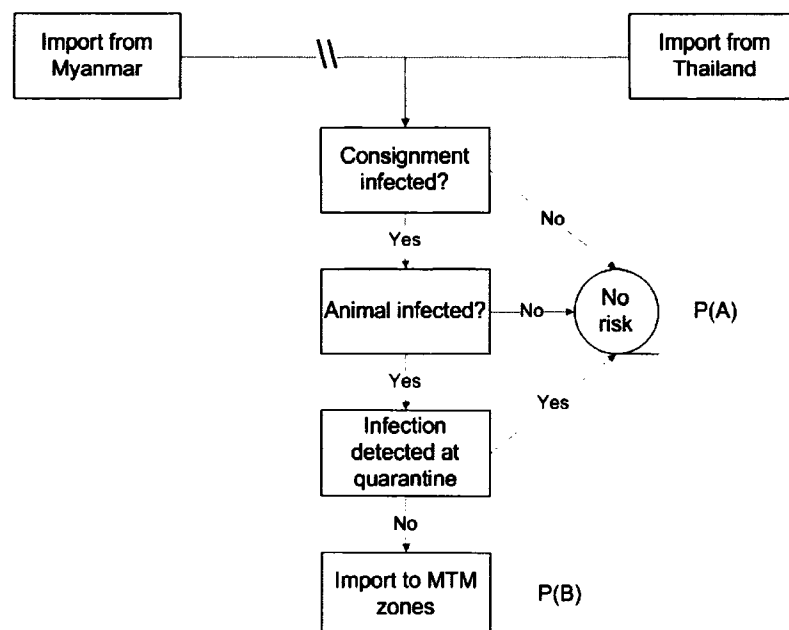


Figure 2.1: Framework of FMD risk assessment model for MTM zones resulting from terrestrial movement of live animals

2.2.3 Operating the Model

Uncertainty and randomness within the model were described using Microsoft Excel[®] 2003 (Microsoft, Redmond, WA) with @Risk 4.0 (Palisade Corporation, Newfield, NY) add on function to simplify uses of probability distributions. Each simulation consisted of 10,000 iterations using Latin Hypercube sampling.

2.2.4 Model Parameters

2.2.4.1 Livestock Movement

Movement of livestock in the MTM countries is somewhat of an obscured cascade. Majority of the movements occur unreported and are largely driven by market prices of livestock in the region. The three countries in the MTM area share terrestrial boundaries, with Thailand as an intermediate country. Attempts were made to realize

patterns as well as magnitude of livestock movement in the MTM areas. Where records were unavailable, experts' opinions were utilized as the best estimates.

Myanmar

No official records were kept for movement of livestock in Myanmar. Thus, information on livestock movement was acknowledged using expert opinions. To solicit the expert opinions, a workshop was conducted in Yangon in January 2004, where participations were received from local veterinary officers of Livestock Breeding and Veterinary Department (LBVD) including Deputy Directors from all 14 states/divisions. The participants were asked to draw maps and directions of livestock movement for both domestic and international traffics. Then they were invited to exert their opinions on the approximated numbers of livestock and the perceived level of risks involved in each direction of the movements. A visit was also made to Tanintharyi division, the Myanmar MTM area. Several discussion forums were initiated in several areas visited in the Tanintharyi division, including five villages in Myeik district and one village in Kaw Thaug district. The workshop sessions—similar to the one held in Yangon—were carried out and included participation from local villagers and livestock traders. Inquiries were made for incoming and outgoing animals, including sources, destinations, amount, and type of animals. The villagers were also questioned whether they had seen outbreaks of FMD before and when the outbreaks were last seen, and any person who had witnessed an FMD outbreak would describe to the others the clinical symptoms and patterns of spread.

There were no movements of cattle and buffaloes from divisions/states north of the MTM zones down to the MTM zones in Myanmar. There were movements of cattle

and buffaloes from small eastern islands to Myeik, but those were considered irrelevant to FMD control because the origins of these animals were free from FMD. It was estimated that 300 to 500 animals per month were walked across the border to Thailand mainly through Maw Htaung point in Tanintharyi Township. Those movements usually involved local animals in Tanintharyi Township; but there might be some animals from Myeik Township or further north if supplies in Tanintharyi Township were not sufficient. Reverse movement from Thailand to Myanmar BZ did not happen. Due to geographical difficulty, only limited numbers of animals were moved south from the BZ to the CZ. All of the movements in the BZ occurred by land. It was estimated that 8,000 cattle and 7,000 buffaloes from other townships were transported by land to Myeik Township yearly.

Thailand

Movements of livestock in Thailand are managed by Animal Quarantine Inspection Services Section (AQISS), under the supervision of Bureau of Disease Control and Veterinary Services (BDCVS), Department of Livestock Development (DLD). Movement permit has to accompany all movements, and all permit records are kept at the animal quarantine stations (AQS), with summary reports submitted monthly to the AQISS headquarter. There are 38 international and 16 domestic AQS in the country. In addition to the governmental AQS, there are numbers of approved private quarantine premises, which have been accredited and routinely inspected by veterinary officers. According to the legislations, animal destined for the proposed FMD control zones in Thailand (Region 8 and 9) have to be accompanied by movement permits issued by DLD provincial office from where the animals originate. At a quarantine station, where

animals are kept for a period of time and are released if no signs of infectious diseases are observed, Movement Release form is given to a consignment if it passes all the quarantine requirements. Information from a movement permit, however, is not a dependable source to gain knowledge of livestock movement due to discrepancies between the records and the actual animals that pass the AQS. Consignments initially proposed to move to the southern regions do not necessarily reach the intended destination. Similarly, some consignments destined for other regions may end up in the regions of concern because of appealing demands. Supposedly all domestic movements to the MTM areas in Thailand must take a transit at Phetchaburi or further south at Prochuab Khiri Khan provinces. Thus, Movement Release form issued by AQS located in the two provinces will be used instead as approved consignments will definitely be transported to the MTM zones.

Malaysia

The Division of Epidemiology and Veterinary Medicine, Department of Veterinary Services (DVS) supervises movements of livestock in Malaysia. There are seven Animal Quarantine Stations and Check Points located in Peninsula Malaysia, most dealing with international trades of livestock. Only animals destined for immediate slaughter are allowed to move south into the Eradication zone (south of Besut district and Perak district). However, there are common grazing areas that straddle the boundary between the two zones in several areas; so, uncontrolled movements do occur. There are no permanent checkpoints on the roads leading from the Control to Eradication zones, but DVS use mobile units to patrol the roads, supported by police.

Local supply of fresh meat in Malaysia cannot meet the demand for local consumption. As a result, Malaysia is now known as a major importer of livestock and livestock products in the region. In 2001, the records showed that 5,279 head of cattle/buffalo were imported from Thailand and 3,558 head from Myanmar. In 2002, total imports of cattle/buffalo from Thailand were slightly decreased to 4,353 head, where import from Myanmar was halted due to the outbreak of FMD in one of the quarantine stations. In September 2003, Malaysia stopped the importation of cattle/buffalo from Thailand due to an outbreak incidence in Padang Besar Quarantine Station. However, DVS officers admitted that there were at least 20,000 head of livestock being traded illegally across the borders yearly to satisfy local demands of flesh meat.

The movement documents, including import license, health certificate, and other supplemental documents, are checked upon arrival at a quarantine station. Veterinary officers carry out a series of physical inspections during the quarantine period to validate the health status of the animals. The records of the movements are kept at the quarantine and are subsequently submitted to the DVS.

2.2.4.2 Prevalence of FMD

A simple calculation of prevalence derives from acknowledging the number of those affected and the number of those susceptible in a defined temporal partition. In Southeast Asia, several systems have been developed to recognize these vital elements in prevalence calculations. At a national scale, some countries develop outbreak reporting systems as evident in Thailand, Malaysia, and the Philippines. Other countries in the region, nevertheless, receive only reports for the virulent cases of FMD due to limited resources. There is also an outbreak reporting system developed by the OIE-RCU, the

member countries of which have agreed to submitted monthly reports of outbreaks in their respective countries to the OIE-RCU database. The number of outbreaks does not, however, reflect the number of animals infected with FMDV. One of the reasons is due to high probabilities of unapparent and persistent infections (Sutmoller and Casas Olascoaga, 2002; Sutmoller and Casas Olascoaga, 2003), especially where FMD is endemic and where vaccination is practiced (Donaldson and Kitching, 1989).

Prevalence Estimation from Regional Surveillance

Premashthira (2004) carried out an active sero-surveillance in Thailand in early 2003 in attempts to determine level of FMD infection in the country. He tested a total of 4,185 cattle from all nine regions in Thailand using ELISA test to detect non-structural protein 3B (NSP-3B). His findings provide valuable information in constructing an assessment model of FMD risk for this study. Parts of the results from his study are presented in Table 2.1.

Region	Number tested	Positive to NSP-3B (%)
1	480	12(2.5)
2	476	3(0.6)
3	480	39(8.1)
4	477	23(4.8)
5	480	32(6.7)
6	360	23(6.4)
7	479	35(7.3)
8	478	0(0.0)
9	475	10(2.1)
Total	4185	177(4.2)

Table 2.1: Geographical distribution of apparent prevalence of FMD infection in cattle

From these findings, hereafter referred to as “regional surveillance”, let p_{ii} denote the probability of disease (prevalence of FMD) in the livestock population within Region i in the IZ in Thailand (Regions 1 to 7), s_{ii} denote number of positive to NSP-3B test within Region i , and n_{ii} denote number of livestock tested within Region i . The NSP-3B test is known to possess a sensitivity of approximately 88.89% (p_{NB}) and the specificity of close to one (Linchongsubongkoch et al., 2002, unpublished data). From this information, it is possible that a few infected livestock were not picked up by the test. The number of false negative m_{ii} can be estimated using the Microsoft Excel[®] formula

$$m_{ii} = RiskNegbin(s_{ii} + 1, p_{NB}).$$

The true prevalence of Region i can then be estimated as:

$$p_{ii} = RiskBeta(m_{ii} + s_{ii} + 1, n_{ii} - \{m_{ii} + s_{ii}\} + 1).$$

This step would yield FMD prevalence for each corresponding Region. After the simulations, there were seven prevalence estimates, which can be combined to produce a distribution of within-consignment prevalence for all other infected consignments. The distribution calculation using a command RiskDiscrete({weighing}, {probabilities}), a discrete distribution where the probability is weighted by the likelihood of it happening, was performed to arrive at the overall prevalence (p_w). In this study, the prevalences were weighted by the likelihood for the Region from which the consignments originated. Therefore, the formula used to combine the prevalences is

$$p_w = RiskDiscrete(\{prevalence\ of\ Region\ 1: Region\ 7\}, \{no.\ of\ consignments\ from\ Region\ 1: Region\ 7\})$$

Prevalence Estimation from Consignment Surveillance

Another investigation was instigated by the DLD, Thailand to investigate imported animals for FMD. For each consignment entering international AQS, a

subsequent number of blood samples were collected for laboratory testing for evidence of FMD infection, henceforth referred to as “consignment surveillance”. Though the information may not be representative of domestic movement of livestock, the information can be utilized for an indirect estimation of the prevalence and for comparative purposes. There were 57 consignments n_C tested for FMD infection using NSP-3ABC from Brommerli/Intervet (Bomm) test; 28 consignments s_C had at least one positive sample. The readers can find the detailed summary of total numbers of samples that tested positive for each positive consignment in Table 2.2.

From the study done by Linchongsubongkoch et al. (2004, unpublished data) on NSP-3ABC (Bomm), the study found that 84.6% of disease positive cattle sera tested positive (152 test-positive out of 180 infected sera), and 1% of disease negative cattle sera tested negative (4 test-positive out of 379 disease-negative sera). A two-by-two table was reconstructed from this information (Table 2.3).

Consignment number	Number submitted	Positive
001	11	1
002	20	4
003	20	7
004	10	2
005	30	7
006	12	3
007	7	3
008	13	5
009	20	2
010	10	2
011	20	3
012	9	2
013	5	1
014	20	4
015	100	9
016	10	2
017	10	2
018	20	3
019	5	1
020	10	2
021	10	1
022	10	1
023	10	1
024	10	2
025	10	4
026	6	1
027	42	2
028	100	6

Table 2.2: Summary of the numbers of animals tested positive to FMD antibody using NSP-3ABC ELISA from the quarantine stations in Thailand.

		Disease		Total
		+	-	
Test	+	152 (<i>a</i>)	4 (<i>b</i>)	156
	-	28 (<i>c</i>)	375 (<i>d</i>)	403
Total		180	379	559

Table 2.3: Results of NSP-3ABC test (Bommeli/Intervet) in naïve and naturally infected cattle sera

A distribution was estimated for the sensitivity p_{Se} as

$$p_{Se} = RiskBeta(a+1, c+1)$$

and for the specificity p_{Sp} as

$$p_{Sp} = RiskBeta(d+1, b+1).$$

a was denoted as the number of disease-positive-test-positive animals, b for disease-negative-test-positive animals, c for disease-positive-test-negative animals, and d for disease-negative-test-negative animals. The distribution of the true consignment prevalence was estimated as

$$P_{Consign} = RiskBeta(s_C + 1, n_C - s_C + 1).$$

Similar simulations as the ones carried out for the regional surveillance were performed to determine the distributions of false negative livestock (m_{Di}), between-consignment prevalence (p_C), within-consignment prevalences for each positive consignment (p_{Vi}), and combined prevalence of all 28 infected consignments (p_V) (here, we used numbers of submitted samples to weigh the respective prevalences). Next, the probability of an imported livestock to be infected with FMDV (p_D) could be simply calculated as $p_C * p_V$.

2.2.5 Release Assessment Model

From the interviews of local villagers and farmers in MTM zones in Myanmar, it was realized that movement from other areas into MTM zones in Myanmar was extremely limited due to difficulties in transporting animals. Most of the movements originated from adjacent areas, which have had no reports of FMD outbreak since 1990. Sero-surveys for antibody to FMD using NSP tests in Tanintharyi Division yielded no positive result since 2001 (Kyin, M.M., 2004, unpublished data). Hence, movement into the MTM zones from the Myanmar side is not considered a major risk in this study, and is not included in the analysis. It was clear that the movements of concern were domestic movement of livestock in Thailand from areas out of MTM zones into the MTM zones.

Legal movement of livestock from Thailand and Myanmar into Malaysia was not happening since 2003 (see 2.4). Though illicit movement of livestock from other MTM countries might occur, the risk of FMD introduction into Malaysia would be perceived as if no additional prevention measures were implemented; i.e. the risk was similar to the risk of FMD introduction prior to coming into Malaysia. Hence, for simplicity of the model, the probability of FMD introduction into Malaysia was excluded from the analysis.

According to the Thai DLD Animal Epidemic Act B.E. 2499 (1956) amendment B.E. 2546 (2003), livestock movement into the MTM zones in Thailand requires at least 21 days quarantine at their origin (JICA, 2003). Throughout the period of the quarantine, animals are inspected for any signs of livestock diseases, FMD in particular. If no signs of disease occurred, animals are released to the destination, as stated in the import permit, where additional 3-days quarantine may be required. Summary of the process is shown in Figure 2.1.

Probability of Infection Not Detected during Quarantine

Unapparent infection of FMD always poses tremendous concerns for the spread of the disease. Multiple factors are involved in the development of clinical symptoms following the infection (Alexandersen et al., 2002; Sutmoller and Casas Olascoaga, 2002; Grubman and Baxt, 2004). Animals may be infected with FMDV, yet clinical signs of FMD may not be so revealing or may be difficult to observe. The unapparent infection is seen especially where there are moderate to high level of immunity in the herds, such as the cases where FMD is endemic or animals are vaccinated against FMDV (Blaha, 1989; Davies, 2002). As a result, the sensitivity of screening for infection in Thailand by only observing clinical symptoms is far from perfect. The efforts to estimate the effectiveness of the quarantine procedures, unfortunately, was not helpful since no data are available for the direct estimation.

The morbidity rates for FMD infection were reported by a few studies done in Thailand and could also be calculated from outbreak reports acquired from DLD. Cleland et al. (1995 and 1996) reported the morbidity rates for FMD outbreaks in northern Thailand to be between 11 and 20%. Outbreak reports from DLD also are in agreement with these estimations and yielded the approximate morbidity rate of 14% (11939 cases out of 85,303 susceptible livestock). These estimates, however, were based on observations of clinical appearances of the disease, and no references were made as to how many were actually infected. Because no such data were available, experts' opinions were used as the best estimates to construct the distribution for the probability of livestock showing adverse clinical appearances given infection. Given the fact that duration of the quarantine will increase the likelihood of infected livestock showing

detectable clinical symptoms, the estimates for the most likely, minimum, and maximum values were given by experts as 70%, 0% and 100%, respectively. Vose (1997 and 2003) recommended using the Pert distribution over the Triangular distribution in dealing with this type of data where the minimum and maximum value were set at extremes. Thus, the probability of infected livestock showing detectable symptoms during quarantine p_S was modeled as RiskPert(0,0.7,1).

It is generally accepted that once the clinical symptoms of FMD infection appears, it is almost certain that the animal will be tentatively diagnosed as FMD infected ($P\{\text{detection}|\text{showing clinical signs}\} \approx 100\%$). Only the animals with the symptoms will be excluded from the shipment. The probability of an infected animal not showing any detectable symptoms was calculated as $1 - p_S$. The probability of a livestock possessing FMDV and not being detected during the quarantine p_A is the product of the likelihood of an infection in a consignment and the likelihood of the animal not showing symptoms:

$$p_A = (p_W \text{ or } p_D) * (1 - p_S).$$

Probability of an Imported Livestock Infected with FMD

The probability of an accepted animal for movement/trade become infected with FMD (i.e., $P(\text{infected}|\text{accepted})$) provides intuitive meaning to the MTM countries. The probability can be determined by dividing the probability of an infected animal being accepted for import (p_A) by the sum of all probabilities of an animal being accepted import; as

$$P(\text{infected}|\text{accepted}) = \frac{p_A}{p_A + p_B} .$$

Figure 2.1 diagrammatically shows an event tree of how the latter probability could be calculated; p_B was calculated as $1 - (\text{prevalence of FMD in incoming animals})$.

2.2.6 Sensitivity Analysis

In this model, we used the experts' opinions to reflect the likelihood of infected livestock revealing symptoms for FMD (p_S), and the most likely value was set as 70%. It is arguable that this may be an inflated evaluation since FMD is considered endemic in the regions with extensive uses of vaccine in some areas. More pessimistic estimations may be suggested, thus, resulting in higher chances for accepted livestock to be infected with FMD. We investigated the effects of this assumption on the level of unapparent infection associated with the risk of importing FMD infected livestock. The model was run for a range of p_S from 5% to 95% in increments of 5%, and the minimum and maximum values were set constants as 0 and 100%, respectively, across all the values of p_S .

2.3 Results

2.3.1 Prevalence Calculation

Statistical summary for the estimated prevalences of FMD is presented in Table 2.4. The simulation produced similar outputs for the most-likely prevalences at 7.37% and 10.95% for the regional surveillance and the consignment surveillance, respectively. The standard deviation calculated from the consignment surveillance data is, however, approximately 4 times larger than the one calculated from the regional surveillance. Test for the equality of variances showed that the variance calculated from the regional surveillance was significantly lower than those derived from the consignment surveillance (p-value < 0.001). This more expansive result (Figure 2.2) observed in the consignment surveillance reflected our level of knowledge and confidence in the data, i.e.

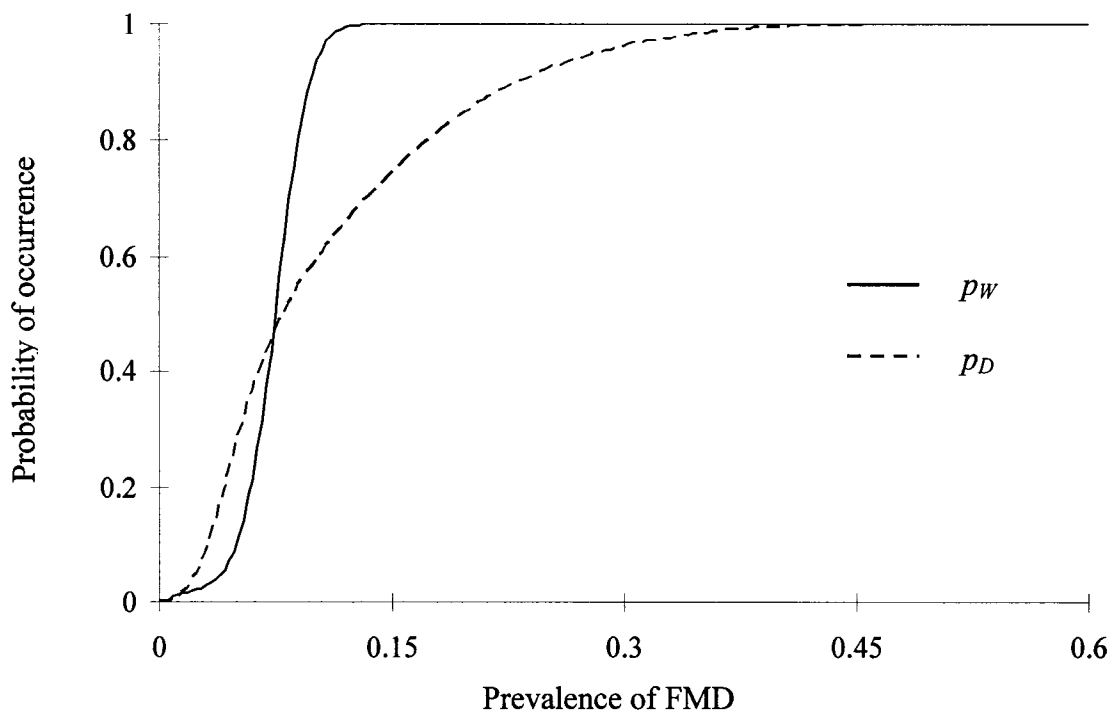
uncertainty, and might be due to smaller number of samples collected for the consignment surveillance as compared to the regional study. Hence, the decision was made to carry out the rest of the analyses with the prevalence calculated from the regional surveillance for the sake of brevity.

Statistic	Prevalence from regional surveillance <i>p_w</i>	Prevalence from consignment surveillance <i>p_D</i>	Probability of unapparent infection in quarantine <i>p_A</i>
Minimum	0.19%	0.04%	0.01%
Maximum	14.91%	58.47%	10.65%
Mean	7.37%	10.95%	2.74%
Std Dev	2.00%	8.37%	1.62%
Variance	0.04%	0.70%	0.03%
Median	7.51%	8.03%	2.50%
Mode	6.83%	4.96%	2.07%
5%	4.02%	2.46%	0.53%
25%	6.20%	4.72%	1.50%
75%	8.68%	15.28%	3.73%
95%	10.39%	28.28%	5.75%

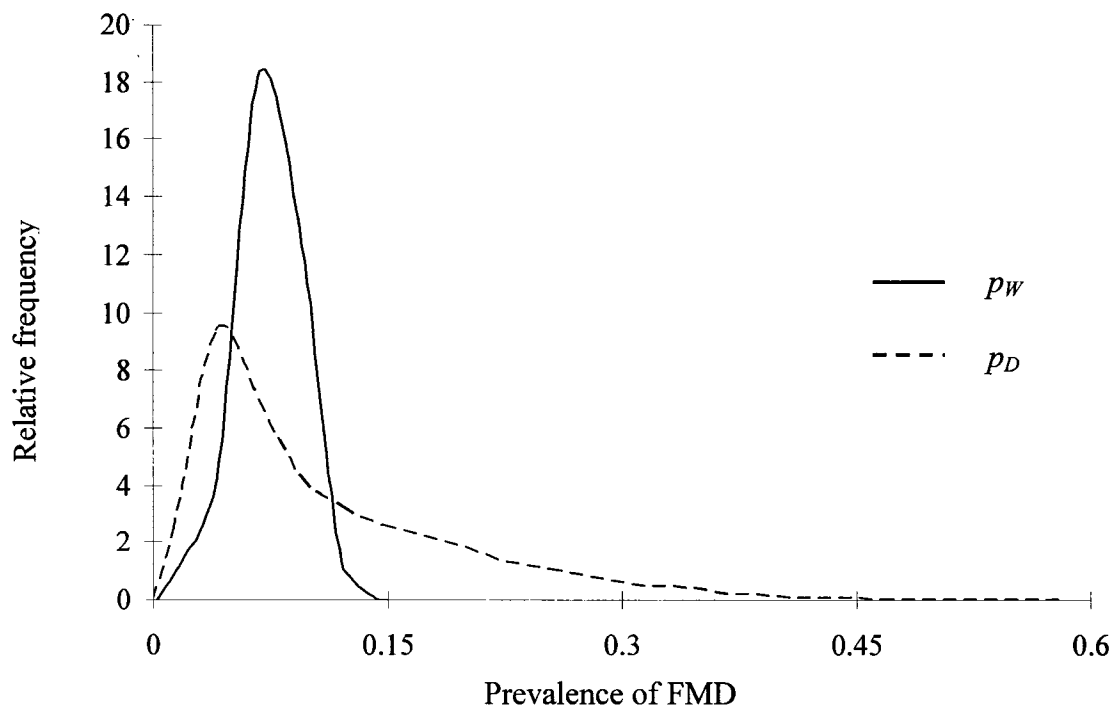
Table 2.4: Summary statistics of the simulation of regional and consignment prevalence calculations, and of the estimated probability of unapparent infection during quarantine

2.3.2 Probability of Infection Not Detected during Quarantine, p_A

Figure 2.3 illustrates the distribution of p_A . For each livestock that comes into a quarantine station, there is approximately an average of 2.74% probability that the quarantined livestock will have an unapparent form of FMD infection. The simulation produced the distribution with similar values for the three measures for central tendency. Summary results of the distribution are presented in Table 2.4.



a)



b)

Figure 2.2: a) Cumulative probability distribution and b) frequency distribution for the prevalence estimated from the regional (p_w) and consignment (p_D) sero-surveillance

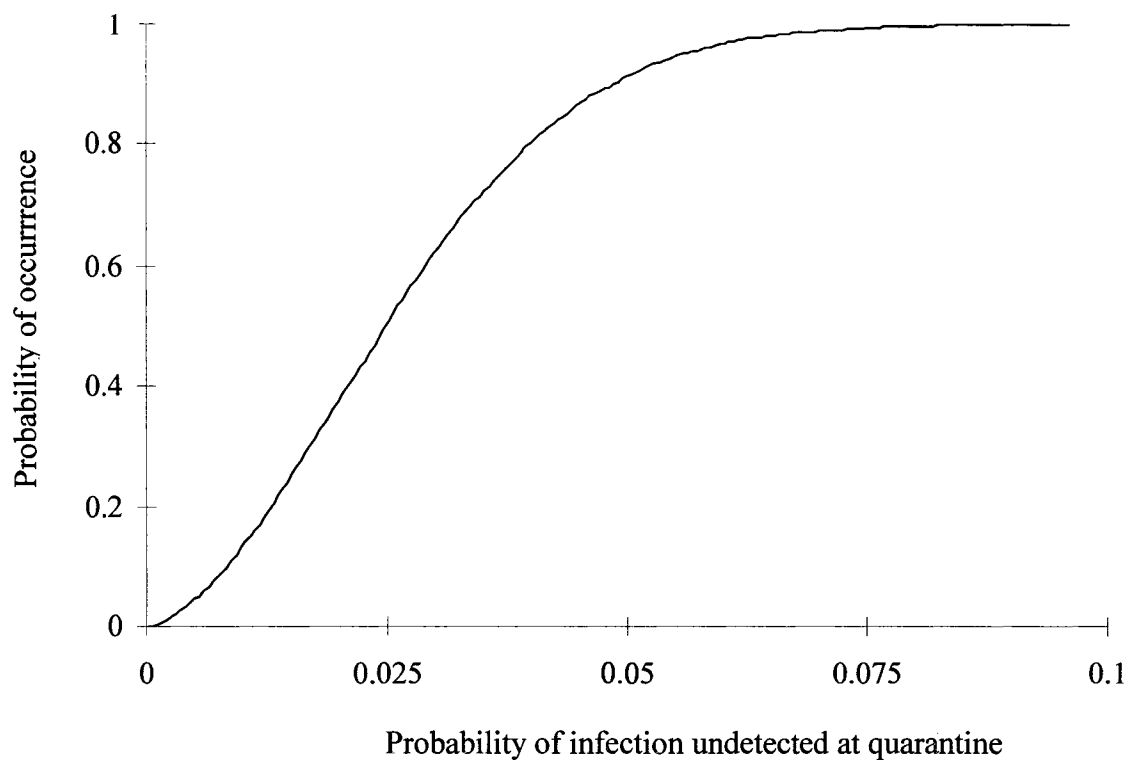


Figure 2.3: Cumulative probability distribution for the unapparent infection of FMD during quarantine

2.3.3 Probability of an Imported Livestock Infected with FMD

For each livestock that meets all the requirements for importation into the MTM zones in Thailand, it is pertinent to understand the level of risk that the individual livestock may carry FMD. The average probability of an accepted livestock containing FMD, estimated from the simulation, was at 2.86%. The risk could be as high as 11% and 95% of the iterations yielded the probability of 6% or lower. Table 2.5 revealed the summary statistics for the probability of infection given the animal was accepted for importation into the MTM zones. Figure 2.4 showed an illustrative representation of the distribution resulting from a simulation of 10,000 iterations.

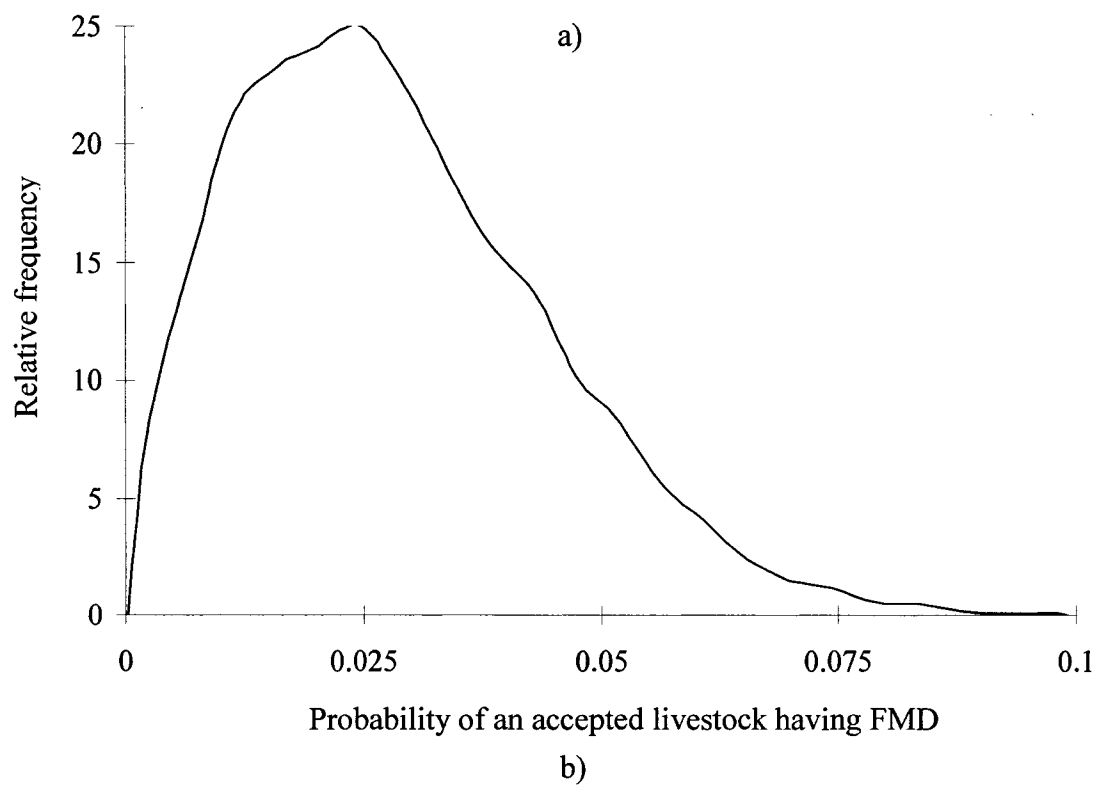
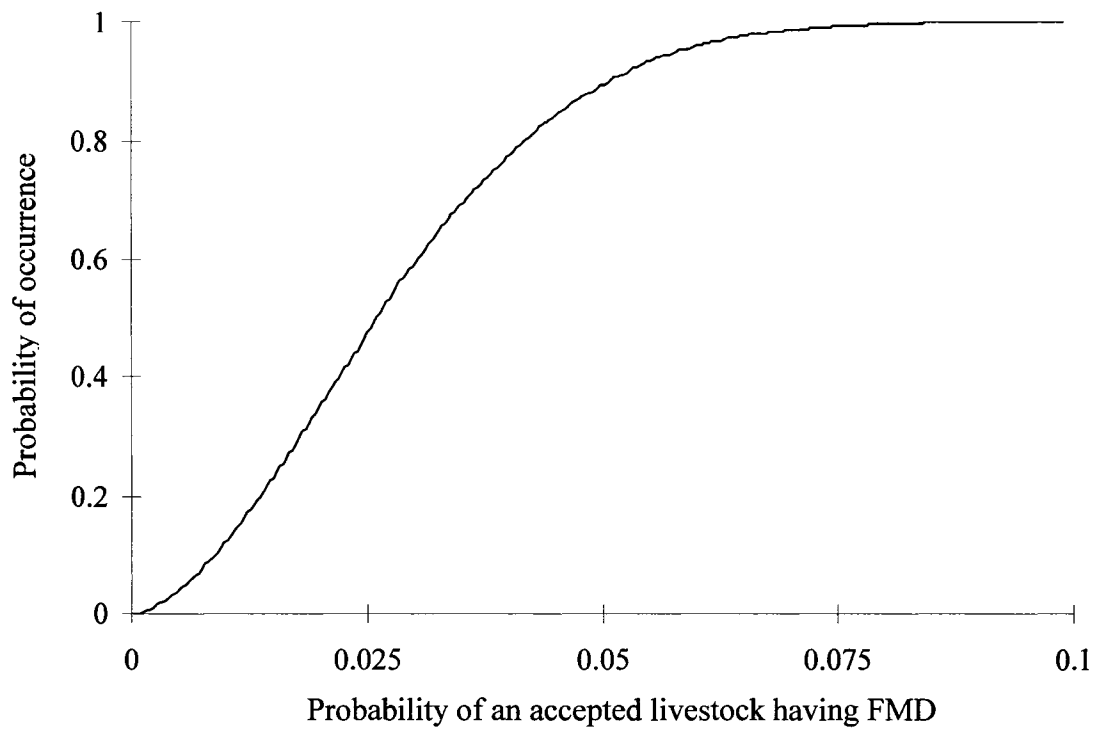


Figure 2.4: a) Ascending cumulative probability distribution and b) frequency distribution for the probability of an imported animal having FMD

Statistic	P(infected accepted)
Minimum	0.01%
Maximum	10.98%
Mean	2.86%
Std Dev	1.67%
Median	2.64%
Mode	3.06%
5%	0.55%
25%	1.58%
75%	3.90%
95%	5.95%

Table 2.5: Summary statistics of the probability of infection given that an animal has been accepted for trade

2.3.4 Sensitivity Analysis

Probability of apparent form of FMD infection has an effect on the level of risk of FMD introduction into the MTM zones (Figure 2.5). Not surprisingly, as the assumed level of apparent form of FMD increases, the probability of the introduction of FMD into the MTM zones decreases. For example, the risk is reduced by almost 70% when p_s increases from 10% to 90%.

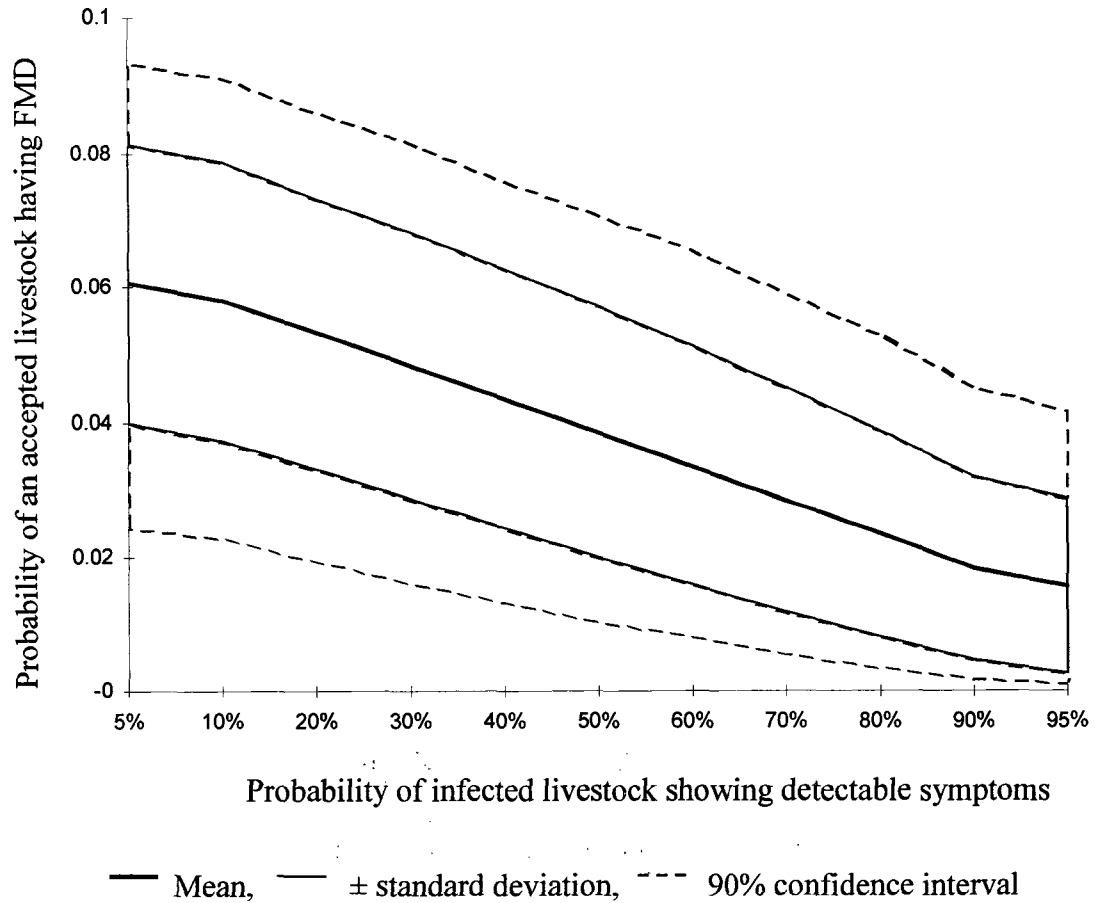


Figure 2.5: Impacts of changes of the probability of detecting symptoms of FMD during quarantine on the probability of FMD infection in an imported animal

2.4 Discussion

The estimated probability of the introduction of FMD involving terrestrial movement of livestock into the MTM zones in Thailand may appear to be small. Considering the amount of livestock moved southward in the MTM each year, nonetheless, concerns over the risk of importing FMD infected livestock shall be highlighted. The formula $1 - \{1 - P(\text{infected}|\text{accepted})\}^N$, where N is the total number of livestock imported, gives almost 100% chance that there will be at least one infected

livestock accepted into the MTM in a year. An approach to manage the risk is to alter movement procedures or regulations. Currently, the only action taken to protect the MTM zones against FMD relies upon the efficiency of the observation of classical signs of the disease. This study shows that the process reduces the probability of FMD introduction by over 60% if no action is taken. It is, however, strongly suggested to employ additional measures to increase the ability of detecting the disease if it is present; thereby further reducing the risk of FMD introduction. This will certainly require practical judgment from decision-makers because no such changes will be without consequences. For example, implementing more stringent measures naturally will reduce the likelihood of traders to comply with the regulations. Applying more rigorous processes will also result in higher costs to manage, and this has always been one of the constraints especially in developing countries. This will eventually drive the movements toward more of the illicit types. Consequently, any decisions made regarding movement regulations will have to be constituted wisely using the best available resources and knowledge. The models described in this study can be utilized as one of the tools for exercising the available options because it is inheritably flexible. The risk of FMD introduction may be reduced by decreasing the risk at the source, i.e. encouraging importation of livestock from the origins where the prevalence of FMD is low. This is always easier said than done. In South East Asia, the rule of demand and supply dictates the prices of livestock and, thus, determines the patterns of livestock movement. It is not practical at this point to designate the movement patterns based on the risks.

It should be kept in mind that this study only describes the risk involving legal transaction of livestock movement, which binds to existing regulations assessed in this

paper. Alternatively, the method of this paper may be used to assess the risk of FMD introduction due to illicit movement if certain assumptions are satisfied. First, it is assumed that the distribution of FMD prevalence in consignments intended to move without report is the same as those of reported transaction. Second, during the illegal movement process, no movement management is practiced that will alter the existence of FMD distribution in the consignment. Third, distribution of the origins of incoming livestock moved legally is the same for those illegal movements. If all the assumptions are met, calculation of the risk of FMD in the incoming livestock transported illegally can be relatively simple. The probability of (illicitly) incoming livestock having FMD would be the same as the FMD prevalence.

It is also important to note that the analysis completed was just designed for quantification of the risk of FMDV introduction, namely release assessment. It does not guarantee that each introduction will result in an outbreak at the receiving end. Another process must be considered to assess the probability of an outbreak from such introduction, namely exposure assessment.

2.5 Conclusion

To our knowledge, this is the first study to attempt a quantitative assessment of the risk of FMD introduction in the region. The results show that current movement regulation is not sufficient to protect the MTM areas from FMD introduction and additional measures are encouraged. The applications of the assessment have proven to be valuable for the achievement of the MTM campaign and can possibly extend to other similar campaigns in the region. Aims of this study were to provide recommendations

based on the best available data to people who make the decisions pertaining to control and eradication of FMD in the MTM areas. It is entirely up to the decision-maker to exercise the options to achieve the goal of the campaign in a practical sense.

2.6 Acknowledgement

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Chapter 3

Impacts of foot and mouth disease introduction into southern Thailand: intrinsic transmission dynamics and outbreak control

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3.1 Introduction

Foot and mouth disease (FMD) is a viral disease in cloven-hoofed animals. The disease is characterized by the formation of vesicles on the epithelial of susceptible animals, although an unapparent form of infection is also common in some species, such as sheep and goats. FMD virus (FMDV) can be transmitted via direct contact between

infectious and susceptible animals, indirect contact through fomites, or exposure of viral particles in the air (wind-borne transmission). FMD is in the list of diseases from the Office of International des Epizooties (OIE) that is easily transmissible and poses a great threat to the world economy and international trade. The presence of FMD in endemic countries diminishes the potential for trade of livestock and livestock products, and poses a great threat to FMD-free countries when sources of FMD re-emerge.

FMD is considered an endemic disease and has been reported in almost all South East Asian (SEA) countries, with the exceptions of Indonesia and parts of Malaysia and the Philippines. Though sporadic cases of FMD outbreaks were reported, parts of SEA, including southern Thailand, southern Myanmar and mainland Malaysia, were believed to acquire FMD from outside sources through movement of livestock. This belief has led to the initiation of a regionalization campaign for FMD freedom, known as MTM campaign. It encompasses Region 8 & 9 of southern Thailand, parts of Tanintharyi Division in southern Myanmar, and mainland of Peninsula Malaysia (Figure 3.1). Rationale and justification for the campaign is described in the reviews by Edwards, J.R. (2004). In recent years, the regionalization scheme has focused on preventing the introduction of FMD into the MTM region by managing the flow of animals. The prevention measures currently employed are not entirely effective in keeping the disease out of the region. A recent study by Wongsathapornchai (2006) has shown that there is still a concerning level of risk of FMD introduction with the present animal movement regulations. The MTM Tristate Commission, therefore, is seeking alternative strategies to deal with the problem. If FMD introduction is inevitable at the moment, there may still be ways to prevent outbreaks or to minimize the impacts of such introductions. It is

therefore pertinent to understand the baseline magnitude of the impact and the parameters that interplay in the FMD transmission chain if FMD is introduced into the concerned areas.

Wongsathapornchai (2006) has reviewed the FMD risk associated with movement of livestock and has demonstrated that only movement into southern Thailand is considered relevant for control of FMD in the MTM areas. The objectives of this study are to quantitatively assess the consequences of FMD introduction via movement of livestock into southern Thailand, to evaluate the relevance of factors influencing the disease occurrence, and to examine model parameters that contribute to such occurrence. Of particular interest are the effects of model parameters that are feasible for modifications. The objectives are accomplished using stochastic epidemiological modeling.

3.2 Materials and Methods

Of fundamental importance, the study began by providing a summary of the FMD situation in southern Thailand and control measures relevant to FMD occurrence in the area. A compartmental epidemiological model was developed for FMD transmission in southern Thailand, with focus on the estimation of the transmission rate, β . The model considered spread of FMD within the areas, as well as introductions of infected animals from outside sources. Using annual cumulative incidence as the outcome of interest, a sensitivity analysis was carried out to investigate effects of disease intervention strategies.

3.2.1 FMD Situation in Southern Thailand

FMD has been documented in Thailand since the 1950s, with the initial reports of type A15 in 1953, followed by type Asia 1 and O in the subsequent years (Chairsrisongkram, 1994). Only sporadic cases of FMD outbreaks have been reported in Region 8 and 9 of southern Thailand (Figure 3.1). Due to geographical locations and livestock demography, FMD outbreaks in the south were perceived as the results of the disease introductions from other parts of the country. However, an increasing trend of FMD outbreaks in recent years and a shift of dominating FMD serotypes from serotype O to A in 2002 have urged the Department of Livestock Development (DLD) to reevaluate the situation.

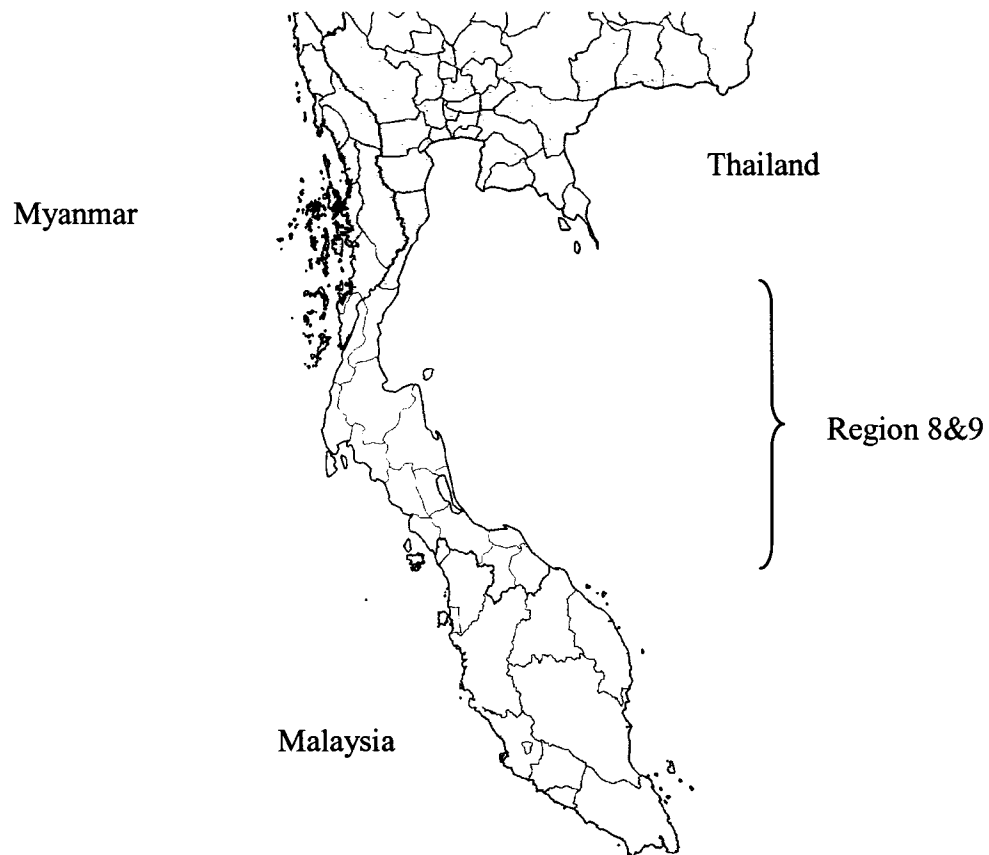


Figure 3.1: Southern Thailand (Region 8 & 9)

The following contains summaries of current FMD situation in southern Thailand from 1999 to 2003; data from 2000 to 2001 were analyzed and presented during the 1st MTM Tri-state Commission Meeting (January, 2003) in Cha-am, Thailand, by Teekayuwat et. al.. In addition, data from 2002 to 2004 were retrieved from South East Asia Foot and Mouth Disease Regional Coordination Unit (RCU), Bangkok, by Suseno and Wongsathapornchai in 2003.

Outbreaks of FMD in southern Thailand have fluctuated in the last five years (Figure 3.2). The number of outbreaks declined from 44 outbreaks in 2000 to 11 outbreaks in 2002; much of the decreasing trend was attributable to use of locally-produced trivalent vaccines in high risk areas. In 2003, the number of outbreaks in the south increased more than six-fold from the previous year. The alarming increase was explained by changes in the serotype of FMDV from serotype O to A. FMDV serotype O predominately occurred in almost all outbreaks from 1992 to 2001. In 2002, 56% of the confirmed outbreaks were the results of FMD serotype A infection. Since then, serotype A has been circulating in the area with 48% and 65% of all confirmed cases caused by serotype A in 2003 and 2004, respectively. A study by Linchongsubongkoch (2003) demonstrated that there were antigenic variations in serotype A viruses circulating within Thailand from 1997 to 2002. Serotype A vaccine (A/Sakolnakorn/97) used at the time did not provide sufficient protection against field isolation (A118/87). As a result, serotype A118/87 has been selected in 2003 as the appropriate vaccine strain and is currently being used in Thailand. Ninety-five percent of all outbreaks in the last five years were reported to affect only cattle and buffalo. There was no report of an outbreak in small ruminant.

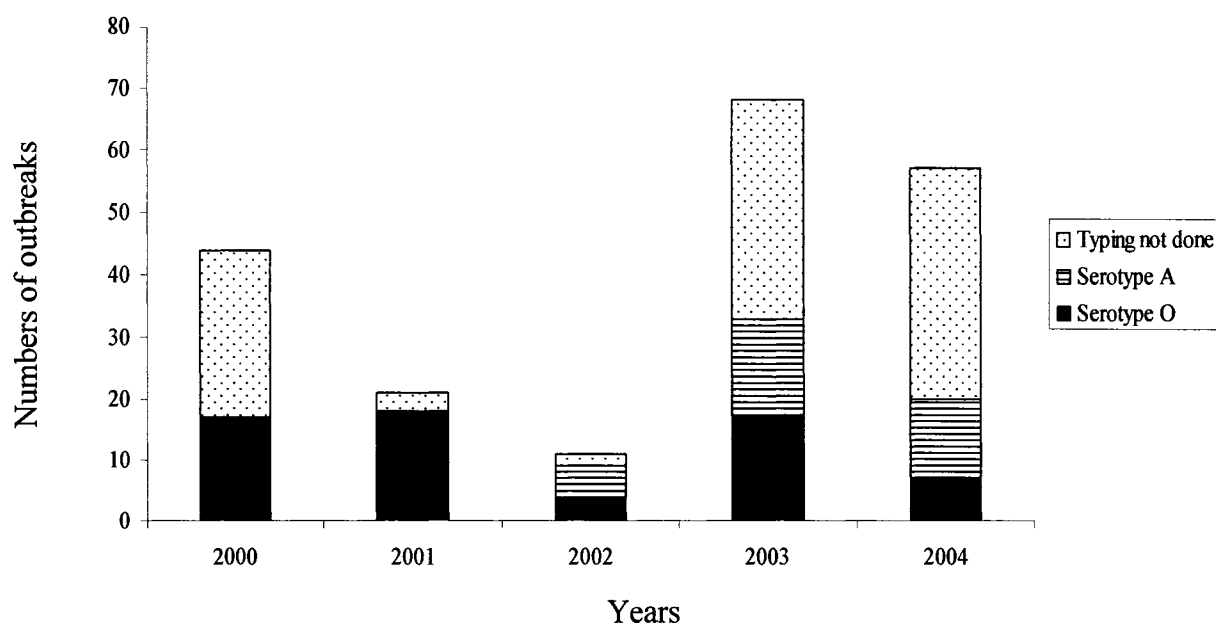


Figure 3.2: Annual cumulative incidence of FMD in southern Thailand from 2000 - 2004

3.2.2 A Simple FMD Transmission Model

The compartmental model was constructed to capture the temporal dynamics of FMD outbreaks. The model is based partly on earlier work on epidemiological models of FMD (Woolhouse et al., 1996; Perry et al., 1999). The model is referred to as a *SLIRV* model. A schematic representation of the model is shown in Figure 3.3. A population of size N is divided into five classes: those susceptible to infection (S); those exposed to infection but not yet infectious (L); those infected and become infectious (I); those recovered from infection and no longer infectious (R); and those vaccinated and become immune to infection (V). At any time t , an animal will be in exactly one of the five classes. The unapparent form of FMD infection in ruminants is relatively more common than in other species; thus, the infectious class is further subdivided into two distinct subclasses of infectious with and without observable symptoms (I_{cli} and I_{sub} , respectively).

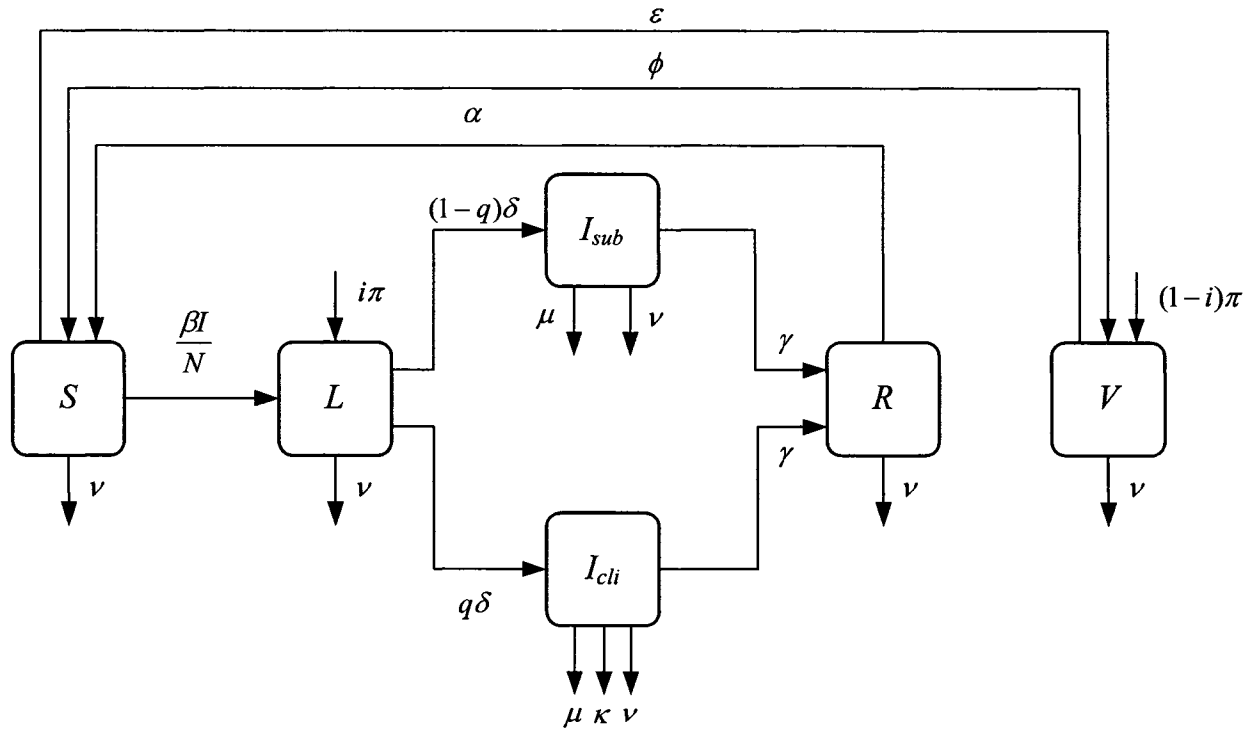


Figure 3.3: A schematic representation of the temporal transition of animals between different classes. At any times, animals may be in one of the five classes: susceptible to infection (S); latently infected with FMDV but not yet infectious (L); infectious (I); recovered from field infection and immune to re-infection (R); and vaccinated (V). The parameters of the model are further described in Materials and Methods section.

After being exposed to FMDV, animals in the S class move to the L class at the rate $\beta I/N$, where β is defined as the transmission rate of FMD infection. Animals stay in the L class for a period of $1/\delta$ and then advance to the I class. A proportion q of animals in the L class will move to the I_{cli} class, while the rest of them will inherit unapparent infection. Animals will remain infectious for the period of $1/\gamma$ and then progress to the R class where they are no longer infectious but still remain in the population. Susceptible animals are subject to routine vaccination, which is commenced bi-annually at rate ϵ . The immunity produced neither from vaccination or from natural infection is life-long.

Animals are protected against FMD infection for a period of $1/\theta$ and $1/\alpha$ following vaccination and natural infection, respectively; and will resume their susceptibility status immediately afterward.

The animal population in southern Thailand is quite dynamic with continual movement of animals in and out of the region. The southern region is a preferred destination for domestic movement of animals within Thailand, because there is a constant demand for general consumption. Southern Thailand is also a major channel for the exportation of animals and products to high-priced markets in neighboring countries. This dynamic nature is described in the model by the following parameters. Importation of animals into the region occurs at the rate π . The study by Wongsathapornchai (2006) estimated that a proportion i of incoming animals will have FMD. Movement regulations require that all incoming animals need to be vaccinated against FMD. Therefore, $1-i$ proportion of all incoming animals will be classified into the V . The population loses some animals at the rate ν due to movement out of the region and death from other causes. Some animals in the infectious class will also suffer and die from FMD at the rate μ . In another word, μ describes the mortality rate of FMD infection. The parameter κ is included in the model to examine the effects of intervention strategies involving isolation of infected animals, or better yet stamping-out policy. The parameters used in the model, along with their descriptions, are summarized in Table 3.1.

Parameter	Definitions	Value		
		β	Uncertainty analysis for ACI	Sensitivity analysis for ACI
β	Transmission parameter	-	0.115	0.115
$1/\delta$	Duration of latent infection	3	Pert(2,3,14)	3
$1/\gamma$	Infectious period	10	Pert(2,10,14)	10
θ	Rate of decay of immunity from vaccination	0.0038	0.0038	0.0038
α	Rate of decay of immunity from natural infection	0.0038	0.0038	0.0038
ε	Rate of vaccination	0.003	0.003	Uniform(0,1)
μ	Loss of animals due to disease	0.00003	0.00003	0.00003
ν	Loss of animals due to other causes	0.00041	0.0041	0.0041
κ	Loss of clinically infected animals due to control measures	0	0	Uniform(0,1)
π	Rate of movement		See Figure 3.4	
i	Probability of incoming animals having FMD	0.0259	*	#
q	Probability of having clinical appearance	0.7	Pert(.5,.7,1)	0.7
p	Proportion of animals becoming immuned after vaccination	0.934	Pert(.7,.9,1)	0.934

* See Wongsathapornchai (2006), where p_A was given as Pert(0.5,0.7,1)

See Wongsathapornchai (2006), where p_A was given as Uniform(0,1)

Table 3.1: Definitions, values, and distribution for the model input parameters in an estimation of transmission parameter, β , and analyses of uncertainty and sensitivity of annual cumulative incidence (ACI)

The model is described by the following nonlinear system of differential equations (Anderson and May, 1991);

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta SI}{N} - p\varepsilon S - \nu S + \alpha R + \phi V \\
\frac{dL}{dt} &= \frac{\beta SI}{N} + i\pi - \delta L - \nu L \\
\frac{dI_{cli}}{dt} &= q\delta L - \gamma I_{cli} - \mu I_{cli} - \kappa I_{cli} - \nu I_{cli} \\
\frac{dI_{sub}}{dt} &= (1-q)\delta L - \gamma I_{sub} - \mu I_{sub} - \nu I_{sub} \\
\frac{dR}{dt} &= \gamma(I_{cli} + I_{sub}) - \alpha R - \nu R \\
\frac{dV}{dt} &= p\varepsilon S + (1-i)\pi - \phi V - \nu V
\end{aligned} \tag{1}$$

The model is based on the concept of the mass action principle: the rate of transmission of the disease at any time is assumed to be proportional to the number of susceptible multiplied by the density of infectious individuals at that time. The proportionality constant, β , is known as the transmission rate, which is defined as the number of animals infected per infectious animal per day. $\beta I/N$ is therefore the rate of conversion from the S to L classes. The rate of change in the number of animals in the S class is then described by the following equation:

$$dS/dt = -(\beta SI/N) - p\varepsilon S - \nu S + \alpha R + \phi V$$

δ is the rate at which animals move from the L to I classes. δ is the reciprocal of the average duration of the latency period of FMD. The number of latently infected animals, L , therefore, obeys the equation:

$$dL/dt = (\beta SI/N) + i\pi - \delta L - \nu L$$

$1/\gamma$ is the mean infectious period for animals in the I groups. Thus, animals recover from I_{cli} and I_{sub} classes at rate γ . Thus, although DLD veterinarians are given the legislative power to cull any confirmed cases of FMD, it is rarely done in the field due to practical and economic difficulties. Normally, the suffering animals will be isolated for

treatment. However, the treatment usually starts between 2-7 days after the infected animals have revealed clinical signs. This suggests that the infectious period perhaps has already elapsed even before the treatment takes effect. Thus, the treatment of infected animals will not have any effects on the course of infection. The model includes a “what-if” scenario to investigate the effect of stamping-out policy on the occurrences of FMD outbreaks. In this “what-if” scenario, it is assumed that animals in the I_{cli} group, once detected, will be removed from the population at rate κ by “stamping-out”. A proportion of deaths resulting from FMD infection, μ , are also observed and it is assumed to be the same for I_{cli} and I_{sub} . The change in number of infectious animals can be explained by the following equations:

$$dI_{cli} / dt = q\delta L - \gamma I_{cli} - \mu I_{cli} - \kappa I_{cli} - \nu I_{cli} \text{ and}$$

$$dI_{sub} / dt = (1 - q)\delta L - \gamma I_{sub} - \mu I_{sub} - \nu I_{sub}$$

Animals that recover from natural infection will have immunity against re-infection for an average duration of $1/\alpha$, and then will resume their susceptibility status. The rate of change in the number of animals in the R group is expressed in the following equation:

$$dR / dt = \gamma(I_{cli} + I_{sub}) - \alpha R - \nu R$$

Susceptible animals in the southern region are vaccinated against FMD during the bi-annual routine vaccinations. ε captures the vaccination capacity of DLD veterinarians and is fairly consistent throughout the year. Vaccines used are locally-produced trivalent vaccines. Not all vaccinated animals will elicit protective level of immunity; instead, Cleland et al. (1994) have shown that only a portion of vaccinated animals, p , were protected against FMD infection. The period of immunity induced by the vaccination is

not life-long. The vaccinated animals will elicit immunity against FMD infection for a period of $1/\theta$. Hence, the following equation specifies the rate of change in the number of animals in the V class:

$$dV / dt = p\varepsilon S + (1 - i)\pi - \phi V - \nu V .$$

3.2.3 Assumptions for the Model

The model described in this paper is based a number of assumptions. Some of the assumptions were created to allow for the completion of mathematical equations; others were formed due to the lack of empirical evidence.

- a) The population was assumed to be homogeneously mixed, in which all animals in the population were hypothesized to have the same management and husbandry. Almost all ruminants in southern Thailand are raised in small-scale farming systems. Farmers will herd their animals to the common grazing areas or paddy fields during the day and will keep their animals within their household during the night. More than 80% of beef cattle, dairy cattle, and buffalo are of the same breed (DLD Information Technology Center, unpublished data). Animals are vaccinated using the same locally produced trivalent vaccine, and all by trained DLD officers. The homogeneity may appear to be a major simplifying assumption. Given the above conditions, however, the cattle and buffalo population can be viewed as a single, homogeneous, free-mixing host population from an epidemiological perspective. Certainly, there are some individual variations; attempts were made to account for such variations using stochastic approaches.
- b) Only direct transmission of FMD is considered in the model. Indirect and airborne transmission is not included because they are regarded as secondary sources of

outbreaks in the areas (Cleland et al., 1995¹; Cleland et al., 1995²; Cleland et al., 1996). The secondary sources in southern Thailand are not significant to FMD transmission. FMDV contaminated aerosols generated by infected animals are likely to be rapidly inactivated by intense sunlight and high temperature in the south. Also, there was no confirmed report of FMD outbreaks caused by fomite transmission (OIE-RCU, 2004; DLD Outbreak Report, 2004).

- c) It was reported that FMD in the area is mainly maintained in village cattle and buffalo population (Chamnanpood et al., 1995; Perry et al., 1999). Only 10% of FMD susceptible species reported in southern Thailand were small ruminants (DLD, 2004), and there were no reports of the involvement of small ruminants in any of the outbreaks that occurred in southern Thailand since 2003 (OIE-RCU, 2004). FMD outbreak in swine population is similar to those in small ruminants. In 2003, pigs were only involved in 3 out of 64 outbreaks (5%) of FMD in the southern Thailand (OIE-RCU, 2004). There is also no evidence of transmission of FMD from swine to other susceptible species. Therefore, it is assumed that no transmission occurs from other species to cattle and buffalo.
- d) Immunization of animals was performed at random. It was also assumed that vaccination in *L*, *I*, or *R* classes will not affect the course of infection.
- e) There is some evidence suggesting that vaccinated animals may still be infected and can become carriers following contact with field FMDV (Grubman and Baxt, 2004). However, studies have shown that transmission of FMD from carrier animals to other susceptible animals does not occur in normal field settings (Moonen and Schrijver, 2000; Sutmoller and Casas Olascoaga, 2002). Because of no supporting evidence to

prove otherwise, those carriers are not considered as being parts of the FMD transmission chain in the model. Thus, for the sake of mathematical simplicity, animals eliciting protective level of immunity are assumed to have the perfect protection against FMD infection for a defined period of time.

3.2.4 Outbreak Data

Outbreak data were retrieved from the records collected by Disease Control Division (DCD), Department of Livestock Development, Thailand. After the DCD is alerted by local veterinarians about a possible FMD outbreak, investigation takes place, and control measures are imposed simultaneously. Outbreak reports are submitted weekly to the DCD headquarters in Bangkok. The reports include weekly incidence and mortality of FMD cases in an outbreak area and control measures used to put out the disease.

The outbreak definition, as defined by DLD, is the same for all outbreaks since 2003 and is consistent with the MTM Minimum Standard Definitions and Rules (SDRs) (Turton, 2003), which states:

An outbreak is a confirmed occurrence of FMD infection, which may affect one or more susceptible animals. Subsequently confirmed cases in close proximity to the initially confirmed case(s) will not be considered to be a separate outbreak unless they occur at a distance greater than the radius of the control area declared from the initially confirmed outbreak (this is generally 3-5 km) or in a timeframe longer than the incubation period for FMD after the last confirmed case in the initial outbreak (14 days).

For convenience and lack of data, DCD uses village locations as reference points for spatial distribution of outbreaks. If cases where FMD occur in adjacent provinces, they will be recognized as one outbreak, given that the cases transpire within 14 days from one another. Outbreaks will be declared to be under control if no new incidence is observed 4 weeks after the last reported case of FMD.

Before 2003, routine, mass vaccination of locally produced trivalent vaccine against FMD was not done in Region 8 & 9 of southern Thailand. Targeted vaccination in the HR in the south was initiated in the first round of vaccination in April of 2003. This predictably has resulted in a change in the composition of animals in terms of their susceptibility to FMD infection. In addition, during the 2003 fiscal year, the government of Thailand has undergone a crucial phase of governmental reform, which has tremendous adverse effects on the ability of DLD to handle outbreaks of FMD in the countries. The adverse impacts were realized when incidences of FMD outbreaks in 2003 increased by almost three-folds from 2002 (from 83 reported outbreaks in 2002 to 209 reported outbreaks in 2003). Hence, outbreaks reported before 2003 were not considered for this study for consistency of the model parameters.

3.2.5 Parameter Estimations

Parameter estimates were taken from literature and from the outbreak report. There is a delay before the FMD cases are reported to DLD officials. Estimated from past outbreaks, this delay is approximately 3 days after the first initial case. The latent period is variable from 2-14 days, but generally varies between 2 to 4 days in cattle (Donaldson, 1987; Kitching, 2002; Suttmoller et al., 2003). The mean latent period was then estimated to be approximately 3 days, giving $\delta = 0.33 \text{ days}^{-1}$. Immediately after the latent period, animals become infectious until they are removed from the population or they are converted to *R* class. Duration of infectiousness includes the period in which animals are infectious but not yet showing detectible symptoms (1-2 days) and the delay before they are removed. DLD veterinarians visit the sites of outbreaks on a weekly basis; the delay of removal thus may vary between 0-7 days, with a mean of 3 days.

Graves (1971) reported that, on average, the infectious period lasts roughly 5 days, and the level of transmission drops dramatically 5-7 days after the development of clinical lesions, giving the infectious period of up to approximately 8-10 days ($\gamma = 0.1 \text{ days}^{-1}$).

Approximately 10% of all animals in southern Thailand were vaccinated in 2003 during the biannually targeted vaccination campaign (DLD vaccination records, 2004). The vaccination process took place twice a year, once in June and then in December, and took about one month to complete. The vaccination is assumed to take place in a pulse, such that during a vaccination pulse, $\varepsilon = 0.1/30 = 0.0033 \text{ days}^{-1}$; and between vaccination pulse, $\varepsilon = 0$. Study by Cleland et al. (1994) reported that 93.4% (p) of all vaccinated animals will become immune to infection after vaccination (assuming that all animals are susceptible at the beginning). The Cleland study also documented that 70% of all vaccinated animals eliciting protective immunity after the vaccination lost their immunity after six month. The rate of decay of protective immunity after the vaccination, \varnothing , was calculated to be 0.0038 days^{-1} . Studies reported that immunity from natural infection will last longer than from vaccination. Due to lack of data, it is assumed that immunity from natural infection lasts as long as animals vaccinated for the second time, giving $\alpha = \varnothing = 0.0038 \text{ days}^{-1}$.

The records from DLD show that there were 89,294 cattle and buffalo moved down into southern Thailand from other regions in 2004. Movements of livestock in these areas are known to follow seasonal patterns which generally peak during the months of October through December and lower during the summer months (Wongsathapornchai, 2001). Values of π are allowed to vary on a weekly basis to adjust for the seasonal movement of livestock. The seasonal patterns will reflect the weekly patterns of livestock

movement in 2004 (Figure 3.4). Despite attempts to screen for FMD infection, the proportion of these incoming animals is expected to be infected by FMDV. Wongsathapornchai (2006) showed that, on average, 2.6% of these incoming animals will have FMD. Information on the uncertainty distribution of this risk probability is also available and will be utilized as the estimated values for i .

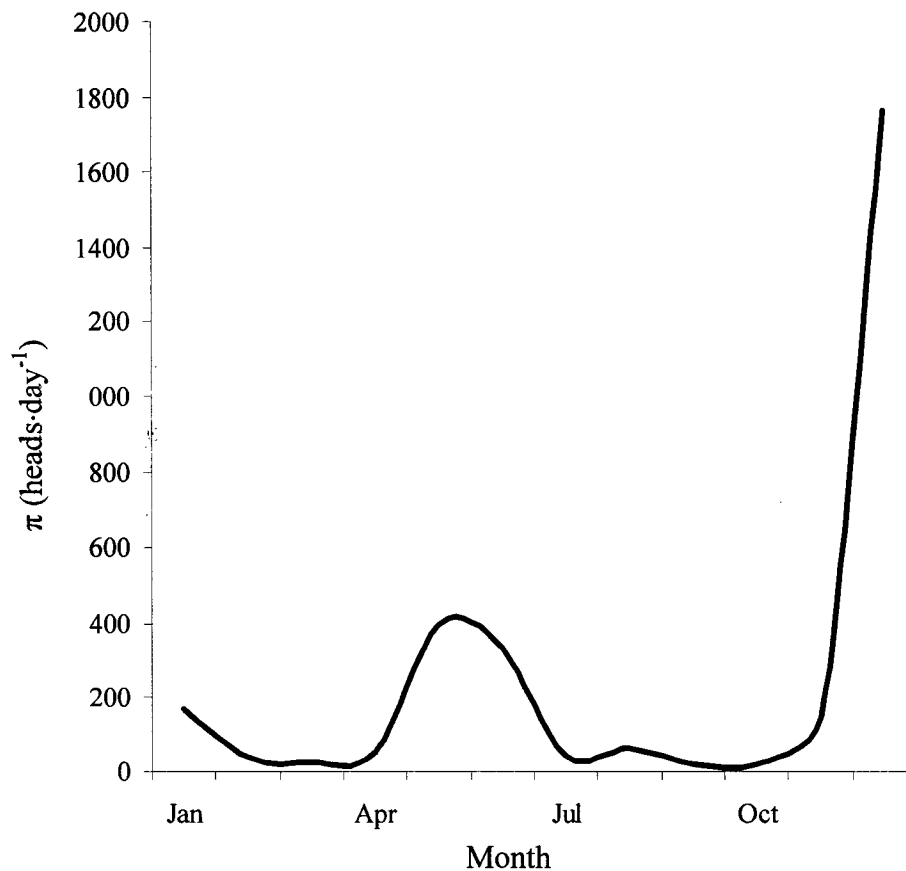


Figure 3.4: Daily patterns of livestock movement into southern Thailand from other regions in 2003

FMD is known to create low mortality in ruminants. The reported mortality of FMD in southern Thailand in 2003 was approximately 1%, giving $\mu=0.000027$. There is no reliable source of data for the estimation of loss of animals due to movement out of

the areas and death from other causes, ν . However, records from DLD show that the animal population in southern Thailand has remained fairly constant despite continual introduction of animals from other parts of the country. From this information, ν was estimated to be around 0.0004 to produce a constant value of N in the model.

β represents a transmission parameter, which is a combination of the average number of contacts between animals per unit of time and the probability of transmission per contact between a susceptible and an infected animals. β inherently simplifies intrinsic, environmental, and social factors that contribute to the ability of the virus to be successfully transmitted to other susceptible animals. Estimation of β is not so straightforward. In this study, β was approximated by comparing observed epidemic data and expected number of observable FMD incidences derived from the model, i.e., values of $q\delta L$. Data from the FMD outbreak reports was used to estimate β . For the estimation of β , other parameters in the model were held fixed using average values. The least square estimation (LSE) method was employed whereby a value for β was estimated such that the sum of squares of the difference between the observed and expected epidemic data was minimal. Rationale and steps for the computation LSE were explained in Heathcote and Nicholls (1990).

3.2.6 Uncertainty and Sensitivity Analysis of Annual Cumulative Incidence of FMD

Some parameters in the model were allowed to vary to incorporate the uncertainties in parameter estimations. These parameters include δ and γ . A probability distribution function, PDF, was assigned to each parameter to describe the range of possible values and probability of their occurrences. Minimum, most-likely, and

maximum values were given. Vose (1997 and 2003) recommended using Pert distribution over a triangular distribution in dealing with the data where the minimum and maximum value were set at extremes. Upper and lower bound for δ , γ and p were derived from the literature (see section 2.5) and from experts' opinions for q (Wongsathapornchai, 2006). See Table 3.1 for parameters' values and their respective distributions.

Sensitivity analysis of the FMD annual incidence is performed so that the effect of changes in the model parameters can be investigated. Attention was given to the parameters that were "modifiable" through changes in control practice. Two parameters from equation (1) were carefully examined, including speed of the vaccination, ε , and removal of infectious population from the population, κ . A uniform distribution was assigned to each of the two parameters to allow the values of the parameters to vary between zero and one. A value of zero implies that the intervention does not exist or is absolutely ineffective. One of the major risks of FMD in southern Thailand is the introduction of the disease from outside sources. Hence, it is also pertinent to examine factors leading to changes in the likelihood of FMD introduction through movement of livestock, i . Wongsathapornchai (2006) suggested that alteration of the sensitivity to detect the disease at quarantine stations, p_s , would dramatically change the level of i . To examine effects of the sensitivity, uniform distribution was again assigned to handle the expert's estimates of p_s . The median values of p_s were allowed to vary from 0 to 1; the value of zero implied that there was virtually no screening at the quarantine, and unity implied that the screening process is considered perfect in ruling out infected animals.

A method of partial rank correlation coefficient (PRCC) was used to evaluate effects of model parameters to the changes in ACI (Sanchez and Blower, 1997; Chowell

et al., 2004). The values of each of the three parameters and the subsequent ACI were ranked; the ranked numbers were then used to calculate correlation coefficients values using methods described by Stuart et al. (1999).

3.2.7 Simulation Steps

A model was constructed and simulated in Microsoft Excel[®] 2003 (Microsoft, Redmond, WA) with @Risk 4.0 (Palisade Corporation, Newfield, NY) add-on-function to simplify stochastic processes. A simulation included 5,000 iterations and was sampled using Latin Hypercube Sampling technique. The model was run in time steps of one day to estimate daily changes in the incidence and prevalence of the outbreaks. The simulation was allowed to run for a period of 2 years (730 days). A one year “burn-in” process, where the results from the first 365 days were ignored from the analysis, was necessary to replicate the endemic situation of FMD in southern Thailand. Only a one year “burn-in” process was sufficient to produce relatively stable patterns of FMD incidences (Figure 3.5).

3.3 Results

3.3.1 Fitting the Model to the Outbreak Data

In Figure 3.6, the sum of the squares of the difference between observed data and the simulated incidence of FMD was plotted against the possible values of β that could produce outbreak similar to what was observed in the x-axis. As shown in the curve, the value of β that gave the smallest sum of squares of the difference was estimated at 0.115. This value of β also produced the estimated cumulative incidence (21,144 cases) close to the observed cumulative incidence (21,591 cases) in 2003.

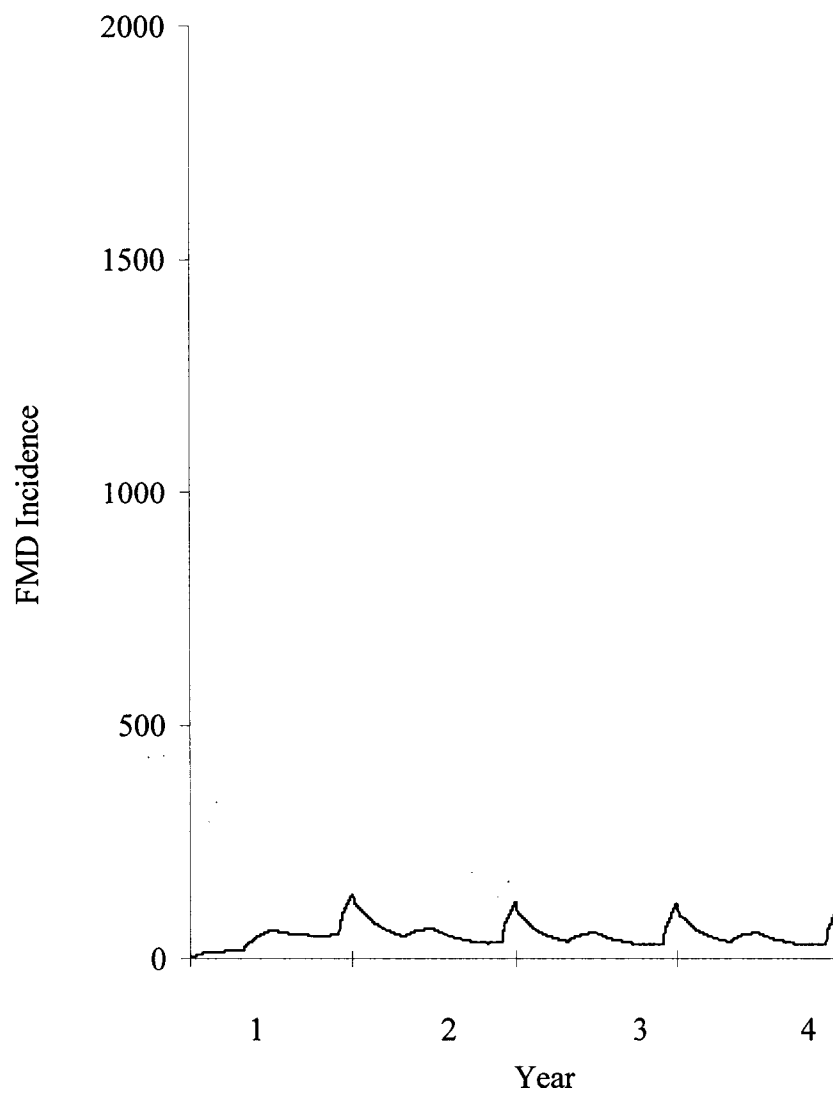


Figure 3.5: Expected daily incidence of FMD simulated from the compartmental model for the period of 1,460 days.

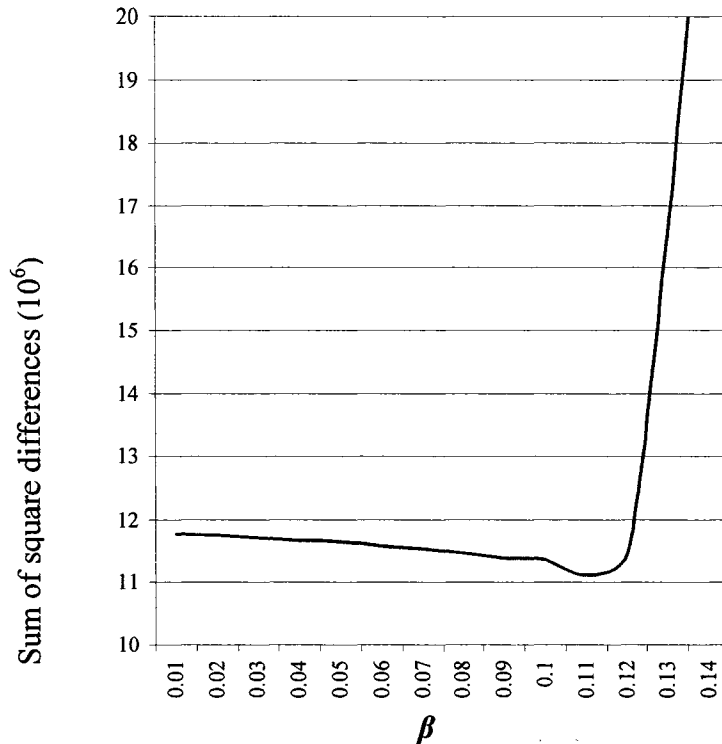


Figure 3.6: Graphical illustration of the sum of squares of the difference between simulated and empirical data on number of FMD incidences for the range of possible transmission parameter, β , values.

3.3.2 Uncertainty and Sensitivity Analysis of Annual Cumulative Incidence of FMD

The annual cumulative incidence (ACI) of FMD was inherently expressed in the model equation as δL . The model parameters, including δ and γ , were chosen according to their probability for use in the calculation. The process was then repeated 5,000 times. Figure 3.7 shows the distribution of the ACI from the simulation. The mean value of ACI is 23,213 with standard deviation of 12,484. Ninety-five percent of the ACI estimates are less than 47,397, with the minimum of 2,576 and the maximum of as high as 88,226. Summary statistics for ACI are presented in Table 3.2.

Statistic	Value
Minimum	2,576.8
Maximum	88,226.9
Mean	23,213.4
Std Dev	12,484.8
Median	20,633.2
Mode	18,152.9
5%	7,570.6
25%	13,889.9
75%	30,121.0
95%	47,397.2

Table 3.2: Summary statistics for the analysis of uncertainty of annual cumulative incidence of FMD in southern Thailand

Sensitivity of ACI to the model parameters was examined. Values of ε , κ , and p_A were allowed to vary uniformly from 0 to 1, while other parameters in the model were held fixed at the average values previously described in section 2.4. For each iteration, a value of ACI corresponding to a set of value of ε , κ , and p_S was stored. The stored values were then used to calculate PRCC for the sensitivity analysis. The PRCC for the ACI estimates and the parameter ε , κ , and p_S are listed in Table 3.3 in descending order. All three parameters appear to have negative correlations with ACI, meaning that the bigger the value ε , κ , and p_S , the smaller the value of ACI. ε and p_S were strongly correlated with ACI with the p-values of 0.0007 and less than 0.0001, respectively.

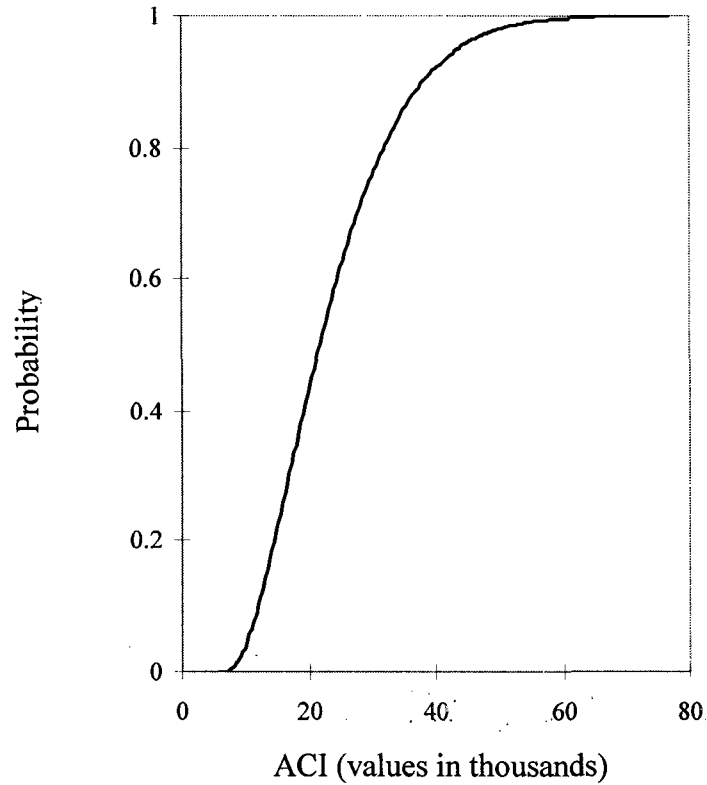


Figure 3.7: Ascending cumulative probability density function resulting from the uncertainty analysis for the range of annual cumulative incidence of FMD in southern Thailand

Input parameter	Annual Cumulative Incidence, ACI	
	PRCC	<i>p</i> value
ρ_S	-0.97924	<0.0001
ε	-0.03183	0.0007
κ	-0.00284	0.7635

Table 3.3: Partial rank correlation coefficients and their corresponding *p* values between the rate of slaughter of infectious animals, rate of vaccination, and sensitivity of the screening process during quarantine versus annual cumulative incidence, ACI

3.4 Discussion

The sensitivity analysis of ACI allows the examination of intervention strategies that affect disease occurrence that otherwise are impractical to study in experimental settings. In this study, the model allows investigation of three pertinent questions in control and eradication of FMD in southern Thailand. First, how important is the preclusion of the introduction of FMD infected animals in relation to eradication of the disease in the areas? Second, should mass vaccination against FMD be considered as an inevitable option in prevention campaign? Third, is killing of infected animals necessary in controlling FMD outbreaks?

Introduction of FMD infected animals into the southern regions from other regions of the country is the most significant determinant in determining annual incidence of FMD. This is evident when the sensitivity of FMD screening process, leading to changes in the likelihood of FMD infected animals being introduced, is strongly correlated with the ACI. Negative correlation suggests that the value of ACI will be lower when the sensitivity is higher. The risk of FMD can be reduced by improving the efficiency of FMD detection prior to the introduction. This can be achieved by implementing additional screening tools, which provide relatively higher level of sensitivity to detect infection, rather than depending solely on clinical observation (Wongsathapornchai, 2006). With the availability of more rapid screening tests for FMD, such as pen-side 3ABC and 2C nonstructural protein (NSP) tests for detection of NSP antibody and antigen (National Veterinary Research and Quarantine Service (NVRQS), Republic of Korea), the incorporation of diagnostic tests to the FMD screening process is more practical than ever. Effects of the improved screening sensitivity, as well as other

measures aimed in reducing the risk of FMD introduction, to alleviate the incidence of FMD are further deliberated in the study by Wongsathapornchai (2006).

Although the p-value shows that the correlation between the rate of vaccination (ϵ) and AIC is statistically significant (at $\alpha = 0.05$), the PRCC value for ϵ was only -0.03. The PRCC value suggests the significance of the correlation; however, the value does not signify the intensity of the correlation, nor does it imply the relative importance between ϵ and other parameters in the model. Large ruminants in southern Thailand are more scattered as compared to other regions of the country, as evident in the estimated value for β . Uses of vaccines are necessary, or even inevitable, during outbreaks; however, the necessity of mass vaccination with the goal to reduce the number of new cases of FMD may not be a sensible option for the situation in the south.

Though DLD is endorsed with legislative powers to adopt the stamping-out policy, culling of infected animals have rarely been done due to economic and social concerns. Farmers are generally very fond of their animals and fail to see why apparently healthy animals should needlessly be destroyed. Sometimes, in spite of adequate compensation, the slaughter policy causes much resentment, particularly from those that have lost their means of livelihood. Notwithstanding the difficulties, slaughter of FMD infected animals and/or high risk in contact animals has been recommended in the Minimum Standards (Turton, 2004) for emergency response to FMD in the MTM regions. The recommendation receives strong attention from the MTM Commission as whether to consider the implementation of the stamping-out policy. Messages from this study reinforce the insignificance of culling of infected animals in the southern regions of Thailand. The results also provide scientific justification for the DLD to avoid the

utilization of the slaughtering strategy. Although the model suggests that culling of infectious animals will not significantly reduce annual cumulative incidence of FMD, the suggestion is only valid for general implementation of stamping-out policy at a regional scale. Each FMD outbreak is a unique event which has to be dealt with on a case by case basis. There may be some circumstances where slaughtering of infected animals are highly recommended (Howard and Donnelly, 2000), for instance outbreaks in a totally naive population. It should also be reminded that there are other aspects of disease control that have to be factored in when making such a decision. Perhaps the most important factor is economical feasibility, in which it had to be economically advantageous to slaughter infectious animals. The model developed in this paper, unfortunately, does not address the economic consequences from the control program. Considerations should also be given to other factors, such as social and environmental impacts and animal welfare, which are essentially difficult to measure.

Because bounds exist on how much a given parameter can change in practice, achieving a goal of FMD free status may require changing parameters other than those included in the sensitivity analysis (or even changing parameters other than those included in this study). For example, reduction of lag time from detection of suspected cases until reporting to veterinary authorities (smaller γ) will speed up intervention processes and eventually reduce the magnitude of FMD outbreaks (smaller ACI). To achieve this objective, it may require good public awareness so that farmers/villagers are aware of possible signs of FMD infection, and effective communication between farmers, villagers, or local staffs and DLD veterinarians can be established. Increasing the awareness will also essentially reduce the likelihood of importing FMD infected animals

into the south. Surveillance for FMD will exert similar effects in reducing the ACI by reducing the value of γ . Together with highly sensitive screening tests, surveillance will also identify a percentage of unapparent infection, which provides a better reduction of γ .

3.5 Conclusion

This study shows that the epidemiological model and its surrounding concepts could be used as tools to investigate outbreak characteristics and related interventions aimed in controlling the outbreak magnitude. The results from the model suggest that improved FMD screening efficiency and vaccination may help reduce the annual number of FMD incidence, while exclusion of infectious animals is currently evitable. The model is a tangible aid for decision-makers to examine mitigation strategies and to prepare for outbreak events. It is, however, subject to a number of assumptions and parameter values based on best-guess estimations and experts' opinions, which need to be considered when interpreting the results. Attention should also be given to the issue of cost and other "immeasurable" factors (i.e. ethics and animal welfare) when the model is used.

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Chapter 4

Control of foot and mouth disease in Southern Thailand: uses of epidemiological risk modeling

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4.1 Introduction

Foot-and-mouth disease (FMD) belongs among the most feared infectious diseases in domesticated livestock because of its high contagiousness and infectiousness. FMD has profound effects on the health of animals and their productivities, and its occurrence results in international restrictions on animal trades which cause tremendous economic losses to the affected countries. Nearly all areas of Southeast Asia are suffering from FMD. To control and eradicate the disease from the region, the countries in Southeast Asia, with assistance from the Office of International des Epizooties (OIE),

have established the collaborative regional campaign, called Southeast Asia Foot and Mouth Disease Campaign (SEAFMD). Following the OIE/ASEAN Mid-Term Evaluation of the SEAFMD Campaign in 1999, the SEAFMD endorsed the concept of progressive zoning approach to progressively deal with FMD. The Malaysia-Thailand-Myanmar Peninsula Campaign for FMD Freedom (MTM) has been instituted to put this into practice. The campaign aims in establishing FMD-free areas with the collaborations from the three MTM countries (Edwards, 2004).

Certain interventions are deployed, aiming to prevent FMD introduction and to minimize possible consequences in the MTM areas. Currently employed interventions include taking livestock from areas known to be disease-free during a required period of time prior to the importation and utilizing quarantine procedures with or without laboratory testing. Once the imported livestock reach their destinations, attempts are made to limit contacts between imported and local livestock. The effectiveness of such interventions in relation to the reduction of FMD incidence, however, has been questionable as the outbreaks of FMD have been experienced despite all the efforts. Although the MTM campaign has received good collaborations and supports from the member countries, resources to deal with such the wide-spread and contagious disease as FMD are currently limited. It is of best interest to the MTM countries to allocate the resources to the areas where they are most needed and that the benefits are at the greatest.

A study by Wongsathapornchai (2006) identified that efficient management of livestock movement into Southern Thailand was important to the FMD control program in the MTM areas. In addition, Wongsathapornchai (2006) reinforced the significance of prevention of FMD introduction through livestock movement. Wongsathapornchai's

study indicated that prevention of FMD introduction was more important than dealing with the disease once it enters the areas. We proposed to examine different control programs, and the efficacies of such programs were then compared. The objective was to identify the optimal programs for controlling FMD in Southern Thailand using epidemiological risk modeling.

4.2 Materials and Methods

The methods began with the reviews of the FMD situation, control and prevention of FMD in Southern Thailand. The likelihood of FMD introduction was evaluated using risk assessment model described in Wongsathapornchai (2006). The consequences of such introduction were then assessed through the use of the compartmental modeling approach (Wongsathapornchai, 2006). Subsequently, this paper attempts to evaluate the baseline scenario and four eradication scenarios through the comparison of estimated FMD incidences from the respective scenarios.

4.2.1 Prevention and Control of FMD in Southern Thailand

Reviews for FMD situations in Southern Thailand are provided elsewhere (Wongsathapornchai, 2006; Black, 2004). In short, despite sporadic cases of FMD outbreaks, the southern region of Thailand, from Petchaburi province southward, has been declared as FMD free region by Department of Livestock Development (DLD) (Figure 4.1). Rationales for such declaration were the low prevalence of FMD as compared to other regions in the country, small-scale farming practices which limit the transmission of the disease, and most importantly geographical location of the region where movement of livestock is hypothetically controllable and the major flow can only

come from one direction. There were only a small number of FMD outbreaks reported in Southern Thailand each year until the recent changes in strains of FMD virus circulating within the region in 2003 (Linchongsubongkoch, 2003), resulting in dramatic increase in numbers of FMD outbreaks in the south.

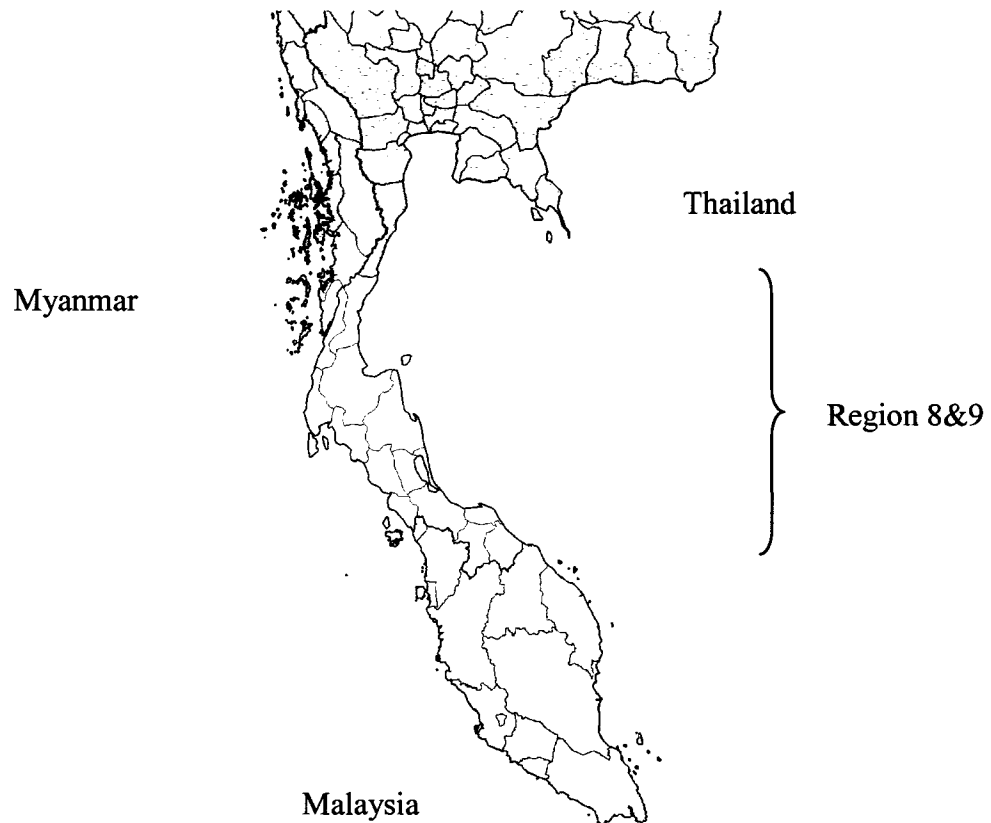


Figure 4.1: Southern Thailand (Region 8 & 9)

Movements of livestock from zones outside of the MTM into these zones in Thailand are complied with the following procedures outlined by the DLD. Movement permits issued by DLD veterinary officers must be adhered to all movements. Animals will be confined in an accredited quarantine station for the period of at least 21 days, and will be released only if the animals do not exhibit clinical symptoms of important contagious diseases, FMD in particular. At the quarantine station, first and second dose of the trivalent vaccines against FMD will be administered to the animal on the first and

14th day, respectively. Subsequently, the animals must be transported directly to an accredited private premise and will be quarantined for at least 3 days at the premise.

4.2.2 Risk Assessment Model

The methods to assess the likelihood of FMD introduction into Southern Thailand were described in details in the previous study conducted by Wongsathapornchai (2006). In short, the probability of infection in an incoming animal (i) was estimated as

$$i = \frac{p_A}{p_A + p_B}, \quad (1)$$

where p_A was the probability of the failure to noticed infected livestock during the quarantine; and p_B was the probability of a healthy livestock in a consignment.

4.2.3 FMD Transmission Model

A compartmental model was developed to capture transmission dynamics of FMD in Southern Thailand (Wongsathapornchai, 2006). The following set of differential equations was used for the model computations;

$$\begin{aligned} \frac{dS}{dt} &= -\frac{\beta SI}{N} - p\epsilon S - \nu S + \alpha R + \phi V \\ \frac{dL}{dt} &= \frac{\beta SI}{N} + i\pi - \delta L - \nu L \\ \frac{dI_{cli}}{dt} &= q\delta L - \gamma I_{cli} - \mu I_{cli} - \kappa I_{cli} - \nu I_{cli} \\ \frac{dI_{sub}}{dt} &= (1-q)\delta L - \gamma I_{sub} - \mu I_{sub} - \nu I_{sub} \\ \frac{dR}{dt} &= \gamma(I_{cli} + I_{sub}) - \alpha R - \nu R \\ \frac{dV}{dt} &= p\epsilon S + (1-i)\pi - \phi V - \nu V \end{aligned} \quad (2)$$

The model and its flow diagram were elaborated elsewhere (Wongsathapornchai, 2006). At each time step, an animal was classified into exactly one of the six disease

classes; susceptible (S), infected but not yet infectious (L), subclinically (I_{sub}) and clinically (I_{cli}) infectious, recovered (R), and vaccinated (V). Animals in the S class were those that were prone to infection with FMD. Once exposed to the FMDV, animals in the S class moved to L class. Though infected, animals in the L class were not yet able to spread the disease to other susceptible animals. The animals would stay in the L class for a defined period of time before they all progressed to the I class. The spread of the infection began when the animals were in the I class. Some animals in the I class did not exhibit observable signs of FMD infection (I_{sub}), while classical signs of FMD were visible in others (I_{cli}). Animals in I class were either severely suffered from infection and died from FMD or recovered from the disease and moved to R class. Animals in V class were those that were vaccinated; they were protected against FMD infection for a period of time and then resumed their susceptibility status. There were continual introduction of livestock into Southern Thailand from other regions. A proportion of the incoming livestock were latently infected with FMD, while others were required to receive vaccination before coming in. Livestock population in Southern Thailand was also decreased due to movement out of the areas and to deaths from other causes. The dynamics of livestock demography were also accounted for in the model.

Thirteen biological parameters were used in equation (2). The descriptions of the parameters are given in Appendix I. Probability distributions were assigned to the parameters to account for levels of uncertainty and variability in the parameter estimates.

4.2.4 Scenarios

Five scenarios were selected for this study. The rationale for the scenario selections included the availability of resources and the feasibility for field applications.

The baseline scenario was the one to which other scenarios were compared. The significant parameters, suggested from previous study (Wongsathapornchai, 2006), was manipulated so that its effects could be inspected. In Eradication Scenario (ES) I, the effects of an improved sensitivity of the screening process during animal quarantine were studied. Eradication Scenario II examined effects of vaccination for the FMD control and eradication programs. ES III and IV examined the consequences of the more modified strategies to eradicate FMD. The combined effects of vaccine and NSP test usages were inspected in ES III, with an addition of the modified stamping-out approach in ES IV. Of particular interest, the comparison between FMD incidences (qL) from each scenario was made. The assumptions for each scenario are explained in more details in the following sections.

4.2.4.1 Baseline Scenario

The baseline scenario was constructed based on the current knowledge of the biology and epidemiology of FMD and the movement regulations imposed on livestock intended for movement southward into Southern Thailand (see 2.1). The values of the model parameters were taken from the previous study (Wongsathapornchai, 2006). Vaccinations were carried out only in high risk areas and during an outbreak (ring vaccination). The transmission rate (β) was identified by comparing the outbreak data retrieved from DLD and SEAFMD to outbreaks estimated by the previous compartmental model (Wongsathapornchai, 2006). Certain parameters were allowed to vary to capture the levels of the uncertainties in their values, including the periods of latency ($1/\delta$) and infectiousness ($1/\gamma$). The probability of importing infectious animals (i) depended upon the ability to detect the disease during import processes ($1 - p_A$), where p_A was the probability of the failure to detect the infection. In the baseline scenario, p_A was based on

the detection of clinical appearances of FMD at a quarantine station. The sensitivity of clinical inspection of FMD signs (p_S) was estimated at 70% (minimum, 50%; maximum, 100%) (Wongsathapornchai, 2006) by the local experts. Under this baseline scenario, FMD control efforts were assumed to continue at this level for the next five years.

4.2.4.2 Eradication Scenario I: Uses of NSP-3ABC

As suggested from previous study (Wongsathapornchai, 2006), attempts were made to investigate the effects of improved sensitivity to detect FMD infected animals during movement processes. A logical use of the ELISA test for the detection of FMD non-structural protein (NSP) antibody was proposed in addition to the detection of clinical symptoms during quarantine. The study conducted by Linchongsubongkoch et al. (2004) indicated that, using NSP-3ABC test provided by World Reference Laboratory (WRL) (Pirbright, United Kingdom), 177 out of 180 disease positive cattle sera were tested positive and 0 out of 379 disease negative cattle sera were tested negative. From this information, the distribution of the sensitivity of NSP-3ABC (WRL) (p_{Se}) was estimated using

$$p_{Se} = \text{RiskBeta}(\text{test positive} + 1, \text{test negative} - \text{test positive} + 1). \quad (3)$$

Animals tested positive with NSP test would be excluded from the shipment or be destroyed. ES II then substituted the values of p_S with the values of p_{Se} in the model.

4.2.4.3 Eradication Scenario II: Effects of Mass Vaccination

Under the ES II, a change in vaccination policies was assumed. Mass vaccinations were carried out to achieve 80% coverage for all susceptible cattle and buffaloes in the southern region. The vaccinations were conducted at a pulse over a period of four weeks, so that the vaccination rate was at 2.9% (0.8/28) per day during the

vaccination pulse and 0% per day during the non-vaccination period. The vaccinations were performed twice yearly; the first and the second round of vaccinations were carried out in January and in July, respectively, of each year. The values for all other parameters in the model remained the same as in Baseline Scenario.

4.2.4.4 Eradication Scenario III: Combined Effects of NSP Test and Vaccine

ES III was constructed to investigate the combined effects of vaccines and NSP tests. A mass vaccination campaign similar to that of ES II was deployed, with improved diagnostic capabilities using the NSP test to identify infected animals before they were brought into the southern region. In this scenario, the vaccination rate was estimated at 0.029 animals per day and the sensitivity of the NSP (WRL) test was referenced at the level described in section 2.4.3. All other parameters in the model remained at their values as in the Baseline Scenario.

4.2.4.5 Eradication Scenario IV: Introduction of Modified Stamping-Out

The first four scenarios assumed that infectious animals were not removed from the population. This somehow assembled the field situation where there were attempts to treat infectious animals on premises. Culling of infected animals and/or immediate contacts (stamping-out) was identified as impractical to apply in this region (Wongsathapornchai, 2006) due to economical reasons. An attempt to introduce a modified strategy to deal with such a highly contagious disease as FMD was described in this ES IV. During the first and the second year, a strategy similar to ES III was applied. Vaccines and NSP test were introduced from year one to year five with their values similar to the values in ES III. From the third year onward, when incidence of FMD was supposedly decreased, modified stamping-out policy was introduced. It was assumed

that all clinically confirmed cases (I_{cli}) of FMD will be removed from the population within an average of 7 days after being identified as infected. The rate of loss of clinically ill animals due to the stamping-out measure was approximated at 0.14 (1/7) animals/day.

4.2.5 Simulation Steps

The model was simulated in a computer running Microsoft Excel[®] 2003 (Microsoft, Redmond, WA) with @Risk 4.0 (Palisade Corporation, Newfield, NY). The simulation contained 5,000 iterations using Latin Hypercube Sampling technique. The model was run on a daily-time step for the period of six years (2,190 days). The results from the first 365 days were ignored from the analysis. This one year “burn-in” process was relevant to assimilate the stable endemic condition of FMD in Southern Thailand (Wongsathapornchai, 2006). Only the results from day 366 to day 2,190 are presented here and are referred herein as year one to five accordingly. The estimated incidence of FMD—presented in the model as the calculated values for qL —was pivotal to the evaluation of the impact of the scenarios. Daily estimated incidences for each 365-day interval were summarized to obtain the estimated annual cumulative incidence (ACI) of FMD, which was used for comparison purpose in this study. For the studied scenarios, the estimated ACIs for the fifth-year simulation were statistically compared using Tukey's Studentized Range (HSD) Test. The statistical significance (alpha) was set at 0.01.

4.3 Results

The results from the simulation showed the estimates of the FMD daily and annual incidence for each studied scenario. For the sake of simplicity, the focus will be put primarily on the averages of these estimates. Average annual incidences of FMD from the studied scenarios were compared side-by-side in Table 4.1. Figure 4.2 illustrated the daily incidences of FMD for all five scenarios. Patterns of FMD incidences in the studied scenarios corresponded to the patterns of livestock movement presented in Appendix II, where the peak of the incidences were observed during the fourth quarter of a year. The peaks were more pronounced in the BS and ES II. The results showed that ES IV produced the smallest ACI as compared to the other scenarios.

	BS	ES I	ES II	ES III	ES IV
1 st Year	44,399	39,205	11,673	8,752	8,752
2 nd Year	33,692	22,866	5,223	1,287	1,287
3 rd Year	35,119	24,596	5,189	1,267	849
4 th Year	35,221	24,817	5,189	1,267	815
5 th Year	35,315	24,893	5,190	1,268	815

Table 4.1: Average annual cumulative incidence estimated from a simulation of 5,000 iterations for the Baseline Scenario (BS), Eradication Scenario I (ES I), Eradication Scenario II (ES II), Eradication Scenario III (ES III), and Eradication Scenario IV (ES IV).

4.3.1 Baseline Scenario

The simulation gave the average of the estimated ACI for the first year at 44,399 cases per year. The average ACI was slightly decreased and stable at approximately 35 thousand infected animals per year by the fifth year (Table 4.1). The underlying daily incidences were estimated at 90 cases per day; however, the average daily incidences

were more than two times as high (more than 160 FMD cases per day) during the peak seasons.

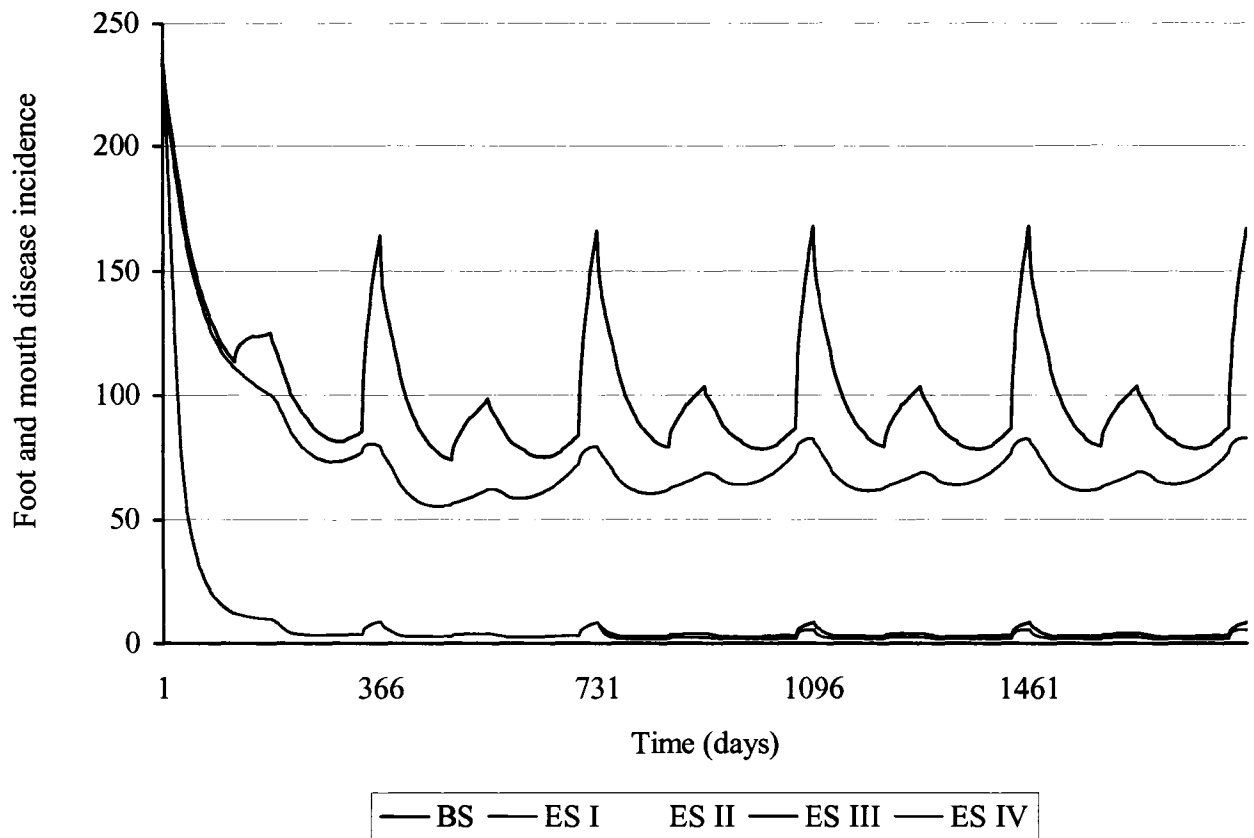


Figure 4.2: Estimated daily incidences of FMD in Southern Thailand over a five-year period for the Baseline Scenario (BS), Eradication Scenario I (ES I), Eradication Scenario II (ES II), Eradication Scenario III (ES III), and Eradication Scenario IV (ES IV).

4.3.2 Eradication Scenario I

The average ACI for the ES I was slightly decreased from the BS by an approximately 11% in the first year (39,205 cases per year) and 30% in the second year onward. The average ACI for the fifth year was estimated at 24,893 cases per year. Though less pronounced than what was observed in the BS, the peak of the incidences was still noticeable in the ES I.

4.3.3 Eradication Scenario II

The first year cumulative incidence was estimated to be 11,673 cases per year, which was more than a 70 percent reduction from the BS. The ACI was intensely decreased in the second year and became steady at approximately 5,190 cases per year from the third year onward. Figure 4.2 shows that the incidences were as high as 70 cases per day during the peak season, where the underlying incidence was calculated to be only 5 cases per day.

4.3.4 Eradication Scenario III

Under Eradication Scenario III, there was more than an 80 percent decrease in the incidence of FMD from the incidence seen in the BS when the combination of mass vaccination and NSP-3ABC tests was utilized. 8,752 cases of FMD were estimated to occur in the first year. Yet, the greater percentage of reduction was observed from the second year onward, where only 1,268 cases of FMD (more than 85% reduction from the first year and more than 96% reduction from the BS) was estimated to emerge yearly. Seasonal patterns of incidences were relatively less noticeable when the peak incidences flattened out.

4.3.5 Eradication Scenario IV

Eradication Scenario IV produced the smallest ACI compared to the other scenarios. The strategy used in the first and the second year in the ES IV was the same as in the ES III; thus, similar patterns were also seen. The modified stamping-out policy was introduced into the ES IV from the third year forward, which resulted in approximately a 36% reduction in the ACI from the previous year (from 1,287 cases per

year in the second year to 815 cases per year by the fifth year). The difference between the underlying and the peak incidences was not so distinct. The underlying incidence was estimated at 3 cases per day, and the peak incidences were about 8 cases per day.

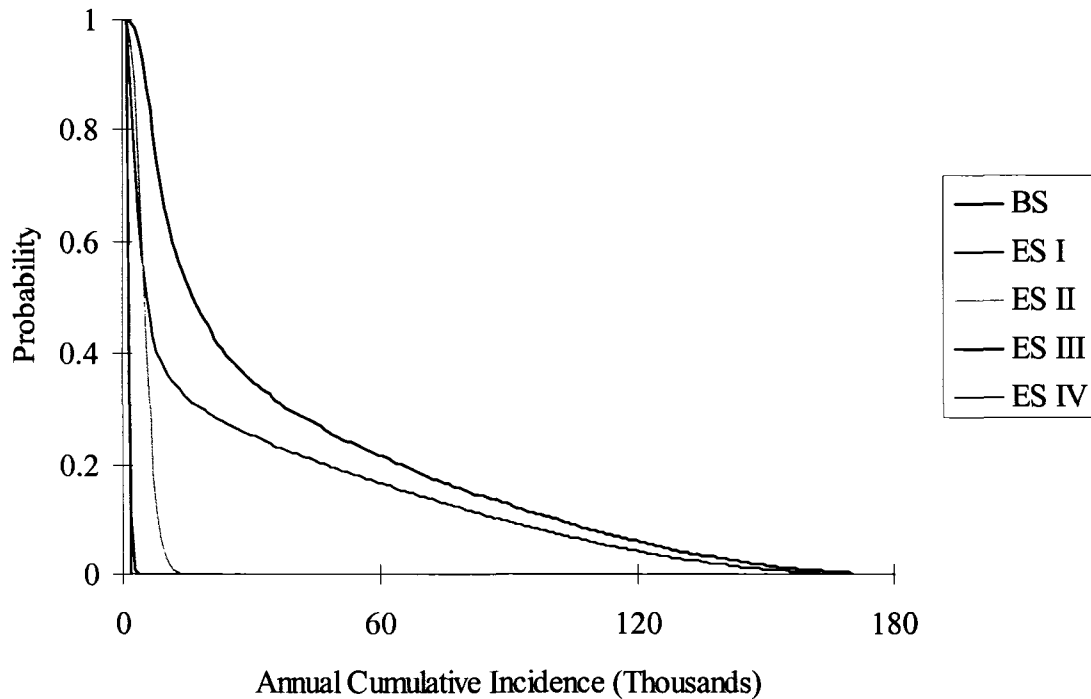


Figure 4.3: Descending cumulative probability distribution of the estimated annual cumulative incidences for the 5th year of the simulation, scenarios comparison

Scenario	Tukey Grouping	Average 5 th -year ACI
Baseline	A	35,315
ES I	B	24,893
ES II	C	5,190
ES III	D	1,268
ES IV	D	815

Table 4.2: Comparison of the average ACIs for the fifth year simulations based on Tukey's Studentized Range (HSD) Test ($\alpha = 0.01$)

Table 4.2 shows results from the application of Tukey's Studentized Range (HSD) Test in comparing the average ACIs for the fifth-year simulations. Means with the different letters are significantly different at the one percent level of significance. In summary, the fifth-year ACIs from BS, ES I, and ES II were all statistically different from the other scenarios. The estimated fifth-year ACIs from ES III and ES IV were significantly different from the BS, ES I, and ES II. However, the difference between the fifth-year ACI estimated from ES III and ES IV did not appear to be significant.

4.4 Discussion

This study shows the potential for the integrated use of modeling approaches in decision making processes related to control of animal diseases, FMD in particular. The complex systems of livestock movement and transmission of FMD in Southern Thailand are partially explicated and simplified. The control efforts begin from reducing the likelihood of new introduction of infectious animals to limiting the probability of exposure of those infectious animals to other susceptible species in the areas.

Use of vaccines has always been the main point of discussions. Southern Thailand had employed a mass vaccination strategy until the policy was changed during the last seven years to only vaccinate animals in the high risk areas. Due to dramatic increases in the FMD incidences after the cessation, the concept of mass vaccination is again brought up. The topic is currently controversial. On one side, the vaccination is believed to bring down the total number of FMD affected livestock. On the other side, the reintroduction of mass vaccination after seven years of its termination is unquestionably viewed as a regression of the process toward FMD-free areas in the south because of problems with

vaccine itself (Brownlie, 2001; Mason and Grubman, 2001; Barnett et al., 2002; Grubman and Mason, 2002). This study showed that mass vaccination (at 80% coverage) would radically decrease the ACI by more than 85%. Yet, this study did not signify whether to consider the use of mass vaccination because the effectiveness of the vaccination depends largely upon several important factors, the efficacy of the vaccines and the efficiency of the vaccine delivery systems, for instance. In this study, the efficacy of vaccine may be scrutinized as an overestimated value (at 93%). Nevertheless, the result from the study by Wongsathapornchai (2006) demonstrates that the FMD epidemiological model is quite robust to the change in vaccine efficacy even when the proportion of animals becoming immuned after vaccination is allowed to vary from 70% to 100%.

While the price of livestock is still a dominating determinant of livestock movement for domestic consumption in Southern Thailand, it is still not feasible to import only livestock from FMD free areas. Importing livestock from FMD endemic area, thus, poses a challenging task to the livestock officials in trying to minimize the probability of the introduction of the infection. The ideal strategy is the one that has the greatest impact on the probability of the introduction of the infection, where the cost is kept at the minimum and the trader's cooperation is still maintained. Most of all, it has to be practical to apply in the field by local officers. There were discussions among DLD officials to introduce the NSP-3ABC tests during the quarantine processes as an addition to the physical examination, hence, reducing the likelihood of the new introduction of the infection. Wongsathapornchai (2006) proved that the use of NSP-3ABC test yielded the highest negative correlation with the probability of the infection among incoming

livestock. Hypothetically, the deployment of the test shall result in a major reduction of FMD infection in the region. In fact, only 30% reduction—smallest among all studied scenarios—from the BS was estimated. The possible explanation for this surprising result is that the great impact of the improved sensitivity of the screening process is only relevant at a certain level of the sensitivity. The change of the sensitivity at a sufficiently high to an even higher level, i.e. changing from using physical examination to NSP-3ABC test, will not dramatically alter the estimated ACI. In this study, approximately 30% change in the sensitivity logically lead to about 30% change in the ACI, which is still very damaging in an epidemiological point of view. This result suggests that alternative strategies shall be considered in the addition to the test.

As expected, collaborative use of multiple control techniques is the most effective strategy to reduce the ACI. More than 96% reduction (from the BS) in ACI is expected when the NSP test and vaccine are used collaboratively. Even greater reduction in ACI is seen when the modified stamping-out is strategically appended. From Figure 4.2, it is logical to assume that the use of the NSP test decrease the ACI by the reduction of the FMD incidence during the peak period, while the vaccine has the major contribution to the reduction of underlying incidences of FMD. This conclusion, however, need to be further studied.

Like most studies, the model described in this paper is subject to the degrees of limitations and assumptions (Wongsathapornchai, 2006). Many parameters used in the model, for example, are derived from the best estimates from experts in the field. Sensitivity of the model to the parameters is addressed elsewhere (Wongsathapornchai, 2006). The uncertainties and variability of the model parameters are also accounted for

when the distributions are used instead of fixed estimates. In addition, the accuracy of the estimation is not of major importance to this study, where the main objective is to compare the effects of different control and prevention approaches.

4.5 Conclusion

The result from this study suggests that the vaccine strategy is necessary for the control of FMD in Southern Thailand at the moment. A strategic use of NSP test to screen infectious animals, thereby reduce the probability of FMD introduction, is also crucial. More importantly, the best mitigation is a collaborative use of multiple techniques to further reduce the incidence of FMD in the MTM.

This study importantly reveals the applications of the model in epidemiology and risk assessment to aid in the decision making processes, especially pertaining to control of FMD in Southern Thailand. Though the model is subject to certain limitations and needs some minor refinements, its current applications are demonstrated to be of a great value to the FMD control campaign in Thailand. The model assists in answering some vital questions that potentially lead to eradication of FMD from the region, i.e. the impacts of the screening test and vaccine to the incidences of FMD. There are certainly other strategic approaches to control FMD that have not been discussed in this paper. Nevertheless, the impacts of such approaches, in relation to the five scenarios discussed here, to FMD incidences must be further studied. Fortunately, such studies are made possible given the flexibility of the model.

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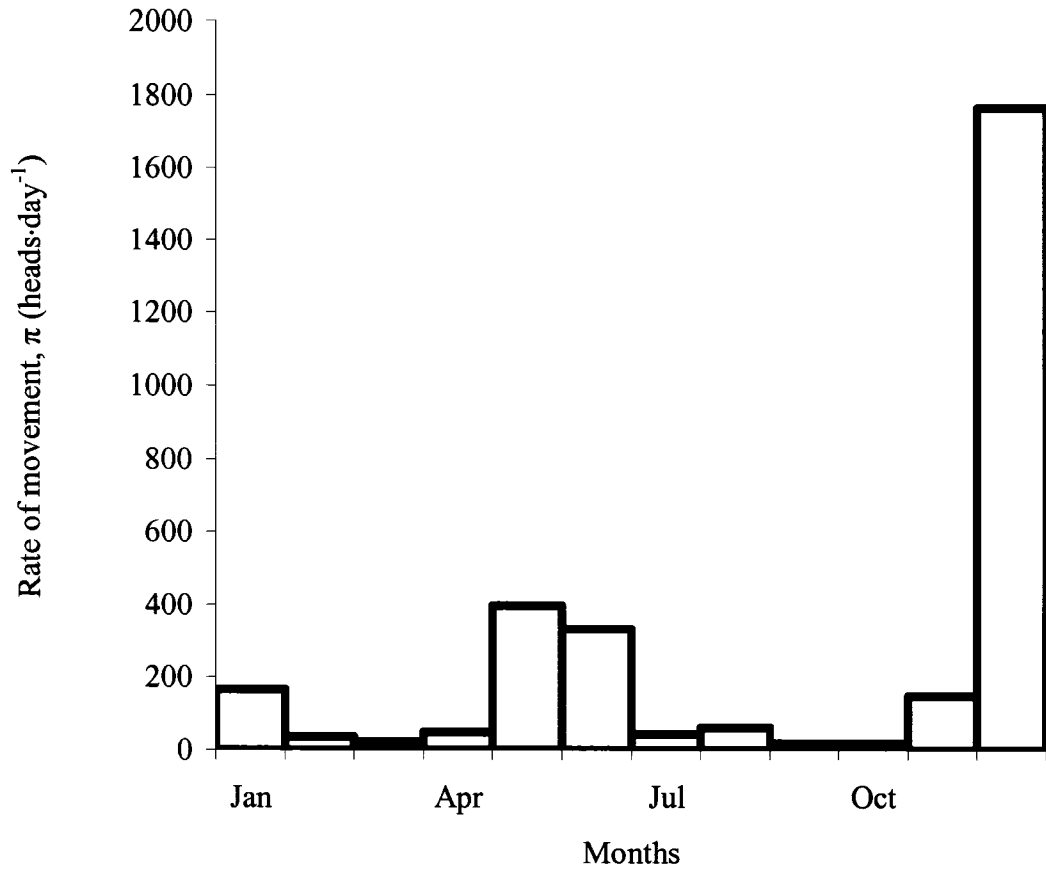
Appendix I: Definitions, values and distribution for the model input parameters in an estimation of annual cumulative incidence (ACI) for the studied scenarios

Parameter	Definitions	Value				
		BS	ES I	ES II	ES III	ES IV
β	Transmission parameter	0.115	0.115	0.115	0.115	0.115
$1/\delta$	Duration of latent infection	Pert(2,3,14)	Pert(2,3,14)	Pert(2,3,14)	Pert(2,3,14)	Pert(2,3,14)
$1/\gamma$	Infectious period	Pert(2,10,14)	Pert(2,10,14)	Pert(2,10,14)	Pert(2,10,14)	Pert(2,10,14)
θ	Rate of decay of immunity from vaccination	0.0038	0.0038	0.0038	0.0038	0.0038
α	Rate of decay of immunity from natural infection	0.0038	0.0038	0.0038	0.0038	0.0038
ε	Rate of vaccination	0.003	0.003	0.029	0.029	0.029
μ	Loss of animals due to disease	0.00003	0.00003	0.00003	0.00003	0.00003
ν	Loss of animals due to other causes	0.00041	0.00041	0.00041	0.00041	0.00041
κ	Loss of clinically infected animals due to control measures	0	0	0	0	0.14
π	Rate of movement	See Appendix II				
i	Probability of incoming animals having FMD	*	#	*	#	#
q	Probability of having clinical appearance	0.7	0.7	0.7	0.7	0.7
p	Proportion of animals becoming immuned after vaccination	0.934	0.934	0.934	0.934	0.934

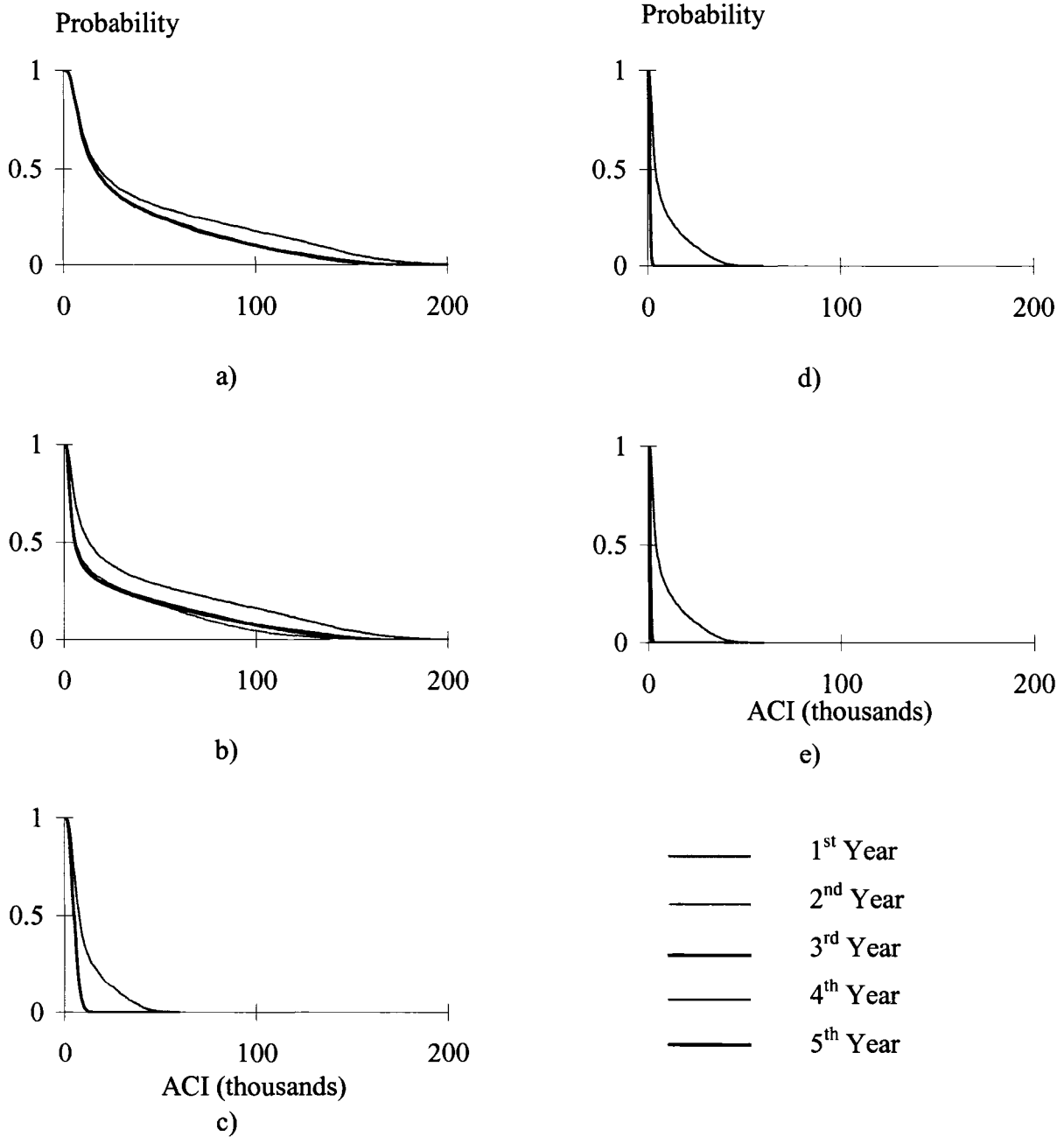
* See Wongsathapornchai (2006), where p_S was given as Pert(0.5,0.7,1)

See Wongsathapornchai (2006), where p_S was given as RiskBeta(178,4)

Appendix II: Patterns of monthly movement of cattle and buffaloes into Southern Thailand in 2003.



Appendix III: Descending cumulative probability of the annual cumulative incidences (ACI) of FMD in five years in Southern Thailand using control strategies as explained in the a) Baseline Scenario, b) Eradication Scenario I, c) Eradication Scenario II, d) Eradication Scenario III, and e) Eradication Scenario IV.



Chapter 5

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5.2 List of Abbreviations

AIDS	Acquired immunodeficiency syndrome
ASEAN	Association of Southeast Asian Nations
BSE	Bovine spongiform encephalopathy
BVD	Bovine viral diarrhoea
BZ	Buffer Zone
CZ	Control Zone
DCD	Disease Control Division (Thailand)
DCs	Dangerous contacts
DLD	Department of Livestock Development (Thailand)
DVS	Department of Veterinary Services (Malaysia)
ELISA	Enzyme-linked immunosorbent assay
EZ	Eradication Zone
FMD	Foot-and-mouth disease
FMDV	Foot-and-mouth disease virus
FZ	Free Zone
HIV	Human immunodeficiency virus
Ig	Immunoglobulin
IPs	Infected premises
IZ	Infected Zone
LBVD	Livestock Breeding and Veterinary Department (Myanmar)
MAP	Mass action principle
MTM	Malaysia–Thailand–Myanmar
NSP	Non Structural Protein
OIE	Office International des Epizooties
OP	Oesophageal–pharyngeal sample
R _a	Effective reproductive ratio

RCU	Regional Coordination Unit
R_0	Basic reproductive ratio
SARS	Severe acute respiratory syndrome
SDRs	Standard Definitions and Rules
Se	Sensitivity
SEAFMD	South East Asia Foot and Mouth Disease
Sp	Specificity
TCID ₅₀	Fifty percent tissue culture infective dose
UK	United Kingdom
US	United States
WRL	World reference laboratory for Foot and Mouth Disease

5.3 Appendices

5.3.1 Appendix I: Illustration of the calculation steps for the **regional** sero-survey using NSP-3B (UBI)

	B	C	D	E	F	G
1						
2	Within region prevalence calculation					
3	Test sensitivity		88.89%			
4	Region	Livestock tested	Positives S_i	Number missed M_i	Total infected	Prevalence P_i
5	1	480	12	4	16	3.64%
6	2	476	3	0	3	0.95%
7	3	480	39	3	42	9.98%
8	4	477	23	3	26	4.47%
9	5	480	32	4	36	7.30%
10	6	360	23	2	25	10.04%
11	7	479	35	3	38	7.90%
12	Within region prevalence estimate			0.95%		
13						

Cell D3 - The sensitivity for the ELISA test for NSP-3B (UBI) was acknowledged from previous study and was fixed at 0.8889

Cell C5:C11 - Total number of cattle tested with NSP-3B ELISA from each region (corresponding with the regions in cell B5:B11)

Cell D5:D11 - Number of test-positive sera

Cell E5:E11 - Number of positive sera that were not picked up by the test (false negative). The values were calculated using the negative binomial distribution and the probability mass function was expressed as;

$$f(x) = \binom{s+x-1}{x} p^s (1-p)^x, \text{ where}$$

s = number of success

p = probability of success.

The values could also be calculated from the Excel[®] formula;

$$=RiskNegbin(Si + 1, test\ sensitivity)$$

Cell F5:F11 - Total number of infection in the tested livestock (= $S_i + M_i$)

Cell G5:G11 - The probability of infected livestock (prevalence, P_i). P_i was calculated using the beta distribution and the probability density function was expressed as;

$$f(x) = \frac{x^{\alpha_1-1}(1-x)^{\alpha_2-1}}{\int_0^1 t^{\alpha_1-1}(1-t)^{\alpha_2-1} dt}, \text{ where}$$

α_1 and α_2 is a continuous shape parameter and $\alpha_1 > 0, \alpha_2 > 0$

P_i could also be calculated from the Excel® formula;

$$=RiskBeta(Total\ infected + 1, Livestock\ tested - Total\ infected + 1)$$

Cell E12 - The regional sero-prevalence of FMD. This was estimated using discrete distribution, weighed by number of livestock tested from the region, as expressed in the following Excel® formula.

$$=RiskDiscrete(G5:G11, C5:C11)$$

5.3.2 Appendix II: Evaluation of the NSP-3ABC (Bommeli) test validity

	B	C	D	E	F	G	H	I
1								
2	Test validation for NSP-3ABC (Bomm)							
3					Disease			
4					+	-	Total	
5		Test	+		160		1	161
6			-		20		99	119
7			Total		180		100	280
8								
9				Sensitivity	88.09%			
10				Specificity	99.11%			
11								

Cell F9 – Test sensitivity (*Se*). *Se* was estimated using beta distribution. For brevity, we used the following Excel[®] function to simplify the calculation;

$$Se = RiskBeta(true\ positive + 1, false\ negative + 1), \text{ or}$$

$$Se = RiskBeta(F5 + 1, F7 - F5 + 1)$$

Cell F10 – Test specificity (*Sp*). *Sp* was estimated using beta distribution. For brevity, we used the following Excel function to simplify the calculation;

$$Sp = RiskBeta(true\ negative + 1, false\ positive + 1), \text{ or}$$

$$Sp = RiskBeta(G6 + 1, G7 - G6 + 1)$$

5.3.3 Appendix III: Illustration of the calculation steps for the **consignment** sero-survey using NSP-3ABC (Bommeli)

Cell F31 - Number of consignments, which contain at least one positive animal, that were tested negative by the test (false negative). The values were calculated using the negative binomial distribution and the probability mass function was expressed as;

$$f(x) = \left(\frac{s+x-1}{x} \right) p^s (1-p)^x, \text{ where}$$

s = number of success

p = probability of success.

The values could also be calculated from the Excel[®] formula;

$$=RiskNegbin(Positive\ consignment + 1, Se), \text{ where}$$

Se = Test sensitivity, which was estimated in Appendix II

	B	C	D	E	F	G	H	I
28	Between consignment prevalence							
29	Consignment tested				57			
30	Consignment positive				28			
31	Positive missed				3			
32	Total infected				31			
33	Estimated consignment prevalence				43.29%			
34								
35	Test sensitivity			90%				
36								
37	Within consignment prevalence							
38	Consignment number	Number submitted	Positive	Negative	Positive missed	Total infected	Estimated prevalence	
39	001	11	1	10	0	1	39.49%	
40	002	20	4	16	0	4	15.51%	
41	003	20	7	13	2	9	33.28%	
42	005	10	2	8	0	2	20.93%	
43	006	30	7	23	2	9	25.26%	
44	007	12	3	9	1	4	26.82%	
45	008	7	3	4	0	3	46.27%	
46	009	13	5	8	2	7	83.47%	
47	017	20	2	18	0	2	11.64%	
48	018	10	2	8	0	2	34.70%	
49	021	20	3	17	0	3	23.21%	
50	022	9	2	7	0	2	55.75%	
51	025	5	1	4	0	1	16.22%	
52	026	20	4	16	0	4	26.64%	
53	028	100	9	91	1	10	13.63%	
54	032	10	2	8	3	5	46.77%	
55	033	10	2	8	0	2	28.68%	
56	036	20	3	17	0	3	20.14%	
57	037	5	1	4	0	1	22.67%	
58	038	10	2	8	0	2	33.89%	
59	039	10	1	9	0	1	15.18%	
60	040	10	1	9	0	1	17.14%	
61	041	10	1	9	0	1	18.94%	
62	042	10	2	8	0	2	53.32%	
63	043	10	4	6	0	4	19.71%	
64	047	6	1	5	0	1	5.53%	
65	053	42	2	40	0	2	5.75%	
66	127	100	6	94	0	6	6.15%	
67								
68	Estimated within consignment prevalence				15.51%			
69								
70	Estimated prevalence of imported animals				6.71%			
71								

Cell F32 - Total number of infected consignments (= F30+ F31). The infected consignment was defined as the consignment which contains at least one infected livestock

Cell F33 - The probability of infected consignment (between-consignment prevalence, *BCP*). *BCP* was calculated using the beta distribution and the probability density function was expressed as;

$$f(x) = \frac{x^{\alpha_1-1}(1-x)^{\alpha_2-1}}{\int_0^1 t^{\alpha_1-1}(1-t)^{\alpha_2-1} dt}, \text{ where}$$

α_1 and α_2 is a continuous shape parameter and $\alpha_1 > 0, \alpha_2 > 0$

BCP could also be calculated from the Excel® formula;

$$=RiskBeta(infected consignment + 1, non-infected consignment + 1)$$

Cell H39:H66 - Similar strategies as explained in Appendix I were employed to estimate the prevalence of FMD within each consignment (*WCP*) that had samples submitted to the laboratory and had at least one animal confirmed as FMD-infected. First, numbers of false negative samples were estimated using the negative binomial distribution to get the total number of animal supposedly infected with FMD. Second, we used the discrete distribution to average the *WCP* for the infected consignment, weighed by the number of sample submitted to the laboratory from each consignment.

Cell F70 – Overall consignment prevalence (*OCP*) was calculated from the intersection of the two independent events ($P(A \cap B) = P(A)P(B)$);

$$OCP = F33 \times F68$$

5.3.4 Appendix IV: Origin and annual movement of cattle and buffaloes into Southern Thailand in 2003

	B	C	D
14	Estimated number of infected livestock being import		
15	Total import in 2003		89,491
	Import from Region	Number of import	Percent of import
16			
17		1	1,897
18		2	1,602
19		3	2,890
20		4	16,305
21		5	5,002
22		6	29,835
23		7	31,960
24			

5.3.5 Appendix V: The summary of the probability of FMD infection in different stages of importation

	B	C	D	E	F
71					
72	Inspection at quarantine				
73	Prob of showing clinical symptoms			78.14%	
74					
		Prob of livestock infected in a consignment	Prob of infection detected at quarantine	Prob of livestock infected and not detected at quarantine	prob of accepted livestock contains FMD
75					
76	RS	8.96%	7.00%	1.96%	2.11%
77	CS	12.21%	9.54%	2.67%	2.95%
78					

The following paragraphs showed the Excel[®] functions used to derive the values for the respective cells.

F33 = *RiskPert(0.5,0.7,1)*, an expert estimate for the probability of the apparent form of infection

For the regional sero-survey;

See Appendix I

$$\text{Cell C76} = \text{RiskDiscrete}(\text{G5:G11}, \text{C17:C23})$$

$$\text{Cell D76} = \text{C76} \times \text{F73}$$

See Appendix IV

$$\text{Cell E76} = (\text{C76} \times (1 - \text{F73}))$$

$$\text{Cell F76} = \text{E76} / (\text{E76} + (1 - \text{C76}))$$

For the consignment sero-survey;

$$\text{Cell C77} = \text{F70} \text{ (see Appendix III)}$$

$$\text{Cell D77} = \text{C77} \times \text{F73}$$

$$\text{Cell E77} = (\text{C77} \times (1 - \text{F73}))$$

$$\text{Cell F77} = \text{E77} / (\text{E77} + (1 - \text{F73}) + (\text{F73} \times (1 - \text{F68})))$$