A RISK ASSESSMENT FOR THE EXPORT OF FRESH BEEF PRODUCTS AFTER AN OUTBREAK OF FOOT AND MOUTH DISEASE IN THE FREE ZONE OF SOUTH AFRICA

by

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ABSTRACT

Foot-and-mouth disease has been recognised as one of the most important diseases constraining international trade in animals and animal products. Economic losses due to reduced exports as well as additional costs of implementation of control measures associated with FMD outbreaks in South Africa have been reported. In order to participate in the international market, countries with FMD endemic areas including South Africa must demonstrate that the likelihood of FMD in fresh beef products is negligible. However, the quantitative risk of FMD virus survival in beef and beef products destined for export from the FMD free zone in South Africa has not been done. This study aims to assess the probability of FMD virus surviving in fresh beef products after implementation of the risk reduction measures at different steps along a beef value chain using quantitative risk assessment stochastic modelling.

A quantitative risk assessment was conducted throughout the beef value chain using data from previously published studies in Science Direct, Google Scholar, Web of Science, and PubMed. In addition, an expert opinion questionnaire survey was used to collect additional data on the likelihood of FMD in South Africa. A scenario tree was developed and equations for input variables were created. A probability distribution using A Monte Carlo simulation with 100 000 iterations to model the probability of occurrence of the FMD virus at each node. The overall likelihood of FMD virus contamination of fresh beef products was calculated by adding the probabilities at farm, feedlot and abattoir. A sensitivity analysis was used to determine inputs in the value chain that are correlated with the overall FMD likelihood in fresh beef products using correlation coefficients. A correlation coefficient is the quantification of a statistical relationship between two variables. In addition, the impact of changes in the initial prevalence of FMD in the country and the likelihood of an animal been asymptomatic on the overall FMD likelihood in fresh beef products were also assessed.

The overall probability of FMD virus contaminating fresh beef products was negligible (2.1×10^{-9}). The probability of FMD virus circulation in the country (correlation coefficient (r) =0.72)

and the inability to diagnose asymptomatic cattle (*r*=0.59) were strongly correlated with the probability of FMD virus in fresh beef products. Weak correlations were observed between FMD transmission rate (r=0.17), antemortem, inspection (r=0.9), post-mortem inspection (r=0.09) and the probability of FMD virus in fresh beef products. When the initial probability was increased to 3.4×10^{-2}, the likelihood increased to 1.6×10^{-4} .Similarly, increasing the probability of not detecting asymptomatic animal to 0.6 increased the probability of FMD virus in fresh beef products to 5.2×10^{-9}.

The likelihood of FMD virus in fresh beef products destined for export from the FMDV free zone was negligible. The initial prevalence of FMD in the country and the asymptomatic status of FMD infected cattle were strongly associated with the probability of the presence of FMD virus in fresh beef products intended for export from the FMD free zone. Therefore, it is important for regulators and farmers to ENSURE that FMD free status is always maintained and that control measures at farms and abattoirs such as biosecurity, vaccination, passive surveillance, and processing must continue in order to maintain the disease-free status of the FMDV free zone. The addition of active surveillance in the FMD free zone could potentially further decrease the likelihood of FMD survival in fresh beef products.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

FMD	Foot-and-mouth-disease
OIE	World organisation for animal health
PEO	Provincial executive officer
NSP	Non-structural proteins
DAFF	Department of Agriculture, Forestry and Fisheries
WTO	World trade organisation
RNA	Ribonucleic acid
SAT	South African territories
r	correlation coefficient
CBT	Commodity Based Trade

CHAPTER 1

1.1 Introduction

Beef and beef products are a source of income for farmers and feedlot owners in South Africa and these products are sold locally and internationally. Therefore, considerable effort is devoted to enabling South Africa to gain equitable access to commodity markets as a mechanism for poverty alleviation (Thomson *et al.*, 2006)(However, Foot-and-mouth disease (FMD) remains an important trade barrier to international markets for trade in animals and animal products (World Organisation for Animal Health, 2017a).

Foot-and-mouth disease is a livestock disease that affects cloven-hooved animals including cattle, goats, sheep, pigs, impala, giraffe, and water buffalo (Garner, East, Kompas, Ha, Roche & Nguyen, 2016; World Organisation for Animal Health, 2012). The causative agent is a single-stranded RNA virus of the genus *Aphthovirus* in the family *Picornaviridae*. Three serotypes of FMD virus have been isolated in South Africa: South African Territories SAT 1, SAT 2 and SAT 3 (Brown, 2003; Longjam, Deb, Sarmah, Tayo, Awachat & Saxena, 2011). Other serotypes that have been reported in other countries including Serotype O, in France and serotype A in Germany (Knowles, 1990). Subsequently, in 2011, serotype C was identified as a new serotype in Germany (Longjam *et al.*, 2011).

Certain areas within South Africa are considered free from FMD without vaccination by the OIE based on the zoning system (World Organisation for Animal Health, 2017b). However, during an outbreak in the FMD free zone, the FMD free status of South Africa is revoked. This results in a substantial loss of income for the farmers and investors, affecting the country’s gross domestic income (Martínez-López, Perez, De la Torre & Rodriguez, 2008). In order to maintain the FMD free status, the South African government manages the risk of FMD outbreaks by implementing active vaccination, biosecurity-surveillance, traceability systems, and animal movement control (Penrith, Cassidy, Osofsky, Atkinson, Thomson & Atkinson, 2013). Additional mitigations such as primary and secondary beef inspections, maturation of the carcass for 24 hours at 2 °C, testing the pH of the longissimus dorsi muscle and removal of lymph nodes are implemented at the abattoir to further reduce the risk of FMD virus in beef commodities (Department of Animal and Plant inspection services et al 2013):

1.2 Justification

Studies have shown that risk management through implementation of mitigations throughout the beef value chain can reduce the likelihood of contamination of fresh beef products with the FMD virus to negligible levels (Astudillo, Sutmoller, Saraiva & López, 1997). Measures such as compartmentalization and commodity-based trade could facilitate the trade of fresh beef and beef products in countries where the disease is endemic provided that risk mitigation measures prescribed in the OIE terrestrial code have been implemented throughout the beef value chain and the risk of the disease been quantified (Astudillo *et al.*, 1997). In South Africa, limited research has been conducted to assess the likelihood of FMD virus contamination of fresh beef products destined for export from the FMD free zone. In addition, no studies have been done to assess factors throughout the food value chain associated with the probability of FMD virus contamination in fresh beef products.

1.3 Aim

This study aims to quantify the probability of FMD virus contamination in fresh beef products in the FMD free zone after implementation of the risk reduction steps along a beef value chain.

1.4 Objectives

1. To describe a beef value chain in the FMD free zone of South Africa

2. To investigate the probability of exporting FMD virus contaminated fresh beef products from the free zone, South Africa
3. To investigate mitigation procedures of fresh beef products from the free zone.

1.5 Research Benefits

This research will contribute to the development of the Veterinary Procedural Notice (VPN) for registration and maintenance of cattle units for export of animal products (split system). In addition, information from this study will be used to develop guidelines for management and control of FMD virus in the FMD free zone and contribute towards the discussion of the possibility of commodity-based trading in African conditions.

1.6 Ethics Approval

This study has been approved by the University of Pretoria, Faculty of Veterinary Science's Animal Ethics Committee EC043-15.

1.7 Dissertation Structure

This dissertation is divided into Chapter 1: Introduction, Chapter 2: Literature review, Chapter 3: Materials and methods, Chapter 4: Results, Chapter 5: Discussions, Chapter 6: Conclusions Chapter 7: References, Addendum and Questionnaires

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CHAPTER 2

2.1 Literature Review

2.2 Background

The World Trade Organisation (WTO) has elected the OIE as the organisation that is responsible for developing standards and guidelines for the safe international trade of animal and animal products. These standards are contained in the Terrestrial Animal Health Code (TAHC) and pertain mainly to animal health standards and the prevention of the spread of animal diseases (Astudillo et al., 1997; Thomson et al., 2013). Foot-and-mouth disease (FMD) is one of the six diseases for which the OIE have developed guidance and policy for management of these diseases for harmonization of international trade. The OIE has also developed procedures for the official recognition of the FMD free status of its member countries (World Organisation for Animal Health, 2017a). In addition, these procedures ensure that countries without FMD free status can acquire FMD free status and are able to participate in international trade. Countries free of FMD can introduce several measures to avoid FMD outbreaks and loss OIE FMD free status. These include movement control, vaccination, and creation of protection zones (World Organisation for Animal Health, 2017a). The OIE is tasked to develop and promote international trade standards and guidelines among member countries to prevent the spread of disease to countries or zones that have currently claimed freedom of disease. While the Codex Alimentarius Commission is responsible for developing food safety standards relating to agricultural products including those from FMD infected areas (Joubert, 2014; Paton, D J; Sinclair, M; Rodriguez, 2009). Although the standards set out by the Codex Alimentarius and the OIE address different issues in terms of FMD control, the two are complementary with respect to setting standards for the international trade food commodities derived from animals.

Foot and mouth disease cause high morbidity and production losses in both commercial and small-scale farmers (Knight-Jones, McLaws & Rushton, 2017). The direct impact of FMD includes reduced fertility, reduced milk and meat production, reduced livestock growth rates, low body condition, loss of draught power and increased in a number of abortion cases. Foot and mouth disease infected bulls and cows sold at salvage received 83% and 88% less than the market value, amounting to an annual loss of up to $1,553 in Uganda (Baluka, Mugisha & Ocaido, in press). In Taiwan, $1.6 billion loss was associated with FMD outbreaks. While losses of between $1.5–10 billion in Australia and $14 billion in the United States have been reported (Ward, Laffan & Highfield, 2007). In 2001, the United Kingdom FMD outbreak was estimated to have cost the country over $6.58 billion. In Zambia, the financial impacts have been estimated at $1.6 billion from the loss of beef and sable antelope exports and an annual cost of over $2.7 million on preventive measures (Sinkala, Simuunza, Pfeiffer, Munang'Andu, Mulumba, Kasanga, Muma & Mweene, 2014). Therefore, FMD free countries spend enormous amounts of money to regain FMD free status after outbreaks have occurred by investing resources into the inspection of animal products at borders, maintaining a strong veterinary infrastructure, and surveillance (Ahmad, Tameru, Nganwa, Ayanwale, Habtemariam & Fite, 2013; Knight-Jones & Rushton, 2013).

2.3 Zoning, compartmentalisation, and commodity-based trade

In order to participate in the international market, the country must demonstrate that the risk of FMD in beef and beef products is negligible ($P<0.01$)(Martínez-López *et al.*, 2008; Rich, Perry and Kaitibie, 2009; Marcos and Perez, 2019) . The creation of FMD free zones in countries in which the disease is endemic has the potential to open access to high-value beef markets for producers including small -scale farmers. Moreover, it is difficult for the majority of southern African countries to declare freedom due to the presence of African buffalo, which are reservoirs for the Southern African Territories (SAT) serotypes of the FMD virus. In addition, compliance with Codex and TAHC in these countries is hampered by insufficient infrastructure, technology, and finances (Thomson et al., 2013). Australia, Central and North America, Europe, and South America countries have managed to control the FMD but remain under constant threat for future outbreaks (Rweyemamu, Roeder, MacKay, Sumption, Brownlie, Leforban, Valarcher, Knowles & Saraiva, 2008). Therefore, demonstrating a liklihood of FMD in the exporting country is important to access these markets as negligible.

2.3.1 Zoning

The OIE described three zones with clearly defined geographical area namely: Infected zone, in which FMD is endemic due to the presence of FMD infected wildlife; the protection zone which is further divided into a zone with vaccination in which geographical areas are adjacent to the infected zones and the zone without vaccination which is adjacent to the FMD free zone. The last zone is FMD free zone without vaccination, this is a zone without FMD where all OIE terrestrial code requirements have been demonstrated. The inspection area of the FMD free zone is an area adjacent to the protection zone where continuous FMD surveillance occurs (Department of Agriculture Forestry and Fisheries, 2012a).

Candidate countries seeking recognition of FMD free zone from must have a record of the following: regular and prompt animal disease reporting; a declaration to the OIE that within the proposed FMD free zone without vaccination, there has been no outbreak of FMD for the past 12 months; there is no evidence of FMD virus circulation found during the previous 12 months and no vaccination has been carried out or vaccinated animals introduced for the past 12 months (United States Department of Agriculture, 2014; World Organisation for Animal Health, 2017a). Whereas, when applying for FMD free status were vaccination is practised, a declaration to the OIE stating that there have been no cases of FMD during the previous two years and there has been no evidence of FMD virus transmission during the past 12 months is required. In addition, there must be documentation on FMD and FMD virus of surveillance, and existing FMD prevention and control strategies. The country must also provide documented and effective strategies for preventing the entry of the virus from the infected zone into the proposed FMD free zone (World Organisation for Animal Health, 2017a).

The waiting period following an outbreak for FMD free zone or country that does not practice vaccination is three months from the disposal of the last animal during stamping out. The waiting period for a FMD free county or zone, without vaccination, that does not practice stamping out is six months. An FMD free country or zone will have a 12-month waiting period in the FMD free country or zone where vaccination is practised. Once the waiting period is complete, an application for an OIE official disease status must be requested by the OIE delegate of the country. A dossier, that contains a relevant questionnaire for FMD or a disease control programme that has been successfully implemented, must be evaluated. The OIE Director General will request an inspection visit by the OIE delegation as part of the evaluation process.

2.3.2 Compartmentalisation and commodity-based trade

Compartmentalisation and commodity-based trade are alternative management strategies to reduce the likelihood of FMD to the importing country when the country or zone from which the beef is derived is not recognized as free from the disease (Brückner, 2011; Rich, Perry & Kaitibie, 2009; Thomson & Penrith, 2015). A compartment is defined as an animal subpopulation with a defined status in respect of the conditions of interest, a geographical identity and integrity in maintenance of its membership and status (Gemmeke, Batho, Bonbon, de Leeuw & Bruschke, 2008). In order for a facility to be approved as a compartment the facility must comply with the following (World Organisation for Animal Health, 2017a): there must be no cases of FMD for the past 12 months; No vaccination for FMD was practised during the past 12 months; there must be documented proof that a surveillance programme was implemented; and there must be an identification and traceability system in place.

Animals within the compartment are isolated to remain epidemiologically separate from populations of unknown health status. The compartment makes use of functional separation through biosecurity management practices. Control measures within the compartment allow for international trade to continue despite an outbreak outside the compartment. Deviation from biosecurity standards increases the likelihood of FMD spread (Astudillo et al., 1997).

The veterinary official of the country has the final authority on all activities in the compartment including compliance with all the requirements for the maintenance of the compartment status. Information relating to the compartment must be readily accessible by the importing countries and any changes must be communicated timeously (Scott, Zepeda, Garber, Smith, Swayne, Rhorer, Kellar, Shimshony, Batho, Caporale & Giovannini, 2006; World Organisation for Animal Health, 2017b).

The veterinary authority is required to conduct an audit according to Chapter 4.4 of the OIE terrestrial animal health code. Regular and prompt FMD disease reporting and a surveillance system around and within the compartment is essential when providing evidence of FMD freedom. Vaccination within the compartment is prohibited and no animal or animal product may enter the compartment unless written consent is given from the Director of Animal Health. The compartment must be approved and certified by a veterinary official attesting that the animals are free of disease on the day of shipment, have not been vaccinated, have remained in the compartment since birth, have been slaughtered in an approved abattoir and have passed ante and post mortem inspection. In addition, there must have been no outbreaks of FMD or evidence of FMD virus infection during the previous 12 months (OIE, 2017).

The system would first entail the pre-selection of animals in local markets, followed by the initial testing, vaccination, and quarantine of animals over a 21-day period. In the second phase, quarantined animals from the first phase would then be finished in the feedlot to ensure that animals are brought up to export weight. The final phase would end in the slaughter of animals in an export approved abattoir that applies Hazard Analysis Critical Control Points (HACCP) procedures to ensure that commodities are safe for human consumption (Brückner, 2011; Rich *et al.*, 2009).

Commodity-based approaches to trade focus on the process by which products are produced, rather than their regional origin, in assessing the likelihood of the disease. This provides the opportunity to export fresh beef products where the likelihood of spread is negligible. To ensure greater market access, such an approach requires local systems throughout the beef value chain to demonstrate negligible likelihood. However, the potential for exports is limited by the high costs of this system (Rich *et al.*, 2009).

Commodity-based trade is based on the application of HACCP principles (Rich & Perry, 2010). When it comes to the implementation of mitigations for processed livestock commodities and ensuring that the hazards are managed effectively, HACCP principles offer a potential way forward (Food Safety Inspection Service 1998). HACCP involves operational control measures and it is a tool that promotes human food safety through the identification of critical control points along food processing and managing them to ensure adequate mitigation. Other operational control measures such as clinical and serological surveillance, movement controls, fencing and vaccination (only in the infected zone) are implemented at the farm and feedlot level to ensure mitigation throughout the beef value chain (Department of Agriculture Forestry and Fisheries, 2012b; Ryu, Park, Yang & Bahk, 2013).

Food quality assurance systems are necessary at every stage of the value chain to ensure the quality and safety of beef and beef products that are destined for export (Orriss & Whitehead, 2000; (Thomson & Penrith, 2015). Therefore, the principle of HACCP can be expanding throughout the value chain for CBT. FMD virus circulation within the value chain can be identified and measures put in place to mitigate the hazard at important critical points (Orriss & Whitehead, 2000). It is suggested that the wider use of a HACCP-based system for hazard identification and management in relation to standards and auditing of livestock commodities should be considered (Thomson, Perry, Catley, Leyland, Penrith & Donaldson, 2006). Value chain-based risk management mitigates the animal disease hazards associated with specific commodities irrespective of the locality of production and HACCP principles can be applied to value chain risk management system incorporating components of value chains such as abattoirs and food processing plants (Thomson & Penrith, 2015). Therefore, by applying HACCP as part of animal disease risk management quality assurance can be maintained or established from ‘farm to fork’ (Thomson, Penrith, Atkinson, Thalwitzer, Mancuso, Atkinson & Osofsky, 2013). Failure to comply with the mitigation steps at any point of the value chain could cause an increased likelihood of FMD virus presence.

2.4 Aetiology of foot and mouth disease

Foot-and-mouth disease is a livestock disease that affects cloven-hoofed animals including cattle, goats, sheep, pigs, impala, giraffe and water buffalo (Garner, Hess & Yang, 2006; Rweyemamu *et al.*, 2008). The causative agent is a single-stranded RNA virus classified in the genus Aphthovirus within the family Picornaviridae. Seven serologically and genetically distinguishable serotypes including O, A, C, Asia-1, SAT 1, SAT 2 and SAT 3 have been identified. Serotype O and A were first detected in 1922 in France and Germany respectively. Subsequently, serotype C was recognised as a new serotype in Germany (Knowles, 1990). While SAT 1, SAT 2 and SAT 3 were first isolated in 1954 in South Africa. The seventh serotype, Asia 1, was identified in specimens from India and Pakistan in 1957 (Brown, 2003; Longjam, Deb, Sarmah, Tayo, Awachat & Saxena, 2011).

Foot-and-mouth disease virus serotypes are not uniformly distributed in the different regions of the world. For example, six of the seven serotypes of FMD (O, A, C, SAT 1, SAT 2, SAT 3) have occurred in Africa. Asia has had FMD outbreaks due to four serotypes (O, A, C, Asia-1), and South America has had three (O, A, C) (Rweyemamu et al., 2008).

2.5 Pathogenesis, transmission and clinical of foot and mouth disease

2.5.1 Pathogenesis, transmission

There are several modes of FMD virus transmission that have been reported in southern Africa (Sinkala et al., 2012). Wildlife including buffalo act remains the most important reservoir for transmission of Southern African Territories (SAT) serotypes of the FMD virus. The transmission can be direct through contact between infected and susceptible cattle. Ingestion of contaminated milk and other animal products, as well as artificial insemination using contaminated semen, have also been reported as a potential mode of transmission. Indirect contact through contact humans and vehicles have also been reported as a potential mode of transmission of FMD.

Foot-and-mouth disease virus multiplication and transmission depend on host species, nutritional and immunological status, population density, animal movements, and contact among domestic and wild species (Longjam *et al.*, 2011). In natural infection, the main route of virus entry is via the respiratory tract (Longjam *et al.*, 2011). However, transmission can also occur through abrasions on the skin or mucous membranes (Longjam *et al.*, 2011; Titus, Herbert-Hackshaw, Bournez, Delgado, Paris-Aaron, Sanford, Trotman & Gongora, 2012). FMD virus has also been detected in the milk, semen, urine and faeces of infected cattle (Lebea, PJ; Bhoora, RV; Maree, 2014).

2.5.2 Clinical signs

The initial virus multiplication usually takes place in the pharyngeal epithelium, producing primary vesicles (Longjam *et al.*, 2011). In cattle, fever and viremia usually start within 24-48 hours after infection and this is followed by a progressive spread of the virus to different tissues and ultimately causing secondary vesicles of the feet and tongue (Longjam *et al.*, 2011). Clinical signs can appear within 2 to 3 days after exposure and can last up to 7 to 10 days. The development of vesicles coincides with the peak of viremia and the highest concentrations of virus in tissues. Rupture of vesicles on the tongue and in the mouth causes the release of large quantities of FMD virus contaminated saliva (Madhanmohan, Yuvaraj, Nagendrakumar, Srinivasan, Gubbins, Paton & Parida, 2014). Additional clinical signs that have been reported included salivation, nasal discharge, mouth discomfort, tongue or lip-smacking, excessive chewing, lameness, and kicking in the air (Kitching & Alexandersen, 2016). In addition, myocarditis in calves and gastroenteritis in piglets have also been reported (Longjam *et al.*, 2011). Morbidity and mortality seem to vary by species, breed, and age of the infected animal with mortality been higher in young animals compared to adults (Longjam *et al.*, 2011).

2.6 Laboratory diagnosis of foot and mouth disease

The demonstration of the presence of the FMD viral antigen or nucleic acid can be used to confirm infection and prescribed tests included Enzyme-linked immunosorbent assays, reverse transcription polymerase chain reaction (RT-PCR) and virus isolation (World Organisation for Animal Health, 2013).

2.6.1 Culture and polymerase chain reaction (PCR)

2.6.1.1 Virus isolation

Virus isolation of primary cultures is laborious, difficult and expensive to perform and takes four to six days to completion (Longjam *et al.*, 2011). A suspension of epithelial samples and phosphate buffer must be centrifuged until a supernatant can be extracted for further processing. The suspension is then inoculated onto tissue culture plates and incubated. Cell cultures are then examined microscopically to check for cytopathic effect (Ferris, King, Reid, Hutchings, Shaw, Paton, Goris, Haas, Hoffmann, Brocchi, Bugnetti, Dekker & De Clercq, 2006).

2.6.1.2 Reverse transcriptase polymerase chain reaction

Real-time PCR is usually the first choice to detect FMD viral RNA (Vandenbussche, Lefebvre, De Leeuw, Van Borm & De Clercq, 2017). PCR has been developed and validated for the detection of the polymerase gene of the FMD virus. PCR has an analytical sensitivity 1000 times higher than that of single passage virus isolation. PCR has advantages over conventional tests, however, false-positive results can occur due to contamination by nucleic acids, particularly from the previously amplified material (World Organisation for Animal Health, 2013).

Traditional PCR the technique is time-consuming and not very accurate. Whereas, real time-PCR is a quantitative PCR which monitors the amplification to the target DNA strand during the early stages of the procedure and not at the end of the test as opposed to the conventional PCR methods. A thermal cycler is used for the real-time PCR to detect the amplification of the DNA and it is also able to heat the chill samples. The Reverse transcriptase PCR (RT-PCR) is a real-time PCR technique that qualitatively detects RNA molecules and has been used for the diagnosis of FMD virus (World Organisation for Animal Health, 2017). The sensitivity and specificity of RT-PCR for FMD virus detection have been estimated as 98% and 100% respectively (Vandenbussche *et al.*, 2017).

2.6.2 Antigen detection methods

2.6.2.1 Antigen detection ELISA

The sandwich ELISA is the preferred method for the detection of FMD viral antigen and identification of viral serotype and can be designed using inactivated or recombinant antigens, thus requiring less restrictive biocontainment facilities. The usual FMD virus antigen detection ELISA is either an indirect or a direct assay that utilises antibodies to detect the presence of FMD virus antigen.

The indirect Elisa is the test of reference described by OIE. Indirect sandwich ELISA: antigen is added to the microtiter plates and incubated for a time period where the antigen is given the opportunity to adhere to the plate. Samples containing primary area added to well contain antigen. Secondary antibodies are then added to the wells contain the primary antibody-antigen complexes. A substrate is then added which elicits a fluorescent reaction in the presence of the antibody-antigen complexes. (World Organisation for Animal Health, 2017)

Direct ELISA antigen is added to plate and given time to adhere to plates. Bovine serum albumin is added to the plate coat the surfaces that are not covered by the antigen. The sample containing the primary antibody is then added to the plate to bind to the antigen. A substrate is then added to which initiates a colour reaction in positive samples (Morioka, Fukai, Yoshida, Yamazoe, Onozato, Ohashi, Tsuda & Sakamoto, 2009; World Organisation for Animal Health, 2017).

2.6.2.2 Complement fixation test (CFT)

The complement fixation test (CFT) has been used for typing antiserum for FMD virus since 1929. The test is used to detect the presence of FMD specific antigens or antibodies in serum samples. The virus of bovine origin has also been successfully typed by CFT using guinea pig antiserum. The CFT has been used extensively for distinguishing different strains of FMD virus and although it is a fast method, it requires samples to contain high virus loads (World Organisation for Animal Health, 2013).

Standard complement proteins are added to the FMD infected serum sample react with antigen-antibody complexes in the serum. FMD antigens are then added to the serum. If the serum contains antibodies that are able to bind to the FMD antigen, complexes are formed. The complement proteins then react with antigen and antibody complexes. Additional anti-SRBC (Sheep Red Blood Cell Stroma) antibodies are then added to the serum which functions as an indicator. If the complement has been depleted, there will be no more complement left in the serum to bind to the anti-SRBC antibody. There will be no colour change in the serum and the results will be positive. If the anti-SRBC antibody binds to the complement protein, lysis will occur and the serum sample will turn pink (World Organisation for Animal Health, 2009a).

2.6.3 Antibody detection

Conventional serological methods for FMD such as the liquid phase blocking ELISA, the solid phase competition ELISA (SPC ELISA) or the complement fixation test all measure antibodies to the against structural proteins of FMD virus. These antibodies against structural proteins are induced by both infection and vaccination limiting the value of these tests in vaccinated populations. Non-structural antibodies of FMD virus are not induced by vaccination, providing that the vaccines have been formulated using FMD antigens purified to remove most of the non-structural viral proteins.

2.6.3.1 Antibody detection Enzyme-linked immunosorbent assay (ELISA)

ELISAs are the most specific and sensitive and faster to realise of all the available serological tests for antibody detection. This method is used for the detection of antibodies against each of the seven serotypes of FMD virus (World Organisation for Animal Health, 2013). There are two general types of ELISA that can detect antibodies against viral structural proteins, namely solid-phase competition ELISA and liquid-phase blocking ELISA.

Solid phase competition ELISA is more specific than the liquid-phase blocking ELISA and it is used for the detection and quantitation of IgG and IgM antibodies in sera A serotype-specific antigen is bound to the solid surface of the well in the microplate. Antibodies in sample serum compete with Guinea-pig anti-FMDV antiserum when binding to this FMD antigen (Şevik & Öztürk, 2013). Guinea-pig antisera will bind to an anti-guinea-pig antibody that is conjugated with an enzyme forming a complex. The unbound material is removed during washing. If the complex is subsequently detected by direct or indirect methods, it reveals the absence of antibodies in the sample serum (Kemeny & Challacombe, 1988).

Liquid phase blocking ELISA methods include the blocking of FMDV antigen by specific antibodies in the sample sera (Şevik & Öztürk, 2013). The pre-titrated antigen is incubated in the liquid phase with serum. The antibodies in the serum can bind to the antigen, these complexes are analysed using a trapping ELISA. Results are obtained by comparing the colour produced in the test wells with the colour produced in the antigen control wells in which test sera were absent (Hamblin, Barnett & Hedger, 1986).

2.6.3.2 Virus neutralisation tests (VNT)

The virus neutralisation test (VNT) for antibodies against structural proteins is a serotype-specific serological test. This test depends on tissue cultures and is, therefore, more prone to variability than ELISA. This assay is also slower and subject to contamination (World Organisation for Animal Health, 2013). Inactivate serum samples are diluted and then fixed on the well plate. Previously titrated FMD virus is then added to the well to bind to the antibodies present in the serum coated to the well. If the FMD virus binds to the antibodies on the plate, it is considered neutralised. The virus will then not be able to infect the cells in the cell suspension that is subsequently added. A stain is added which binds to intact cells containing neutralized antibody-virus complexes giving a positive colour change. (World Organisation for Animal Health, 2017).

2.6.3.3 Non-structural protein (NSP) detection

The detection of antibodies to non-structural proteins (NSPs) is a method that can be used to identify FMD virus-infected animals within vaccinated populations. Tests for antibodies to NSPs of FMD virus are useful in providing evidence of previous or current viral replication in the host, irrespective of vaccination status (Paton, de Clercq, Greiner, Dekker, Brocchi, Bergmann, Sammin, Gubbins & Parida, 2006). NSP antibodies can be used to differentiate animals that are infected and those that are vaccinated. When susceptible animals become infected with FMD virus, the body produces antibodies against both viral structural proteins and non-structural proteins. The inactivated FMD vaccine contains minute amounts of NSP. Animals that are vaccinated theoretically should not products antibodies against NSP. There are several methods that can be used to detect NSP antibodies such as agar gel immunodiffusion, latex bead agglutination test and ELISA (Chen, Lee, Lin, Pan, Shih, Lee & Tsai, 2013). These methods are not FMD serotype specific.

2.7 Foot and mouth disease control

The likelihood of FMD circulation in beef and beef products determines if a country is able to market fresh (chilled or frozen), maturated, or deboned beef. The likelihood of FMD virus survival in deboned beef is said to be negligible.(Henderson; Brooksby, 1948; Paton, D J; Sinclair, M; Rodriguez, 2009).

The risk characterization takes into consideration the epidemiological characteristics of the FMD virus in the infected country and the presence of mitigation measures appropriate to reduce the likelihood to a negligible level. Appropriate mitigations include imposing trade restrictions based on the origin of animals, maturation of the carcass for 24 hours at 2 °C testing the pH of the longissimus dorsi muscle, surveillance, farm-level inspection, ante-mortem and post-mortem inspections (United States Department of Agriculture, 2014)

Yu (Yu, Habtemariam, Wilson, Oryang, Nganwa, Obasa & Robnett, 1997) in the USA reported that the initial prevalence of FMD in the country was an important determinant of the overall likelihood of FMD virus in deboned beef. In the same study, the likelihood of FMD virus increased as the prevalence of FMD virus infected herds increases. While, Paton and researchers (Paton, D J; Sinclair, M; Rodriguez, 2009) in the UK indicate that the presence of mitigating measures including surveillance, competent veterinary authority, zoning, movement control, fencing, and vaccination reduces the likelihood of FMD virus transmission in deboned beef. Similarly, bleeding out of carcasses, lymphatic nodes and blood vessels have been shown to reduce the likelihood of FMD virus in beef and beef products (Paton, D J; Sinclair, M; Rodriguez, 2009). In addition, Henderson and Brooksby (1948) have also reported that pH and pathological conditions play a significant role in the survival of the FMD virus in deboned beef.

2.8 Epidemiology of foot and mouth disease in South Africa

Livestock provide a potential pathway out of poverty for rural and commercial producers that supply export feedlots and abattoirs. There are approximately 14 million heads of cattle in South Africa and 60% of these is owned by commercial farmers and 40% by rural farmers (Department of Agriculture Forestry and Fisheries, 2014; Meissner, Scholtz & Palmer, 2013). It is reported that between 2007 and 2013 South Africa was a net importer of beef and beef products. However, by the end of 2016, South Africa was a net exporter of beef and beef products, exporting on average of 39 000 tons of beef valued at R2 billion. This has been attributed to change in the South African OIE FMD status from infected to freedom resulting in increasing export of beef and beef products. (Department of Agriculture Forestry and Fisheries, 2017). However, an outbreak of FMD can reduce exports by up to 32% due to trade embargoes. Additional economic loss can occur as a result of the implementation of control measures or due to production losses (Baluka *et al.*, in press).

2.8.1 Wildlife reservoirs

South Africa has a wide diversity and number of large ungulates, wildlife and associated predators which have been known to be reservoirs for FMD virus (Penrith *et al.*, 2013b). For example, the African buffalo is said to be the maintenance host of the virus and is considered the primary source of infection for domestic and wild ungulates (Bastos, Boshoff, Keet, Bengis & Thomson, 2000). While, clinical diagnosis of FMD in impala has been regularly recorded since 1944 (Bastos *et al.*, 2000). Nonetheless, the disease in South Africa is typically confined to the free-living African buffalo and impala populations of the Kruger National Park (KNP). (Bruckner, Vosloo, Du Plessis, Kloeck, Connoway, Ekron, Weaver, Dickason, Schreuder, Marais & Mogajane, 2002). Despite the high incidence of outbreaks in impala and buffalo in recent years, direct evidence of natural transmission between wildlife species is lacking (Bastos *et al.*, 2000).

2.8.2 South African zoning system

The majority of South Africa is FMD free without vaccination (World Organisation for Animal Health, 2013). However, there is an FMD infected zone defined as a geographical area in which FMD infected buffaloes are present (Department of Agriculture Forestry and Fisheries, 2012a). While the protection zone is divided into two parts: the protection zone with vaccination and without vaccination. The protection zone with vaccination is geographical areas adjacent to the infected zones.

Only FMD free buffalo are allowed in this zone subject to specific requirements for fencing and regular testing. The protection zone without vaccination are areas adjacent to the FMD free zone and some international boundaries. Only FMD free buffalo are allowed, subject to the specific requirements for fencing and regular testing. The FMD free zone without vaccination is a zone without FMD where all OIE terrestrial code requirements have been demonstrated (Department of Agriculture Forestry and Fisheries, 2012a). Except for the Kruger National Park, the surrounding protection zone, and the surveillance zone that encompasses the infected zone in Mpumalanga and KwaZulu-Natal provinces, a large proportion of South Africa is considered free of FMD **(Figure 2.1)**

All domestic cloven-hooved animals in FMD controlled areas (protection zone) are officially registered by means of a stock brand, stock cards and must be identified by owner branding and ear tag according to the Animal Identification Act, 2002 (Act no 6 of 2002). The "South African Identification System Standard Operational Procedure" (SAFIAS SOP) has been compiled and describes the ear tag specifications (Department of Agriculture Forestry and Fisheries, 2012a). Ear tag information is captured and kept on a central electronic database. The ear tag specifications vary according to the different zones as follows: Infected zone and Protection zone with vaccination have green ear tags, Protection zone without vaccination: pink ear tag

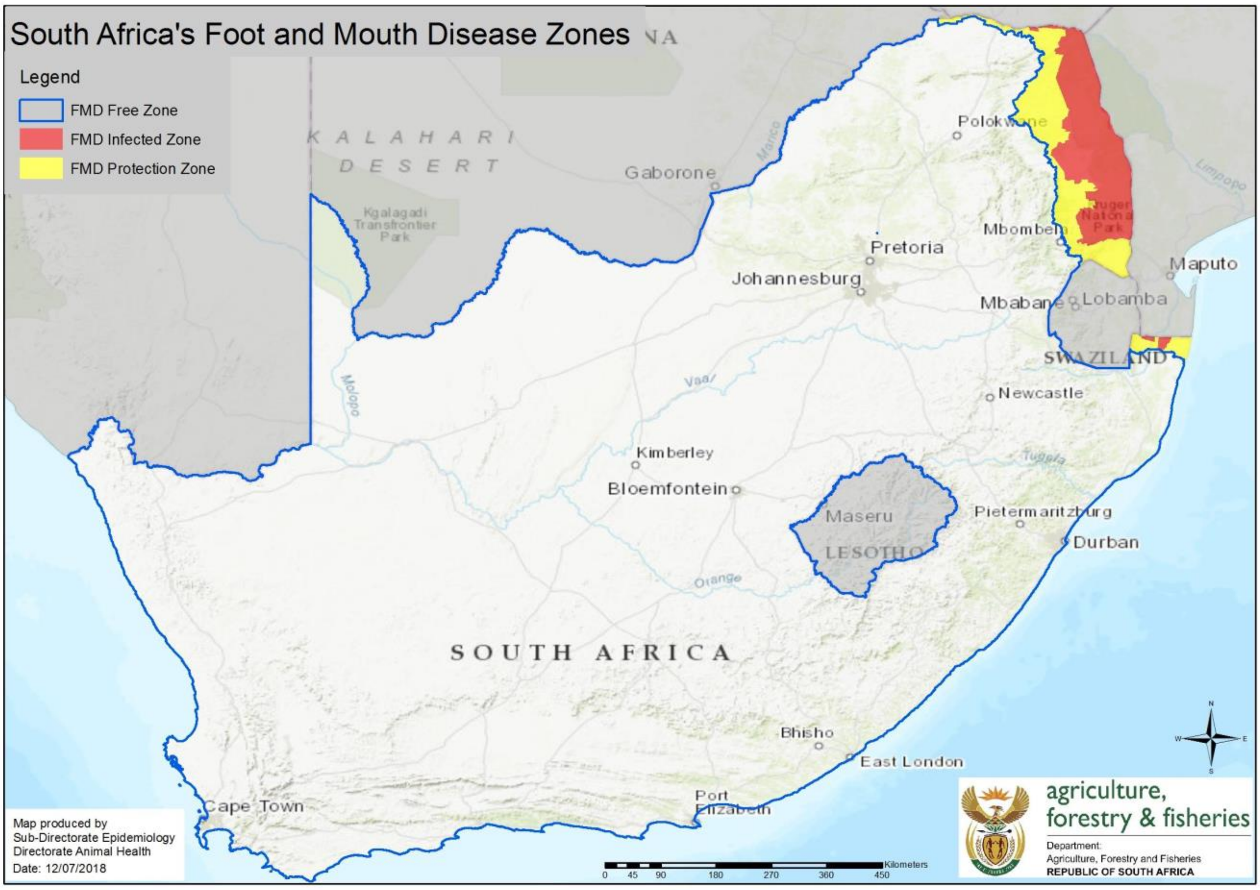

Figure 2. 1 Map of the FMD control areas used with permission from the Department of Agriculture, Forestry and Fisheries. Directorate Animal Health. Sub-directorate Epidemiology

2.8.3 Foot and mouth disease control

2.8.3.1 Surveillance

Surveillance in South Africa is implemented in accordance with Veterinary procedural notice for Foot and mouth disease control (Department of Agriculture Forestry and Fisheries, 2012b) and divides surveillance into active and passive. Active disease surveillance is defined as a purposeful and comprehensive searching for evidence of disease in animal populations or for verification that such populations are free of specific diseases (Department of Agriculture Forestry and Fisheries, 2012c,b). Clinical active surveillance is performed by trained animal health officials and once the lesions have been identified, the state veterinarian at the national or provincial level must be notified about the suspect FMD case (Department of Agriculture Forestry and Fisheries, 2012c,b). In the infected zone and protection zone with vaccination, active clinical surveillance of cattle is done every 7 days. Routine mouth examinations are required for at least 10 randomly selected cattle on each inspection day at every inspection point (dip tank). In addition, active serological surveillance is performed every month on 25 cattle at randomly selected dip tanks and suspect cases are sent for PCR (World Organisation for Animal Health, 2014). In the protection zone without vaccination, clinical inspections of cattle are performed every 14 days as previously described. In addition, passive surveillance of susceptible game species is also opportunistically performed, and PCR testing is performed only when there is suspicion of FMD.

Passive disease surveillance is defined as a the routine gathering of information on disease incidents from sources including requests for assistance from farmers, regular visits to farming communities, reports from veterinary and livestock officers, and submission of diagnostic specimens to laboratories (Department of Agriculture Forestry and Fisheries, 2012c,b). Abattoirs and livestock markets may also provide routine disease reports. In South Africa, cloven-hoofed livestock are inspected at auctions, farms, and dip tanks within the FMD free zone. Serological and virus testing is only performed when there is a clinical suspicion of FMD.

Foot and mouth disease in South Africa compared what has been reported Europe is typically a mild disorder. Therefore, there is potential for a high proportion of asymptomatic animals which are missed during clinical examination. In addition, differences in production systems will also likely to influence the probability of detecting lesions (Vosloo, Bastos, Sangare, Hargreaves & Thomson, 2002).

2.8.3.2 Movement control

Livestock movements and trade play a key role in the spread of FMD, hence, movement and trade restrictions at domestic and international levels are first to be implemented during an outbreak (Knight-Jones and Rushton, 2013). In South Africa, all movements of animals or animal products between different zones within South Africa require written FMD inter-state veterinary or inter-zonal approval from the relevant provincial executive officers. Movement between two provinces requires approval from both provincial executive officers from the origin and the destination (Department of Agriculture Forestry and Fisheries, 2012a).

Movement of cloven-hooved animals and products are regulated by a permit system in South Africa. There are two types of permits: Red Cross permits and ordinary movement permits. A red cross permit is used for movements from infected or protection zones to the FMD free zone. This permit is also used when an animal is sent to an abattoir in the surveillance or FMD free zone for direct slaughter. The state veterinarian at the destination must be informed of the movement of animals from the infected or protection zone. Whereas, an ordinary movement permit is used for all other movements that are subject to veterinary movement control. The state veterinarian at the destination does not need to be informed of movements permitted by an ordinary movement permit.

Movement is only allowed if the animal originates from a herd that was fully vaccinated during the last vaccination campaign (Department of Agriculture Forestry and Fisheries, 2012a).

2.8.3.3 Fencing

Separation of wildlife and domestic stock in South Africa is accomplished by using fences (Jori, Vosloo, B, Benqis, Brahmbhatt, Gummow & Thomson, 2009; Sangare, Bastos, Venter & Vosloo, 2003). Similarly, it used to establish disease-free zones in countries with endemic disease including FMD (World Organisation for Animal Health, 2017c). In the 1930s, game-proof fences were erected around the KNP to prevent the spread of the disease from infected buffalo to susceptible livestock (Jori & Etter, 2016; Scoones, Bishi, Mapitse, Moerane, Penrith, Sibanda & Thomson, 2010). These fences are maintained and patrolled to prevent any breakdown in the fence structure by animals, natural elements and communal farmers (Jori, Brahmbhatt, Fosgate, Thompson, Budke, Ward, Ferguson & Gummow, 2011) and the cost of fencing is borne by the South African government (Department of Agriculture Forestry and Fisheries, 2012a).

2.8.3.4 Vaccination

Prophylactic vaccination for FMD is only performed within the FMD infected zone and the protection zone with vaccination. All cattle within these zones are prescribed to be vaccinated every 4 months using Aftovax which is an inactivated trivalent vaccine (SAT 1-3) produced in Botswana by BVI (Botswana Vaccine Institute) since 2006. Date of vaccination, herd information including a number of cattle vaccinated are recorded. An “F” is branded on the right side of the neck of each vaccinated animal (Department of Agriculture Forestry and Fisheries, 2012b). Vaccination in South Africa has not been practised in areas outside the FMD protection zone since 1957 (Bruckner *et al.*, 2002).

2.8.4 Foot and mouth disease outbreaks in the FMD free zone

South Africa lost its FMD-free status without vaccination after an outbreak of serotype O was diagnosed in a piggery in the district of Camperdown in KwaZulu-Natal on the 14th of September 2000. It was the only time that serotype O has been diagnosed in South Africa. The cause of the outbreak was identified as the feeding of galley waste from a ship at Durban harbour to pigs in Camperdown. The disease was confined to a small 15 km radius area within the Camperdown District. Stamping out was instituted immediately with limited vaccination after the disease spread to communal grazing areas (Department of Agriculture Forestry and Fisheries, 2001).

On 29 November 2000, a serotype SAT 1 outbreak of FMD was diagnosed in cattle at a feedlot in the FMD free zone of the Mpumalanga Province. The outbreak was linked to cattle in the FMD control zone south of the Kruger National Park (KNP). The game-proof fence was severely damaged by floods and this enabled buffalo to move into the FMD protection zone and have direct contact with cattle outside the KNP (Bruckner *et al.*, 2002). Emergency vaccination was applied at the feedlot with the aim of slaughtering all vaccinated cattle within a reasonable time. Slaughtering of almost 15 000 cattle in the feedlot was done on 19 March 2001 (Department of Agriculture Forestry and Fisheries, 2001).

On the 1st of February 2011, the KwaZulu-Natal Veterinary Services performed routine sampling for FMD within the FMD free zone of KwaZulu-Natal Province (KZN). On the 11th of February 2011, samples came back positive for SAT 1 and SAT 3 based on liquid-phase blocking ELISA. The non-structural protein (NSP) ELISA tests were all negative and no clinical signs were observed (Department of Agriculture Forestry and Fisheries, 2011). Subsequent investigations implicated the illegal movement of cattle from the surveillance zone close to the KNP as the possible source of the outbreak (Bruckner *et al.*, 2002).

In 2014 South Africa regained OIE FMD freedom without vaccination following a visit from the OIE scientific committee to evaluate South Africa’s FMD control measures that were implemented at the time (Zokwana, 2015).

2.8.5 Contingency plan during an outbreak

In terms of the Animal Diseases Act (Act 35 of 1984), the responsible state veterinarian must be informed immediately by the private veterinarian or AHT if an outbreak of FMD is suspected. The state veterinarian is responsible for the collection of appropriate specimens and implements all necessary biosecurity precautions to prevent FMD spread. Upon confirmation of an FMD case, the affected farm will be placed under quarantine, no movement of animals and animal products will be allowed. The information relating to all animals, feed, and animal products on the farm under the quarantine restrictions must be recorded. Forward and backwards tracing will be performed to determine the history of the herd, as well as feed and animal supplements and if possible, all susceptible animals on the farm must be moved centripetally from peripheral camps to the centre of the farm in order to create an animal-free buffer zone. In the case of a communal area in which livestock are managed collectively, biosecurity will be performed at the dip tank level rather than at the level of the affected herd (Department of Agriculture Forestry and Fisheries, 2012c,b)

2.8.6 Economic implications of foot and mouth disease

In South Africa, there are approximately 240 000 small scale farmers and three million subsistence farmers whose income depends on livestock farming in South Africa (Department of Agriculture Forestry and Fisheries, 2017; Knight-Jones *et al.*, 2017; World Organisation for Animal Health, 2012). South Africa currently exports beef products to Mauritius, China, Namibia, Botswana, Hong Kong, and Dubai. In the event of an outbreak in the FMD free zone, all international exports will be prohibited from countries with FMD free status. The impact will be production losses affecting farmers livelihoods. In addition, the economic implementation of movement control makes it difficult for small scale farmers to access the local market and some cases communal grazing (Knight-Jones *et al.*, 2017). Additional consequences include an increase in the cost of control programs and the loss of lucrative markets (Knight-Jones and Rushton, 2013). In 2016, South Africa exported beef to the value of two billion USD and should South Africa lose the FMD free status, embargoes will result in a loss in export revenues. In addition, once status is lost it will take time and resources to regain the FMD free status (Department of Agriculture Forestry and Fisheries, 2017). FMD outbreaks require a large amount of money to be channelled into an intensification of surveillance both at the farm and dip tank levels (Brückner, 2011; Knight-Jones and Rushton, 2013). The erection and maintenance of fences are important for controlling movement. Maintenance of these fences is essential however costly. The maintenance of approximately 100 km fence is likely to cost $32, 000 per year (Lindsey, Masterson, Beck & Romañach, 2012).

2.9 Risk analysis

Risk analysis is the process of identifying hazards, assessing, managing, and communicating about the risk associated with the hazard. It is a tool that is used to manage risks associated with transmission and importation of disease through plants, pests, animals and their products (Murray, 2004). Risk analysis applied to animal and animal products importation comprises of four distinct but closely linked components: 1) hazard identification, 2) risk assessment, 3) risk management and 4) risk communication (World Organisation for Animal Health, 2017d).

A risk is defined as the likelihood of the occurrence of an adverse event or hazard and the magnitude of the biological and economic consequences of this adverse event that impacts animal or human health. It has two components namely, the chance or probability of an event occurring and the magnitude of the consequences (Murray, 2004).

The sanitary and phytosanitary (SPS) agreement involves the application of food safety, animal, and plant health sanitary measures to reduce the likelihood of importing commodity with hazard into the country. Member countries have the right to implement measures that protect human, animal and plant health in line with the SPS agreement (World Trade Organisation, 2014). Measures must be based on a risk assessment that takes available scientific evidence into account. The economic implications must also be considered when considering ways to limit the likelihood of FMD survival. This measure must not discriminate between member countries and thereby restricting international trade (World Organisation for Animal Health, 2009b; World Trade Organisation, 2014). In addition, member countries must be open to negotiating equivalent SPS measures when others do not adopt international standards set out by the OIE (World Trade Organisation, 2014).

Disease risk assessments evaluate the likelihood of entry of a pathogen to an importing country that is free of the disease. This type of risk analysis addresses the consequences arising from diseases; Human and animal health risks from diseases transmitted by animals, plants and their products (Murray, 2004):

The Terrestrial code describes the requirements necessary for importing and exporting countries. These guidelines ensure that mitigations are in place that reduces the likelihood of disease being present in beef and beef products are identified and mitigated (World Organisation for Animal Health, 2009b). The OIE recommends trade standards for member counties that are infected with FMD where there is an official control program that is implemented (World Organisation for Animal Health, 2017a). In the guidelines, the veterinary authority of that country must certify that the beef and beef products comply with the requirements of the importing country. Cattle must have been in the country of export for at least 3 months where vaccination is practised. Cattle must be slaughtered in an approved abattoir where carcases are deboned and matured (World Organisation for Animal Health, 2017a).

2.9.1 Hazard identification

Hazard identification is a categorisation step used to identify all pathogenic agents or vectors capable of being introduced by a commodity considered for importation and that could negatively impact the animal health status of the country. This step requires an understanding of the epidemiology of the hazard and its adverse effects (Murray, 2004).

2.9.2 Risk assessment

The risk assessment estimates the probabilities associated with a hazard using a qualitative or quantitative approach. The qualitative assessment does not require mathematical modelling and it is used for routine decision making (World Organisation for Animal Health, 2017d). Whereas, quantitative risk assessment employs a mathematical model where inputs are expressed numerically (World Organisation for Animal Health, 2017d). In both methods, a risk assessment and estimating the likelihood of an adverse outcome is an exercise in predicting the future. Risk assessment requires an estimation of the probability that one of many potential future events will transpire and also estimates the degree and source of uncertainty associated with predicting the likelihood of the event occurring (Brückner, 2013).

2.9.2.1 Qualitative risk assessment

In a qualitative risk assessment, the risk is best described by using adjectives in an ordinal scale, for the risk assessment component. The ordinal scale can have several levels. Each risk levels resembles a risk zone that is characterized by the number of levels on the scale (AFSSA, 2008). A qualitative compared to quantitative analysis is useful when there is a lack of quantitative information available. In addition, it faster and less time-consuming.

Table 2. 1: Description of the qualitative terms that can be used in a qualitative scale (AFSSA, 2008)

Qualitative description	The probability of the event	The consequences
Negligible	Rare but likely to occur	Little to no impact
Low	Possible in certain circumstances	Minor impact
Moderate	Event is likely to occur	Moderate impact
High	High possibility for the event to occur	Serious impact

A qualitative risk assessment involves the following stages:

i. Evaluation of the epidemiology of the pathogen
ii. Identifying variables that would contribute to the spread and exposure of the pathogen
iii. Determining the consequences following exposure to the hazard
iv. Data collection and evaluating feedback from experts
v. Developing a probability tree where each branch represents a series of related events or probabilities
vi. Release assessment is the analysis of the data collected for the pathogen or hazard and assigning a descriptor for the variable
vii. Exposure assessment is the analysis of the data collected for the population at risk and assigning a descriptor for the variable
viii. Evaluating the magnitude of the consequences

2.9.2.2 Quantitative risk assessment

Quantitative risk assessment employs a mathematical model where inputs are expressed numerically (World Organisation for Animal Health, 2017d). Inputs can be expressed using single numbers or point values that may represent the best guess, average or expected case or perhaps the worst possible situation (OIE, 2004).

Quantitative risk assessment can be either deterministic or stochastic. Deterministic risk assessments use single values such as means or percentiles to describe model variables. Whereas stochastic risk assessments use probability distributions for model variables (Food and Agriculture Organization & FAO, 2009).

2.9.2.3 Sensitivity analysis

Sensitivity analysis determines how much of the variability in output can be attributed to the different input sources in the model. It is a method that determines which variables are the most influential in determining the outcome (Murray, 2004; Saltelli, 2002; Thabane, Mbuagbaw, Zhang, Samaan, Marcucci, Ye, Thabane, Giangregorio, Dennis, Kosa, Debono, Dillenburg, Fruci, Bawor, Lee, Wells & Goldsmith, 2013). The sensitivity analysis can be used to determine the important correlations between inputs and the risk estimate output (Murray, 2004).

Sensitivity analyses methods can be classified into three approaches: mathematical, statistical and graphical. Mathematical methods involve calculating the output for certain input values that represent a range of inputs. This method assesses the impact of the range of variation in the input values on the output. Statistical methods assigned probability distributions to inputs and assessing the effect of input variation on the output distribution. The results of the sensitivity analysis can be presented in the form of graphs, charts, or surfaces (Frey & Patil, 2002). For example, a tornado graph gives a quick overview to identify the most influential input parameters (Vose, 2008).

2.9.2.4 Risk management

Risk management implementing identified measures to address events that pose a risk to the system. In doing so it must ensure balance between a country's desire to minimise the likelihood or frequency of disease spreads and their consequences and its desire to import commodities and fulfil its obligations under international trade agreements (World Organisation for Animal Health, 2017d). For example, heat treatment or processing of beef exported from FMD infected countries can be used as risk management steps. Therefore, OIE guidelines for FMD virus inactivation can be used to develop management and mitigation measures (World Organisation for Animal Health, 2013). Additional control measures such as movement control, border control, biosecurity measure, and disease surveillance in the FMD infected country are also part of the risk management strategy for FMD (United States Department of Agriculture, 2014; United States Department of Agriculture, 2013; World Organisation for Animal Health, 2017a,b).

Following a risk assessment, the proposed risk management measures are assessed in terms of feasibility focusing on the technical, operational and economic factors. After the implementation of the risk mitigation measures, the effect of these measures in risk reduction is that the intended results are achieved through continuous auditing and monitoring (World Organisation for Animal Health, 2017d).

2.9.2.5 Risk communication

Risk communication includes the process of gathering information and opinions regarding hazards and risks from potentially affected parties during risk analysis. A risk communication strategy should be designed at the start of the risk analysis. The results of the risk assessment and proposed risk management measures are also communicated to all stakeholders such as authorities in the exporting country, domestic and foreign industry groups, domestic livestock producers and consumer groups. Assumptions and uncertainty in the model, model inputs and risk estimates should also be communicated. Communication methods may include, peer review articles, reports, workshops, and presentations at congresses (World Organisation for Animal Health, 2017d).

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CHAPTER 3

3.1 Materials and Methods

3.2 Study Location and Study Population

The study was conducted in an export abattoir located in the FMD free zone in Mpumalanga Province, South Africa (Figure 2.1). The abattoir processes up to 2,040 heads of cattle daily, and exports deboned beef to the following countries: United Arab Emirates, , Mauritius, Asia, Seychelles, and various African countries. It receives animals for slaughter from a feedlot owned by the same company and the feedlot is located in close proximity to the abattoir. The feedlot sources animals from local farms as well as the neighbouring country of Namibia. These cattle while in the feedlot, are monitored on a daily basis, and a full-time veterinarian is employed by the feedlot for this purpose.

The company operates four holding stations throughout South Africa that are used as stopover points prior to feedlot delivery. These are situated in Northern Cape, Free State, and Eastern Cape. The three provinces as mentioned above are located in the FMD free zone. Approximately 20-30% of the total number of animals entering the feedlot goes through these holding stations.

National and provincial state veterinarians were invited to participate in the present study. The contacts of national state veterinarians were obtained from the Department of Agriculture, Forestry and Fisheries (DAFF) and provincial state veterinarian contact lists were obtained from the Directorate of Animal Health and the Directorate of Veterinary Public Health.

3.3 Data Collection

3.3.1 Published Literature

The electronic databases Science Direct, Google Scholar, Web of Science and PubMed were searched for information related to FMD epidemiology. The study included articles written in English and published in a peer reviewed international journal.

Keywords used during the research included: "Beef value chain"[All Fields] AND "South Africa"[All Fields], commodity-based[All Fields] AND trade[All Fields], commodity-based[All Fields] AND trade[All Fields] AND ("red meat"[MeSH Terms] OR ("red"[All Fields] AND "meat"[All Fields]) OR "red meat"[All Fields] OR "beef"[All Fields]), "foot-and-mouth disease"[MeSH Terms] OR ("foot-and-mouth"[All Fields] AND "disease"[All Fields]) OR "foot-and-mouth disease"[All Fields] OR ("foot"[All Fields] AND "mouth"[All Fields] AND "disease"[All Fields]) OR "foot and mouth disease"[All Fields], ("foot-and-mouth disease"[MeSH Terms] OR ("foot-and-mouth"[All Fields] AND "disease"[All Fields]) OR "foot-and-mouth disease"[All Fields] OR ("foot"[All Fields] AND "mouth"[All Fields] AND "disease"[All Fields]) OR "foot and mouth disease"[All Fields]) AND ("south africa"[MeSH Terms] OR ("south"[All Fields] AND "africa"[All Fields]) OR "south africa"[All Fields]), Qualitative[All Fields] AND ("Risk Anal"[Journal] OR ("risk"[All Fields] AND "analysis"[All Fields]) OR "risk analysis"[All Fields]), Qualitative[All Fields] AND ("Risk Anal"[Journal] OR ("risk"[All Fields] AND "analysis"[All Fields]) OR "risk analysis"[All Fields]) AND ("foot-and-mouth disease"[MeSH Terms] OR ("foot-and-mouth"[All Fields] AND "disease"[All Fields]) OR "foot-and-mouth disease"[All Fields] OR ("foot"[All Fields] AND "mouth"[All Fields] AND "disease"[All Fields]) OR "foot and mouth disease"[All Fields]), Quantitative[All Fields] AND ("risk assessment"[MeSH Terms] OR ("risk"[All Fields] AND "assessment"[All Fields]) OR "risk assessment"[All Fields]), Quantitative[All Fields] AND ("risk assessment"[MeSH Terms] OR ("risk"[All Fields] AND "assessment"[All Fields]) OR "risk assessment"[All Fields]) AND ("foot-and-mouth disease"[MeSH Terms] OR ("foot-and-mouth"[All Fields] AND "disease"[All Fields]) OR "foot-and-mouth disease"[All Fields] OR ("foot"[All Fields] AND "mouth"[All Fields] AND "disease"[All Fields]) OR "foot and mouth disease"[All Fields]), “("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields]) AND ("methods"[Subheading] OR "methods"[All Fields] OR "methods"[MeSH Terms]) AND ("foot-and-mouth disease"[MeSH Terms] OR ("foot-and-mouth"[All Fields] AND "disease"[All Fields]) OR "foot-and-mouth disease"[All Fields] OR ("foot"[All Fields] AND "mouth"[All Fields] AND "disease"[All Fields]) OR "foot and mouth disease"[All Fields]), "sat"[All Fields]) AND Type[All Fields] AND FMD[All Fields], FMD[All Fields] AND ("etiology"[Subheading] OR "etiology"[All Fields] OR "pathogenesis"[All Fields]), FMD[All Fields] AND Clinical[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "signs"[All Fields] OR "diagnosis"[MeSH Terms] OR "signs"[All Fields]), FMD[All Fields] AND ("epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms]).

Inclusion Criteria

Articles were included in this study if they were:

1) published abstracts of final data or fully published reports on FMD;
2) systematic reviews or meta-analyses of FMD;
3) experimental studies of FMD published in English and
4) official government reports, veterinary procedural notices and guidelines.

3.3.2 Opinion Survey

3.3.2.1 Questionnaire Development

Expert opinion was used to estimate some quantitative input parameters for the model. The data was collected using a semi-structured questionnaire administered via telephone interview. The questionnaire included questions related to farms and feedlots, ante-mortem, primary and secondary meat inspection, and removal of lymph-nodes. The respondent was required to give the minimum, most likely and maximum values. In addition, the respondent was requested to indicate the confidence level with respect to the answer given **(Addendum A).** The other information requested in the questionnaire for a veterinarian in animal health included clinical surveillance at farm and feedlot, the sensitivity of clinical surveillance to detect FMD, and clinical presentation of infected animals based on SAT types found in South Africa. The study selected veterinarians working in the veterinary public health section, particularly in abattoir inspection and hygiene management systems. In addition, veterinarian working at national and provincial levels in animal health section, experienced in FMD surveillance and control were also included in the study. The selected veterinarians must also have in depth knowledge on FMD policy implementation with at least five-year experience in the field.

3.3.2.2 Questionnaire Administration

All questionnaires were pretested on colleagues who are veterinarians in the Directorate Animal Health in the Department of Agriculture, Forestry and Fisheries. The information obtained in the pilot study was used to improve the questionnaire. This involved mainly making questions much clearer to the respondents. State veterinarians in the FMD free zone of South Africa were interviewed on the following aspects: surveillance, detection of FMD, and control of FMD. Both national and provincial level government veterinarians from all nine provinces in South Africa (Mpumalanga, Limpopo, Kwa-Zulu Natal, Free State, Western Cape, Gauteng, and Eastern Cape) were contacted and only 14 state veterinarians were interviewed telephonically. No feedback was received from 4 state veterinarians

3.4 Probability of FMD virus contamination in fresh beef products

A risk assessment of the beef value chain was conducted to estimate the probability OF THE FMD BEING exported in fresh beef products from the FMD free zone. This probability was calculated as $P_{fmd} = P_{farm} + P_{feedlot} + P_{abattoir}$ where P_{farm} denote the probability of FMD virus, $P_{feedlot}$ the probability of FMD virus in the feedlot, and $P_{abattoir,}$ the probability of FMD virus at the abattoir.

The principles for conducting a risk analysis for international trade were followed according to the OIE guidelines from the handbook on import risk analysis for animals and animal products (World Organisation for Animal Health, 2010)

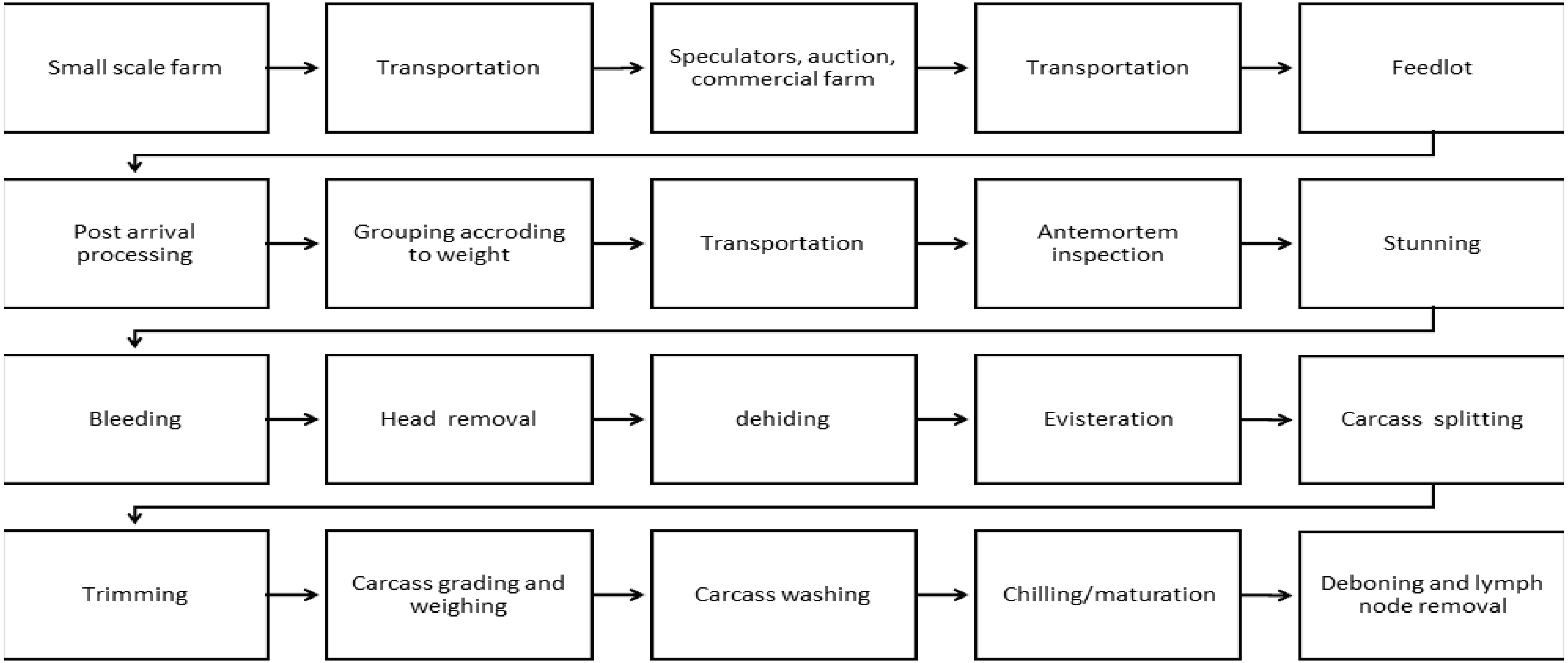


Figure 3. 1: The beef value chain pathway for cattle slaughtered in the FMD **free zone in South Africa**

Cattle born on a farm within the FMD free zone remain on the farm for six months and then get sold to the feedlot directly, or through speculators, and auctions. When the feedlots collect cattle at the various pick up points, records of each farm that supplies cattle are obtained for traceability purposes. However, when cattle are purchased from auctions and speculators there are no records for the farm of origin for the cattle. This creates a problem when the farm of origin needs to be traced during a disease investigation.

Upon arrival at feedlots, cattle are processed and remain at the feedlot until they reach slaughter weight. Animals enter the feedlot at a weight of 200 – 220 kg and remain in the feedlot for 90 – 100 days. During this time the animal gains an additional 100kg. During the finishing period, animals can become stressed and are susceptible to disease (Department of Agriculture Forestry and Fisheries, 2002). Once cattle reach their target weight, they are transported to the abattoir for slaughter **(Figure 3.1).**

As illustrated in Figure 3.1, ante-mortem inspection is performed in the holding pens at arrival point at the abattoir. Cattle are rested for at least an hour prior to slaughter. The last delivery of cattle for the day will remain in the holding pens overnight and will be slaughtered the next morning. Cattle are stunned and bled before the head and hooves are removed and inspected. The skin and internal organs are then removed, and the carcass is split in half, and matured during the chilling stage at 2° C for a minimum of 24 hours. The pH of the *longissimus dorsi* muscle must drop to 5.8 during this time. Carcasses destined for export will be deboned only if the importing country has stipulated that imported beef must be deboned in the trade agreement. Lymph nodes and blood vessels are removed after maturation.

3.4.1 Hazard Identification

FMD virus BEEN identified as A hazard which could adversely affect the export of fresh beef products from South Africa should the FMD free status be revoked (World Organisation for Animal

Health, 2017). FMD virus is highly contagious and causes high morbidity and poor production in cattle. Although there are no public health implications associated with FMD virus, it has the potential to cause devastating economic consequences (Department of Agriculture Forestry and Fisheries, 2017; Knight-Jones, McLaws & Rushton, 2017)

Currently, there are no FMD surveillance programs implemented in the FMD free zone, and since there is no active surveillance of FMD in the free zone, a risk assessment is needed to determine the likelihood of at least one animal being infected with FMD in the free zone as well as the probability of the FMDV surviving all mitigations (Figure 3.2) currently in place prior to export of beef (World Organisation for Animal Health, 2017). The likelihood of FMD contaminated fresh beef products being exported during an outbreak will be calculated according to the following formula: P_{fmd}=Pfarm+Pfeedlot+Pabattoir.

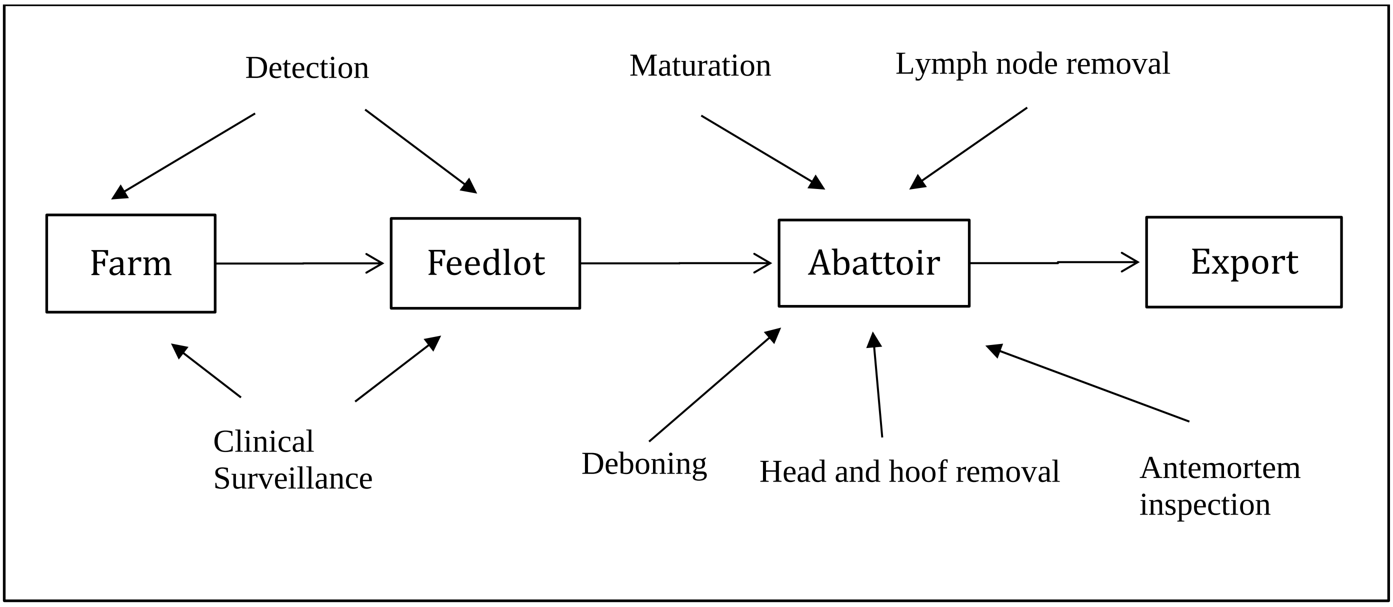


Figure 3. 2: A simplified conceptual model of the beef value chain illustrating the control measures that are currently implemented at each point of the value chain to reduce the

likelihood of FMD virus survival in fresh beef products.

South Africa implements disease control measures to prevent the entry and spread of FMD to FMD free zones or countries. Passive surveillance is implemented at farm and feedlot level for early detection of FMD. Ante-mortem inspection is conducted at the abattoir for the detection of clinically infected animals in terms of the Animal Diseases Act 35 of 1984. Whereas maturation, deboning, and lymph node removal reduce the likelihood that FMD virus survives in fresh beef products (Figure 3.1 and 3.2).

3.4.2 Qualitative Risk Assessment

3.4.2.1 Risk pathway

A risk pathway assessment was used to estimate the probability of FMD detection or survival along the value chain (Astudillo, Sutmoller, Saraiva & López, 1997). The risk pathway begins with considering the probability that an animal or a group of animals is infected with FMD virus at the source farm. In order to calculate the probability of at least one animal on a farm within the FMD free zone being infected, the following information was required:

1. The probability that the infected animal(s) will not be identified as being infected
2. The probability that the infection will remain undetected at each subsequent inspection.
3. The probability that FMD virus will survive processing, storage and distribution.

The likelihood of FMD detection or survival throughout the value chain was quantified using probability distributions within a stochastic risk assessment model **(Figure 3.1-3.3).** In addition to published literature and expert opinion, information from historical data available from the 2012 application for FMD Prevalence survey conducted in KwaZulu Natal (Health and Africa, 2012) was used to calculate the initial prevalence of FMD in the free zone. The probability along the chain for each modelled event was considered a conditional probability, which is the probability of occurrence of that event given that all the previous events had occurred (Vose, 2008).

The first step of the model assumed that there was a random selection of animals from the population of cattle in the FMD free zone. Each branch represents potential scenarios that are likely to occur in a cattle population within the FMD free zone, in the event an animal becomes infected with FMD. The first probability is the prevalence of cattle infected with the FMD virus in the FMD free zone. Branching out from each box are arrows to the next modelled event and attached to these arrows are the conditional probabilities of events occurring. All probabilities within a branch are multiplied to determine a final probability for each branch. Then the probabilities of each branch of the risk pathway are added to calculate the overall likelihood of FMD detection and survival throughout the beef value chain (Vose, 2008).

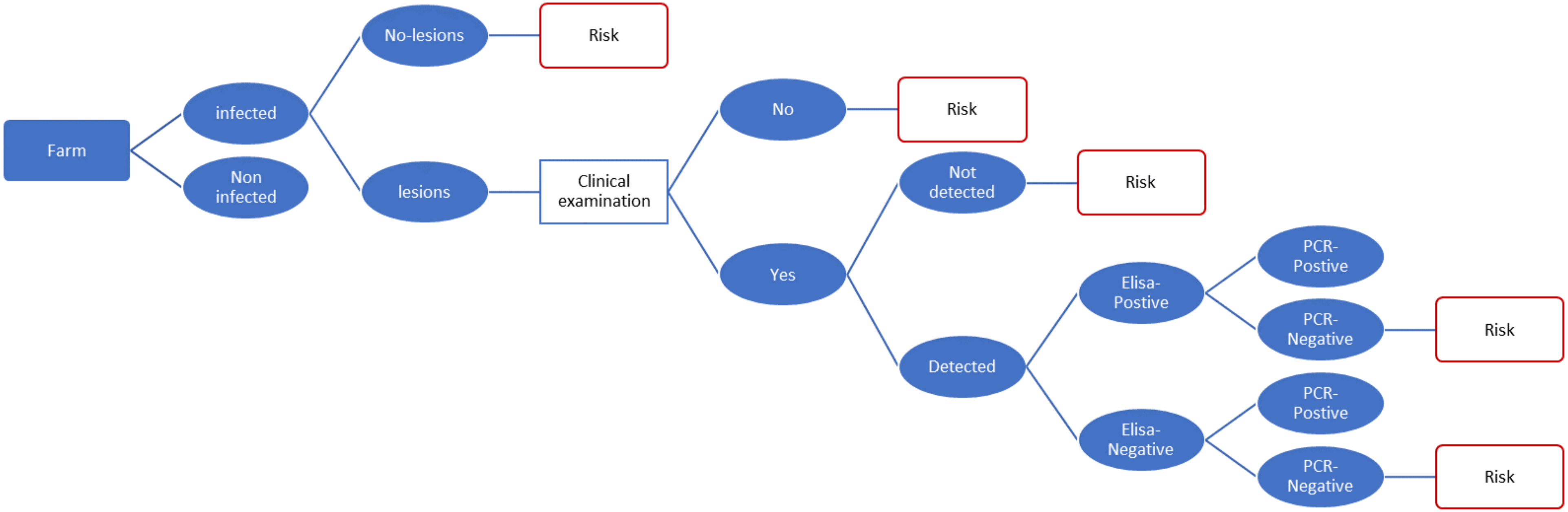
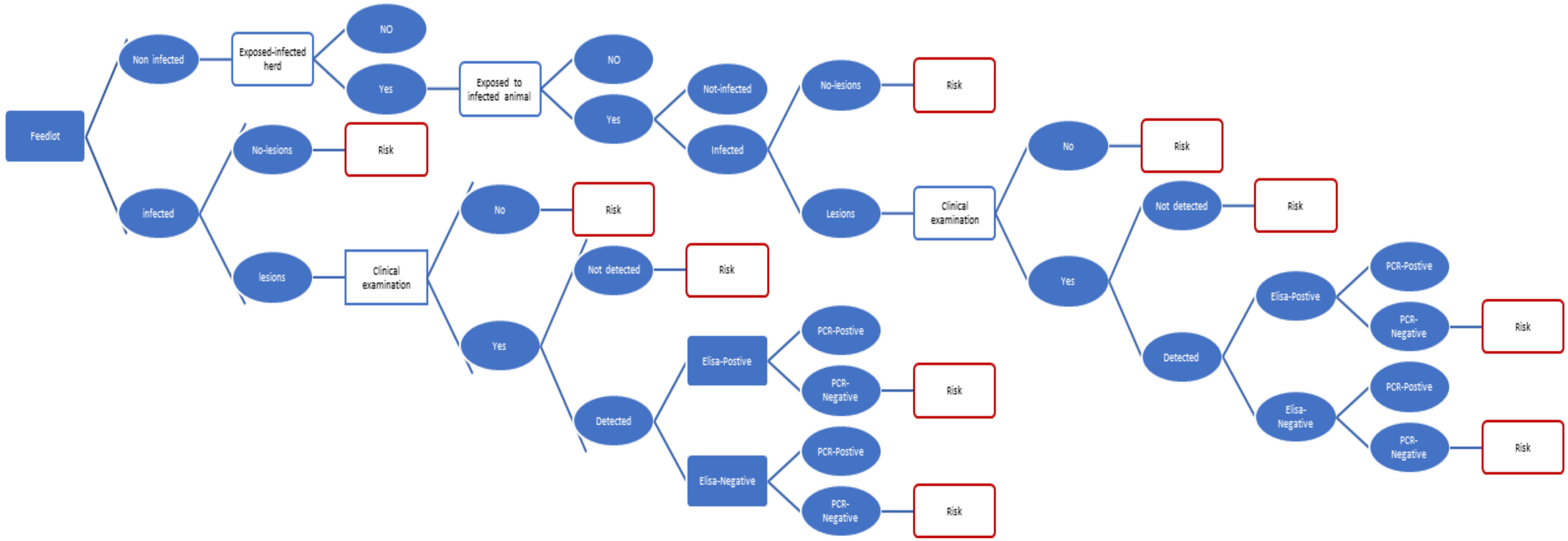
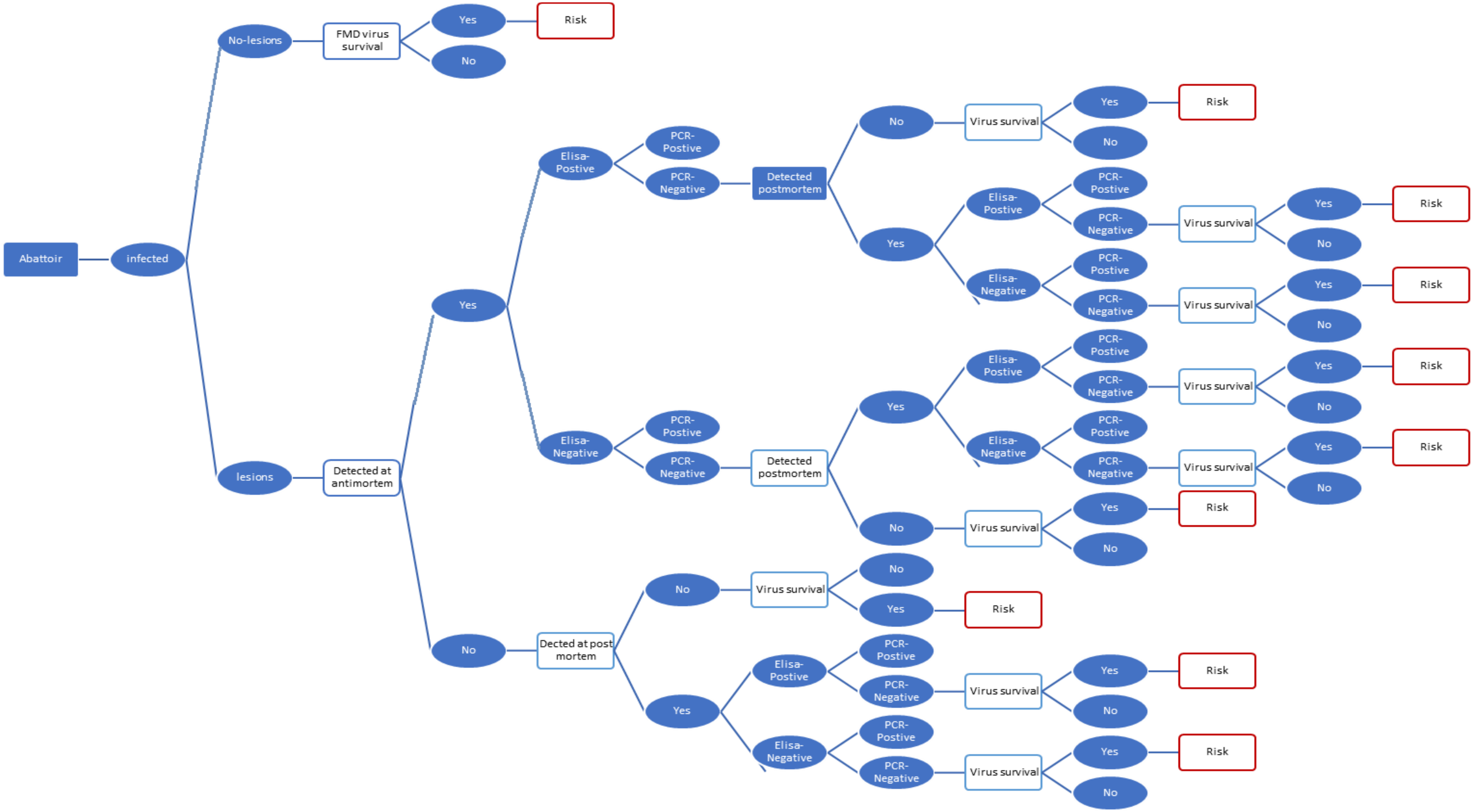


Figure 3.3 Risk pathway for the likelihood of FMD virus using a stochastic risk assessment model at farm level.



3.4 Risk pathway for the likelihood of FMD virus using a stochastic risk assessment model at feedlot level.



3.5 Risk pathway for the likelihood of FMD virus using a stochastic risk assessment model at abattoir level.

3.4.2.2 Expert opinion

The percentages provided by state veterinarians as experts were modelled using a PERT distribution, the preferred distribution to model expert opinion. The experts need only to provide estimates of the minimum, most likely and maximum values for the variable. The PERT function finds a shape that fits these restrictions. It is a version of the beta distribution, that requires the same three parameters as the triangular distribution, namely minimum, most likely, and maximum.

Each state veterinarian was also asked to evaluate their level of confidence in the provided responses. In addition, the level of confidence based on their experience in the field was estimated by the assessor during the interview of each state veterinarian. Both values were multiplied, and an overall level of confidence was allocated to each state veterinarian. This uncertainty from each expert was included into the model by using the inputs from each expert (PERT distributions), weighting them, using the overall level of confidence for each expert, within a discrete distribution.

3.4.2.3 Beef value chain

Probability of circulating FMD virus in the FMD free zone (Pf) was modelled as a beta distribution with parameter α= ni+1 and β= Nu1– ni +1 where ni denotes the number of outbreaks per year. An average number of outbreaks per year (*ni*) was assumed to follow a Gamma distribution (Vose 2008), with a shape parameter α=2 and a scale parameter β=1/18. The α represented the number of FMD outbreaks that had occurred from 2000 till 2018 and β represented the number of years of this period. The Nu1 =3.0 x10^6, which is the estimated number of commercial and subsistence farms in South Africa.

3.4.2.4 Farm of origin-P_{farm}

The P_{farm} value indicates the probability of FMD infected animal not being detected at farm level with the current surveillance in place was calculated as P_{farm}= P2a+P2b+P2c+P2d+P2e . The number of farms in South Africa was modelled using information reported by the Department of Forestry and Fisheries (Department of Agriculture Forestry and Fisheries, 2012a). The probability of FMD virus-infected cattle transmitting the virus to a susceptible animal following contact was assumed not to be influenced by external factors; exposure to FMD virus can either result in infection or no infection. An average number of outbreaks per year denoted by *ni* was assumed to follow a Gamma distribution (Vose 2008), with a shape parameter α=2 and a scale parameter β=1/18. The α represented the number of FMD outbreaks that had occurred from 2000 till now and β represented the number of years of this period. The number of farms (nf) being infected in the FMD free zone during a year was calculated using the Poisson distribution with ni (the previously defined Gamma distribution) as a parameter. Poisson distribution is often used to model rare events when there are a few numbers of events that occur over a long period of time (Nydam, Mohammed and Mohammed, 2005). Therefore, the probability of FMD at the farm level was assumed to follow a beta distribution with parameter $\alpha_1 = nf+1$ and $\alpha_{2=}$ $Nu1 - nf + 1$ (Vose, 2008).

3.4.2.5 Passive surveillance and detection of lesions

Passive surveillance alone is performed in the FMD free zone for FMD (Department of Agriculture Forestry and Fisheries, 2012b). Here veterinarians, observe the herds for clinical signs during routine herd health visits or farm call outs to attend to sick animals.

3.4.2.5.1 At farm level

The initial probability of a farm being infected (Pf) was calculated by first estimating the probability of an animal being infected within a farm. The conservative estimate was that the intra-herd prevalence (*ihp*) was 10% before the farmer identifies FMD animals and before calling the veterinarian and before quarantine and movement control are implemented. Thus, 10% was used as the probability for an animal been infected within herds. Then three other steps namely the probability of the animal developing lesions (*Pl),* the probability of the farm not undergoing clinical surveillance in the FMD free zone (*Psfa*) and the probability of not detecting lesions on one animal during the passive surveillance (*Pdfa)*. These three probabilities were obtained from the expert elicitation process.

3.4.2.5.2 At feedlot level – P(feedlot)

The P(feedlot) value indicates the probability of FMD infected animal not being detected at feedlot level with the current surveillance in place was calculated as P(feedlot) = P3a+P3b+P3c+P3d+P3e+P3f+P3g+P3h+P3i+P3j. The probability of not conducting passive surveillance in the FMD free zone at feedlot level *Psfe* and the probability of not detecting lesions on one animal during the surveillance (*Pdfe)* were modelled using PERT distribution based on expert opinion.

3.4.2.5.3 Diagnostic tests

The aim of diagnostic testing is to identify and confirm infected animals. Foot and mouth disease virus-infected animals that do not test positive (false negatives) contribute the highest likelihood risk to the trade in beef products. The probabilities of the screening antibody ELISA test and that of the confirmatory PCR test to detect FMD virus in infected cattle (ie. their sensitivity) were modelled using beta distributions.

The ELISA and PCR have not been validated in South Africa. Therefore, information regarding the sensitivity of the two tests was obtained using previously published literature (personal communication from the Department of Agriculture, Forestry and Fisheries). The sensitivity (Se) was estimated by dividing the number of animals that tested positive over the total number of infected animals. This estimation of Se is a very conservative approach as infected animals with clinical signs show a higher probability to be positive on ELISA and PCR tests. The sensitivity of the ELISA is an estimation of the probability that an FMD clinically infected animal will test positive for FMD virus.

The probability of ELISA test not detecting an infected animal *Pe* was calculated as *1-Se*. The sensitivity of the ELISA was calculated to be 0.99% based on the study done by Niedbalski (2004). The *Beta (α, β)* distribution was used to model the sensitivity of the ELISA to take into account the uncertainty due to the sample size of the study. The *α* denotes *(n+1), n* being the number of infected animals (180) that test ELISA positive. The *β* denotes *N-n+1*, where *N* is equivalent to the sample of known infected animals (181) (Niedbalski, 2004).

The sensitivity of the PCR was calculated to be 0.98 based on the study done by Vandenbussche *et al.* (2017). Therefore, the probability of the PCR test not detecting an infected animal *Pp* was calculated as *1-Se*. The *Beta (α1, α2)* distribution was used to model the sensitivity of the PCR test to take into account the uncertainty due to the sample size of the study. The *α1* denotes *(n+1), n* being the number of infected animals (*n*=82) that test PCR positive. The α2 denotes *N-n+1*, where *N* is equivalent to the sample of known infected animals (*N*=83) (Vandenbussche, Lefebvre, De Leeuw, Van Borm & De Clercq, 2017).

3.4.2.6 Feedlot

Cattle bought from speculators or auctions generally arrive at the feedlot as a mixed batch. Animals are subsequently grouped according to weight and body condition. This practice of mixing cattle of different health statuses potentially exposes cattle to several diseases. There is a possibility that FMD can be spread through contact with animal in neighbouring pens. Cattle remain in the feedlot for 90 days on average. This makes it possible to detect the FMD virus-infected cattle before leaving the feedlot. However, this is contingent on animals getting infected during the early stages of the production cycle (Vergne, Grosbois, Durand, Goutard, Bellet, Holl, Roger & Dufour, 2012)

The probability of a single non infected animal being exposed to at least one FMD infected herd in the feedlot was calculated using the following formula: *1-(1-Pf)^n*, where *Pf* is the probability for one herd to be infected by FMD in the FMD free zone and *n*=17 is the number of herds that are grouped together at the feedlot coming from n different farms after they are picked from the pickup point and taken to the feedlot .

The probability of a non-infected animal coming into contact with at least one infected animal from the infected herd considered previously was also calculated using the following the formula: $ia=1-(1-ni)^n$ where ni denotes the within-herd prevalence and n=30 average number of animals per pen at the feedlot.

The probability that a naive animal that originates from the FMD free zone could become infected after being exposed to FMD virus was calculated using a PERT distribution with minimum (0.12), most likely (0.432), and maximum (0.80) values (Chis Ster, Dodd & Ferguson, 2012). The transmission rate was also calculated based on a study by Chis Ster and colleagues (Chis Ster *et al.*, 2012). Although it has been suggested that the FMD Serotypes found in EU differ from FMD SAT types that occur in South Africa, there is no research to support the theory that the transmission rate of the FMD SAT types differs from the European serotypes. Therefore, the transmission rates for the SAT types found in South Africa were assumed to be the same as the one reported in Europe. Notwithstanding, differences in the climatic conditions, environmental factors, husbandry and management practices.

3.4.2.7 Abattoir – P(abattoir)

The P(abattoir) value indicates the probability of FMD infected animal not being detected at abattoir level during antemortem and post mortem inspections and surviving processing. In the following sections, the multiple processes within the abattoir that mitigate the risk of FMD virus surviving in the fresh beef are discussed and it is calculated as P(abattoir) = P4a+P4b+P4c+P4d+P4e+P4f+P4g+P4h+P4i+P4j+P4k

3.4.2.7.1 Ante-mortem inspections

Animals arriving at the abattoir are rested for at least one hour or overnight. This means that animals remain in the holding pen for 1 to 24 hours depending on the time of arrival. Therefore, should a naive animal come into contact with an infected animal at this time, the animal would be slaughtered before they develop viremia. Cattle infected with FMD virus in the feedlot are expected to develop visible lesions that would be detected during antemortem and meat inspections. Lesions are likely to be detected at antemortem inspection and during head and hoof inspections. However, animals infected late in the production cycle, they might be missed during abattoir inspections. The probability of lesion detection during antemortem inspections (Pam) was modelled using a PERT discrete distribution based on expert opinion (Table 3.1 and 3.2).

3.4.2.7.2 Primary meat inspection

On average number (n=average) of animals slaughtered in a year is 844518. Primary meat inspection includes inspection of the eviscerated carcass, cattle heads, feet, and red offal, (Department of Agriculture Forestry and Fisheries, 2004). The probability of detecting lesions during primary meat inspections (Phh) was modelled using a discrete distribution based on expert opinion (Table 3.1 and 3.2).

3.4.2.7.3 Deboning, maturation, lymph node removal and blood vessel removal

The implementation of control measures to reduce the likelihood of FMD virus survival in potentially FMD infected beef and beef products that are destined for export. Maturation of the carcass reduces the likelihood of FMD virus survival in muscle (Brückner, 2011). During carcass processing the inside is washed and the carcass is moved into a chiller at 2 °C for at least 24 hours before it is stored at 5° C. Therefore, the chilling room must be designed to provide enough room for storage and for adequate air movement to ensure rapid carcass cooling which is also crucial for food safety and quality. In the study area, beef carcasses are kept in the chilling rooms at temperatures of 4–7° C.

For purposes of this risk assessment model, it was assumed that the beef and beef products were completely deboned, matured, and without any lymphoid tissue or blood vessels. However, it is important to note that residual blood, fragments of bones and small lymph nodes are likely to remain in the final product and may be a source of FMD virus (Paton, Sinclair & Rodríguez, 2010). In addition, FMD virus is most likely be found in the bone marrow rather than the bone itself. Since there are no available data to quantify amounts of fragments of bones or lymph node tissues that remain in beef cuts, it was assumed that the probability of bone fragments and a small amount of lymph node tissue that remains in the carcass, is negligible. (Paton *et al.*, 2010).

The probability of FMD virus surviving processing was calculated by using the data from a study by Cottral, (1969) where 10% FMD virus survived in tissue culture after 14 hours of maturation. In order to model the probability of survival of the virus according to time (i.e. the percentage of survival), a lognormal distribution was fitted with this value and it was assumed that after 28 hours 99% of the virus would have been destroyed. We set the maximum of the lognormal function to be 100% of survival at t=0 and truncated the distribution in order to consider only the portion for t=0 and above. LognormAlt, which uses alternative parameters was the distribution used. This distribution function uses three percentiles, 0 time as 0.001%, 14 hours as 90% and 28 as 99%, therefore the probability of virus survival was calculated as LognormAlt (0.001%,0,90%,14,99%,28,) Truncated for t≤0. RiskTheoXtoP(Pln;24) was then used to return the exact theoretical cumulative probability of virus survival after 24 hours.

Table 3. 1 Summary of inputs and distributions used in the modelling

Input	Description	Description/Model	Reference
Nu1	Estimated number of cattle farms in South Africa	3000000	(Department of Agriculture Forestry and Fisheries, 2014)
ni	Number of outbreaks during a year	Gamma (2;1/18)	(Department of Agriculture Forestry and Fisheries, 2012a)
Pf	Farm probability of FMD in the free zone (based on previous outbreaks over the last 18 years)	Beta (ni+1; Nu1– ni +1)	(Munz, 2017)
Pl	Probability for no lesions developing in an animal when infected with FMD	Discrete (xi; pi); xi=PERT (minimum, most likely: maximum); pi= expert certainty x observed certainty	expert opinion **(Table 3.2)**
Psfa	Probability of not doing clinical surveillance in the FMD free zone at the farm level	Discrete (x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
Pdfa	Probability of not detecting FMD lesions at the farm level	Discrete (x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
ihp	The intra-herd prevalence FMD animals and before calling the veterinarian and before quarantine and movement control are implemented.	10%	This is a conservative estimate of the intra-herd prevalence.
P2a	Probability of an infected animal not showing clinical signs	(Pf) x (ihp) x(P1)	
P2b	Probability of an animal showing clinical signs, but no clinical examination performed	(Pf) x (ihp) x (1-P1) x (Psfa)	
P2c	Probability of clinical examination not detecting an infected animal	(Pf) x (ihp) x (1-P1) x (1- Psfa) x (Pdfa)	

P2d	Probability of animal been positive on clinical examination but negative on ELISA and PCR	(Pf) x (ihp) x (1-P1) x (1- Psfa) x (1-Pdfa) x (1-Pe) x (Pp)
P2e	Probability of animal been positive on clinical examination but positive on ELISA and negative on PCR	(Pf) x (ihp) x (1-P1) x (1- Psfa) x (1-Pdfa) x (Pe) x (Pp) + (1-Pf)
P2f	Probability of an animal with clinical signs infected in a farm	=P2b+P2c+P2d+P2e
Pfarm	Probability of an animal infected in a farm	=P2a+P2b+P2c+P2d+P2e

Table 3. 1 Summary of inputs and distributions used in the modelling continues

Input	Description	Description/Model	Reference
Psfe	Probability of not doing clinical surveillance in the FMD free zone at the feedlot level	Discrete (x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
Pdfe	Probability of not detecting FMD lesions at the feedlot level	Discrete (x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
nf	Average number of farms supplying the feedlot in one day	17	Karan Beef personal comment:
ih	exposed to infected herds	1-(1-Pf)^nf	
Ppe	Average number of animals per pen	30	Karan Beef personal comment:
Pe	Probability of ELISA not detecting an infected animal	Beta (n+1; N– n +1), 1-Beta (180+1,181-180+1); Sensitivity:0.99	(Niedbalski, 2004)
ia	exposed to an infected animal	1-(1-ni)^pe	(Department of Agriculture Forestry and Fisheries, 2012c)
ie	infected after exposed	Pert (minimum, most likely, maximum)	(Chis Ster *et al.*, 2012)
Pp	Probability of PCR not detecting an infected animal	1-Beta(82+1,83-82+1), Sensitivity: 0.98	(Vandenbussche *et al.*, 2017)

P3a	Probability of an infected animal in the feedlot not showing clinical signs	(Pf) x (ni) x(P1)
P3b	Probability of an infected animal when not doing clinical examination is performed	P2f x Psfe
P3c	Probability of identifying an infected animal when clinical examination is performed but lesion not detected	P2f x (1-Psfe) x(Pdfe)
P3d	Probability of an infected animal in the feedlot been ELISA positive but PCR negative	P2f x (1-Psfe) x(1-Pdfe) x (Pep) x (Pp)
P3e	Probability of an infected animal in the feedlot been ELISA and PCR negative	P2f x (1-Psfe) x(1-Pdfe) x (1-Pe) x (Pp)
P3f	Probability of a susceptible animal been infected animal and show no clinical signs	(1- Pf) x (ih) x (1-ia) x (ie) x (P1)
P3g	Probability of a susceptible animal been infected animal and show clinical signs, but no clinical examination is performed	(1- Pf) x (ih) x (1-ia) x (ie) x (1-P1) x (Psfe)
P3h	Probability of a susceptible animal been infected animal and show clinical signs, but no clinical examination is performed but not lesions are detected	(1- Pf) x (ih) x (1-ia) x (ie) x (1-P1) x (1-Psfe) x (Pdfe)
P3i	Probability of a susceptible animal been infected animal and show clinical signs, but no clinical examination is performed but not lesions are detected, negative on ELISA and PCR	(1- Pf) x (ih) x (1-ia) x (ie) x (1-P1) x (1-Psfe) x (1-Pdfe) x (Pe) x (Pp)
P3j	Probability of a susceptible animal been infected animal and show clinical signs, but no clinical examination is performed but not lesions are detected, positive on ELISA, negative on PCR	(1- Pf) x (ih) x (1-ia) x (ie) x (1-P1) x (1-Psfe) x (1-Pdfe) x (1-Pe) x (Pp)
P3h	Probability of symptomatic animals infected with FMD not identified at the feedlot	=P3b+P3c+P3d+P3e +P3f +P3g+P3h +P3i+ P3j
Pfeedlot	Probability of an infected animal neither symptomatic or asymptomatic been identified in the feedlot.	=P3a+P3b+P3c+P3d+P3e +P3f +P3g+P3h +P3i+ P3j

Table 3. 1 Summary of inputs and distributions used in the modelling continues

Input	Description	Description/Model	Reference
Pam	Probability of not detecting lesions during antemortem inspection	Discrete(x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
Phh	The probability of not detecting lesions during meat inspection when the head and hooves are removed	Discrete(x_i; p_i); $x_{i=}$PERT (minimum, most likely: maximum); $p_{i=}$ expert certainty x observed certainty	expert opinion **(Table 3.2)**
Pln	The probability of virus survival after time t	Lognorm (0.001%,0,90%,14,99%,28,) Truncated for t≤0	derived from (Cottral, 1969)
RT	The probability of virus survival after 24 hours	RiskTheoXtoP(Pln;24)	
AR	Likelihood of having an FMD outbreak each year	(1-R)^n n=average number of animals slaughtered in a year=844518 R=Total risk	Department of Forestry and Fisheries Directorate Veterinary Public Health
NY	Estimated number of years before the next FMD outbreak	1/AR	
P4a	Probability of an infected animal showing no clinical signs and virus surviving in fresh beef	(P4a) x (RT)	
P4b	Probability of an infected animal with clinical signs detect during antemortem, positive on ELISA and negative on PCR, negative during post-mortem inspection, virus surviving in fresh beef	Ph3 x (1-Pam) x(1-Pe) x (Pp) x (Phh) x (RT)	
P4c	Probability of an infected animal with clinical signs detect during antemortem, positive on ELISA and negative on PCR, positive during post-mortem inspection, negative on ELISA and PCR virus surviving in the fresh beef	Ph3 x (1-Pam) x(1-Pe) x (Pp) x (1-Phh) x (Pe) x (Pp) x (RT)	
P4d	Probability of an infected animal with clinical signs detect	Ph3 x (1-Pam) x(1-Pe) x (Pp) x (1-Phh) x	

	during antemortem, positive on ELISA and negative on PCR, positive during post-mortem inspection, positive on ELISA and negative on PCR virus surviving in fresh beef	(1-Pe) x (Pp) x (RT)	
P4e	Probability of an infected animal with clinical signs detect during antemortem, negative on ELISA and PCR, negative during post-mortem inspection, virus surviving in fresh beef	Ph3 x (1-Pam) x (Pe) x (Pp) x (Phh) x (RT)	
P4f	Probability of an infected animal with clinical signs detect during antemortem, negative on ELISA and PCR, positive during post-mortem inspection negative on ELISA and PCR, virus surviving in fresh beef	Ph3 x (1-Pam) x(Pe) x (Pp) x (1-Phh) x (Pe) x (Pp) x (RT)	
P4g	Probability of an infected animal with clinical signs detect during antemortem, negative on ELISA and PCR, positive during post-mortem inspection positive on ELISA and negative on PCR, virus surviving in fresh beef	Ph3 x (1-Pam) x (Pe) x (Pp) x (1-Phh) x (1-Pe) x Pp X (RT)	
P4h	Probability of an infected animal with clinical signs not detect during antemortem, detected during post-mortem inspection positive on ELISA and PCR, virus surviving in fresh beef	Ph3 x (Pam) x (1-Phh) x (1-Pe) x (Pp) x (RT)	
P4i	Probability of an infected animal with clinical signs not detect during antemortem, detected during post-mortem inspection negative on ELISA and PCR, virus surviving in fresh beef	Ph3 x (Pam) x (1-Phh) x (Pe) x (Pp) x (RT)	
P4j	Probability of an infected animal with clinical signs not detect during antemortem and post-mortem inspection and virus surviving in fresh beef	Ph3 X (Pam) x (Phh) x (RT)	
Pabattoir	Probability of an infected meat at the abattoir with FMD virus	P4a+P4b+P4c+P4d+P4e+P4f+P4g+P4h+P4i+P4j	
P_{fmd}	The probability of FMD virus occurrence in fresh beef products	P_{fmd}=Pfarm+Pfeedlot+Pabattoir	(Vose, 2008)

Table 3.2 Summary of inputs from expect survey used in the modelling of the likelihood of FMD

					Certainty		
	Min	Middle	Max	Pert	Expert	Observed	Total
Probability for no lesions developing in an animal when infected with FMD							
1	0	0,05	0,1	0,05	3	5	15
2	0	0,1	0,3	0,25	4	4	16
3	0,15	0,2	0,25	0,20	5	4	20
4	0	0,1	0,2	0,10	5	3	15
5	0	0,01	0,05	0,02	3	2	6
6	0,6	0,65	0,7	0,65	4	2	8
Probability of not doing clinical surveillance in the FMD free zone at the farm level							
1	0,4	0,55	0,7	0,55	3	5	15
2	0,8	0,85	0,9	0,85	4	5	20
3	0,4	0,5	0,6	0,50	5	5	25
4	0,4	0,5	0,6	0,50	6	4	24
5	0,7	0,75	0,8	0,75	3	3	9
6	0,7	0,75	0,8	0,75	2	2	4
7	0,95	0,97	1	0,97	4	1	4
Probability of not doing clinical surveillance in the FMD free zone at the feedlot level							
1	0,7	0,85	1	0,85	4	4	16
2	0	0,1	0,2	0,10	5	6	30
3	0,1	0,15	0,2	0,15	5	5	25
4	0,65	0,7	0,75	0,70	6	4	24
5	0,8	0,85	0,9	0,85	4	3	12
6	0	0,02	0,05	0,02	2	2	4
7	0,2	0,25	0,3	0,25	4	1	4
Probability of not detecting FMD lesions at the farm level							
1	0,6	0,65	0,7	0,65	4	6	24
2	0,5	0,55	0,6	0,55	4	5	20
3	0,4	0,45	0,5	0,45	3	5	15
4	0,7	0,75	0,8	0,75	5	4	20
5	0,8	0,85	0,9	0,85	3	4	12
6	0,9	0,95	1	0,95	1	3	3
7	0,1	0,15	0,2	0,15	4	1	4
Probability of not detecting FMD lesions at the feedlot level							
1	0,3	0,35	0,4	0,35	2	5	10
2	0,25	0,3	0,35	0,30	5	6	30
3	0	0,1	0,2	0,10	3	5	15
4	0,8	0,85	0,9	0,85	5	3	15

5	0,5	0,6	0,7	0,60	3	3	9
6	0,6	0,65	0,7	0,65	1	2	2
7	0	0,05	0,1	0,05	3	2	6
Probability of not detecting lesions during antemortem inspection							
1	0	0,1	0,2	0,10	6	6	36
2	0,5	0,6	0,7	0,60	6	2	12
3	0,1	0,3	0,5	0,30	4	5	20
4	0	0,03	0,05	0,03	5	4	20
5	0	0,1	0,3	0,12	4	3	12
6	0	0,2	0,4	0,20	5	3	15
7	0,4	0,5	0,6	0,50	4	1	4
The probability of not detecting lesions during meat inspection when the head and hooves are removed							
1	0,4	0,5	0,6	0,50	6	5	30
2	0	0,1	0,2	0,10	6	6	36
3	0,2	0,25	0,3	0,25	4	5	20
4	0	0,01	0,02	0,01	4	4	16
5	0,15	0,2	0,25	0,20	4	4	16
6	0,2	0,25	0,3	0,25	5	2	10
7	0	0,1	0,2	0,10	4	2	8

The overall likelihood at the farm level was calculated by adding the high-risk pathways in the farm component of the model. The resulting likelihood that was calculated from the farm was nevertheless kept broken down to be used as the initial probabilities for the feedlot component of the model regarding the different events of entry in this component (animal infected vs animal not infected, and animal infected with lesions vs animal infected with no lesions).

The overall likelihood of the feedlot was then used in the same manner for the initial probabilities for the abattoir component of the model (and animal infected with lesions vs animal infected with no lesions). Overall likelihood of FMD survival throughout the value chain (R) was calculated by adding the high-risk pathways in the abattoir component of the model

3.5 Model Implementation

The following assumptions were made:

- Fever and viremia do not occur before 24 -48 hour following infection
- All animals present in the FMD free zone were born in the FMD free zone
- All animals in the FMD free zone are not vaccinated

The model was created in a Microsoft Excel spreadsheet and the @RISK (version 7.5, Palisade Corporation, New York, USA) add-in was used to perform the simulations. The model was run for 100,000 iterations using Latin hypercube sampling of input distributions. FMD virus survival was the outcome variable and the inputs included the various mitigation factors (Ahmad, Tameru, Nganwa, Ayanwale, Habtemariam & Fite, 2013; Vose, 1997). The median and percentiles of the results of the simulations were used to quantify the likelihood and its expected variability (Astudillo *et al.*, 1997).

3.5.1 Probability of virus commination

The probability of FMD virus contamination in fresh beef products was calculated as Pfmd =Pfarm +Pfeedlot +Pabattoir where Pfarm = P2a+P2b+P2c+P2d+P2e; Pfeedlot = P3a+P3b+P3c+P3d+P3e+P3f+P3g+P3h+P3i+P3j and Pabattoir= P4a+P4b+P4c+P4d+P4e+P4f+P4g+P4h+P4i+P4j

3.5.2 Sensitivity Analysis

Spearman’s ranked correlation coefficients were calculated for all stochastic inputs and the overall likelihood of FMD virus survival. The Spearman’s ranked correlation is preferred to the Pearson regression coefficients due to the monotonic relationship between X and Y rather than the linear relationship (Vose, 2008). The correlation coefficient (r) lies between -1 and 1. Negative values suggest a negative relationship while positive values suggest a positive relationship. The correlation coefficient of more than 0.7 suggests highly correlation between the two variables. Correlation coefficients of between 0.5 and 0.7 suggest a moderate correlation, while those between 0.3 and 0.5 suggests a low correlation. A correlation coefficient (r) of less than 0.3 indicates little correlation.

3.5.3 Foot and Mouth Disease Scenarios Modelling

3.5.3.1 Scenario 1: Change in the FMD prevalence

In this scenario, the initial prevalence was changed and the effect on the overall likelihood of FMD in the FMD free zone was evaluated. In order to assess the impact of the increase in the initial prevalence the input value was increased by 10 fold (3.83 x 10^{-5}), 100 fold (3.83 x 10^{-4}), 1000 fold (3.83 x 10^{-3}) and 10 000 fold (3.83 x 10^{-2}).

3.5.3.2 Scenario 2: Change in the likelihood of infected animal showing clinical signs

The probability of not detecting clinical signs will be influenced by the presence or absence of lesions in clinically infected animals. The impact of the level subclinical cases undetected on the likelihood of FMD virus in the fresh beef products was assessed by doubling (0.4) and tripling (0.6) the likelihood of an animal been asymptomatic.

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CHAPTER 4

4.1 Results

The median probability of FMD virus contaminating fresh beef products was calculate as 5.7×10^{-10}**(Figure 4.1; Table 4.1).**

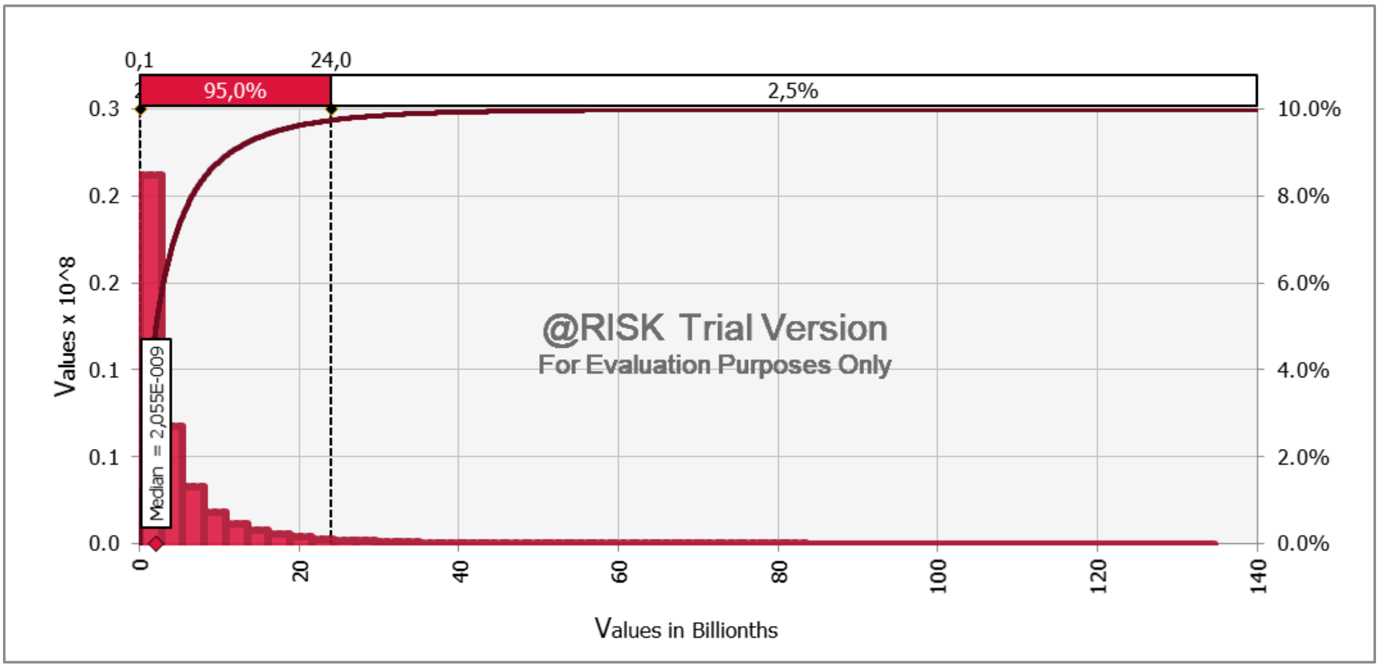

Figure 4.1 The likelihood of foot and mouth disease virus contamination of fresh beef products, South Africa

Table 4.1 The probability of introducing foot and mouth disease virus into the FMD free zone from fresh beef products, South Africa

Description	Probability
Median	2.1×10^{-9}
Minimum	3.5×10^{-14}
Maximum	1.3×10^{-7}
Mode	1.2×10^{-10}
5%	1.1×10^{-10}
95%	1.7×10^{-8}

4.1.1 Sensitivity analysis

The initial prevalence of FMD (r=0. 72) in the country and the asymptomatic status of FMD infected cattle (r=0. 59) were strongly associated with the probability of foot and mouth virus contamination of fresh beef products in the FMD free zone. Weak correlations were observed between FMD transmission rate (r=0. 17), ante-mortem (r=0. 09), post-mortem inspections during head and hoof inspections (0.09) and the likelihood of FMD virus contamination of fresh beef products from the FMD free zone. Negative correlations between the sensitivity of PCR as a confirmatory test (-0.02) and the likelihood of FMD virus contamination of fresh beef products **(Figure 4. 2).**

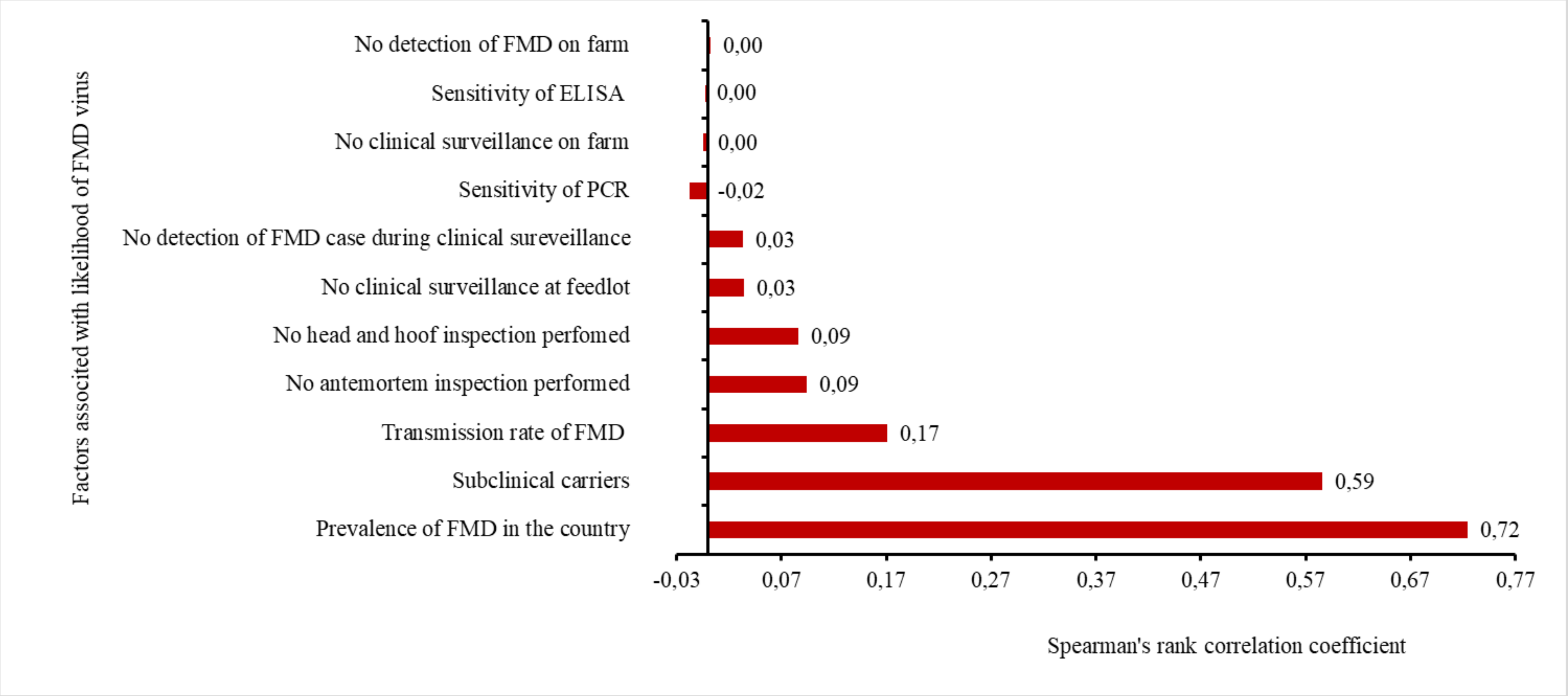

Figure 4. 2 Sensitivity analysis for factors associated with the likelihood of foot and mouth disease virus contamination of fresh beef products, South Africa

4.1.2 Foot and mouth disease probability scenarios

The initial prevalence of FMD in the country and the probability of an animal showing FMD virus clinical signs were strongly associated with the likelihood of foot and mouth disease virus contamination of fresh beef products. Increasing the initial prevalence's of FMD from 3.4×10^{-7} by 10 to 100000 folds shows an increasing trend in the probability of FMD in the FMD free zone **(Table 4.2; Figure 4.3-4.7)**. Similarly, increasing the probability of an animal not showing clinical signs of foot and mouth virus infection increased the probability of FMD virus in fresh beef products in the FMD free zone **(Table 4.2; Figure 4.8, 4.9).**

Table 4.2 Changes in the probability of foot and mouth virus in the FMD free zone as (1) the prevalence of FMD and (2) the probability of subclinical cases increases

Factor	Input value	Likelihood of FMD in the free zone
Prevalence of FMD*		
	3.4×10^{-6}	2.1×10^{-8}
	3.4×10^{-5}	2.1×10^{-7}
	3.4×10^{-4}	2.0×10^{-6}
	3.4×10^{-3}	2.0×10^{-5}
	3.4×10^{-2}	1.6×10^{-4}
Subclinical infections‡		
	0.4	3.6×10^{-9}
	0.6	5.2×10^{-9}

*Increasing the initial prevalence of foot and mouth disease by 10 to 100000 folds

‡Increasing the probability of subclinical foot and mouth virus infected cases

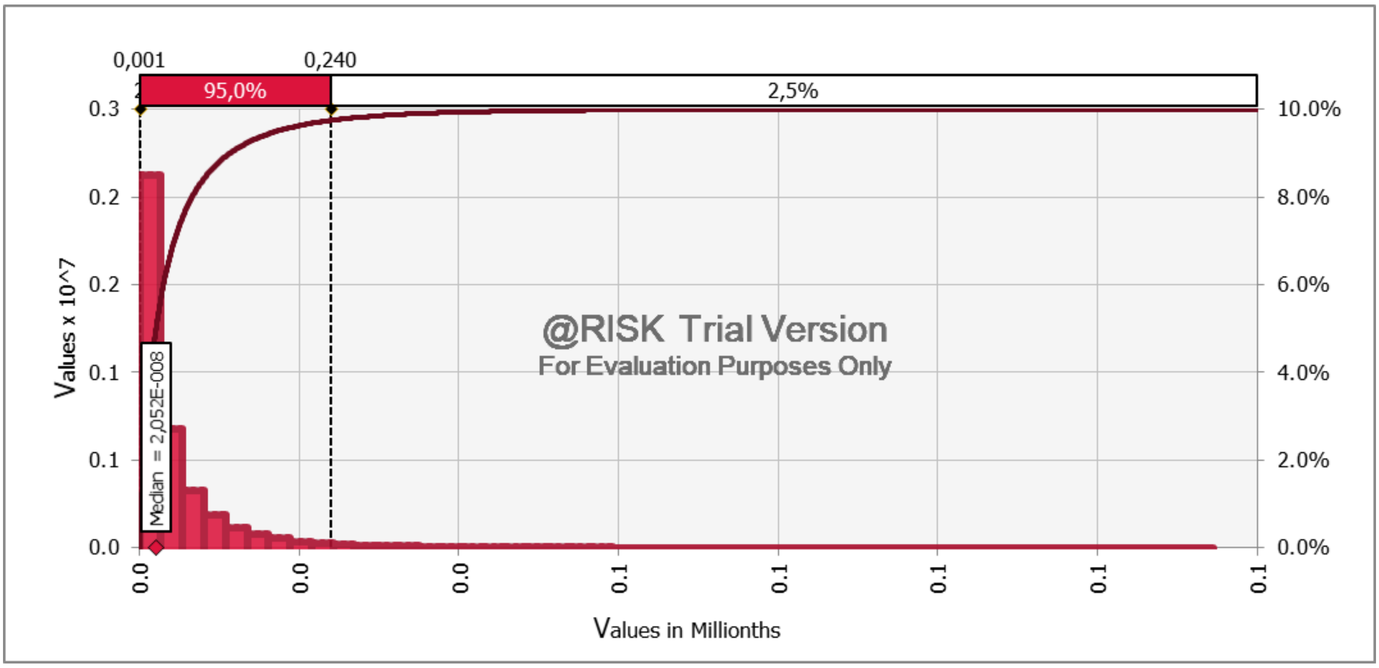

Figure 4.3 The likelihood of foot and mouth disease virus contamination of fresh beef products when the prevalence of the disease is increased to 3.4×10^{-6}

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone was determined as 2.1×10^{-8} (mean: 4.5×10^{-8}, SD: 7.0 $x10^{-8}$) **(Figure 4.3; Table 4.1).**

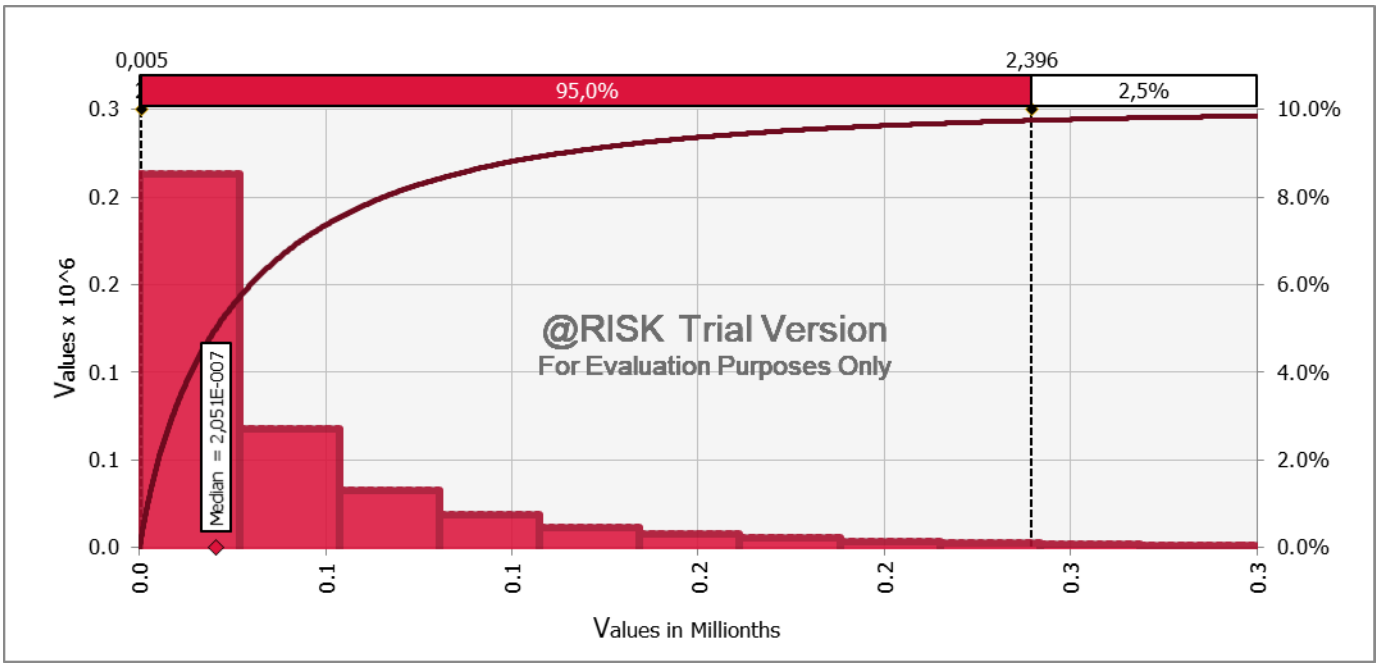

Figure 4.4 The likelihood of foot and mouth disease virus contamination of fresh beef products when the prevalence of the disease is increased to 3.4×10^{-5}

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone was determined as 2.1×10^{-7} (mean: 4.5×10^{-7}, SD: 7.0 x 10^{-7}) **(Figure 4.4; Table 4.1).**

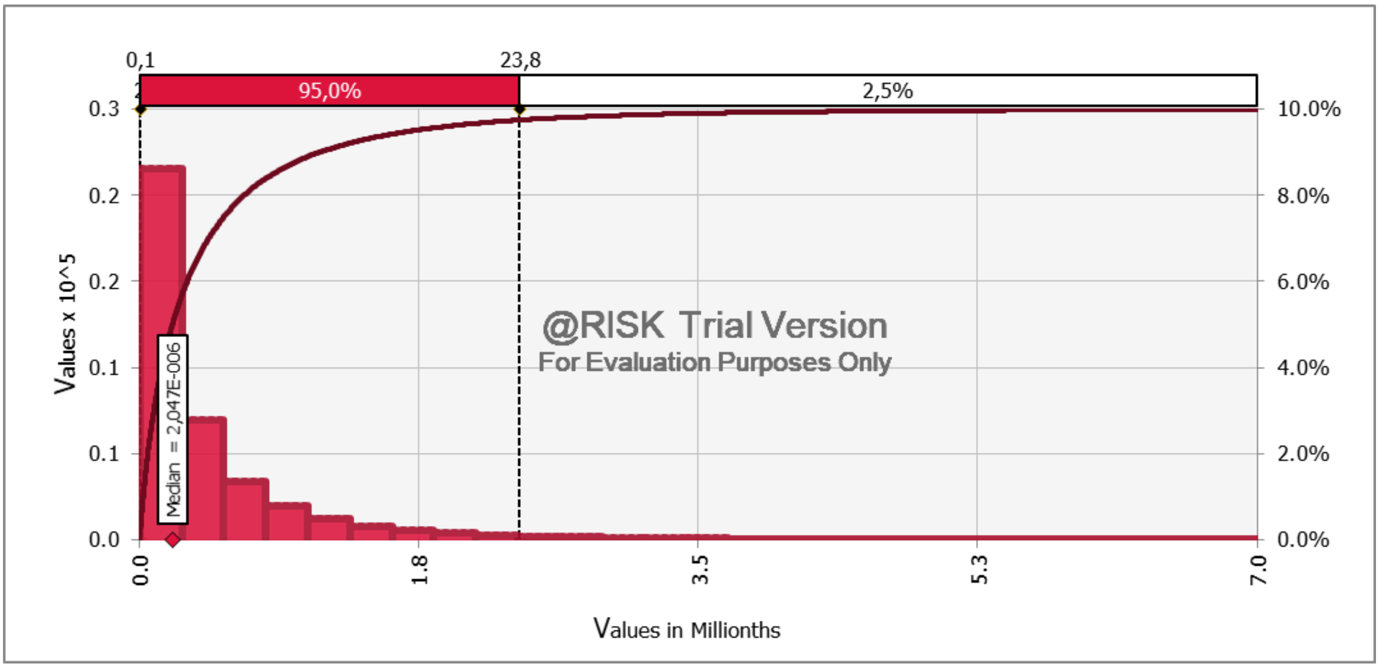

Figure 4.5 The likelihood of foot and mouth disease virus contamination of fresh beef products when the prevalence of the disease is increased to 3.4×10^{-4}

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone was determined as 2.0×10^{-6} (mean: 4.5 x10^{-6}, SD: 6.9 x 10^{-6}) **(Figure 4.5; Table 4.1).**

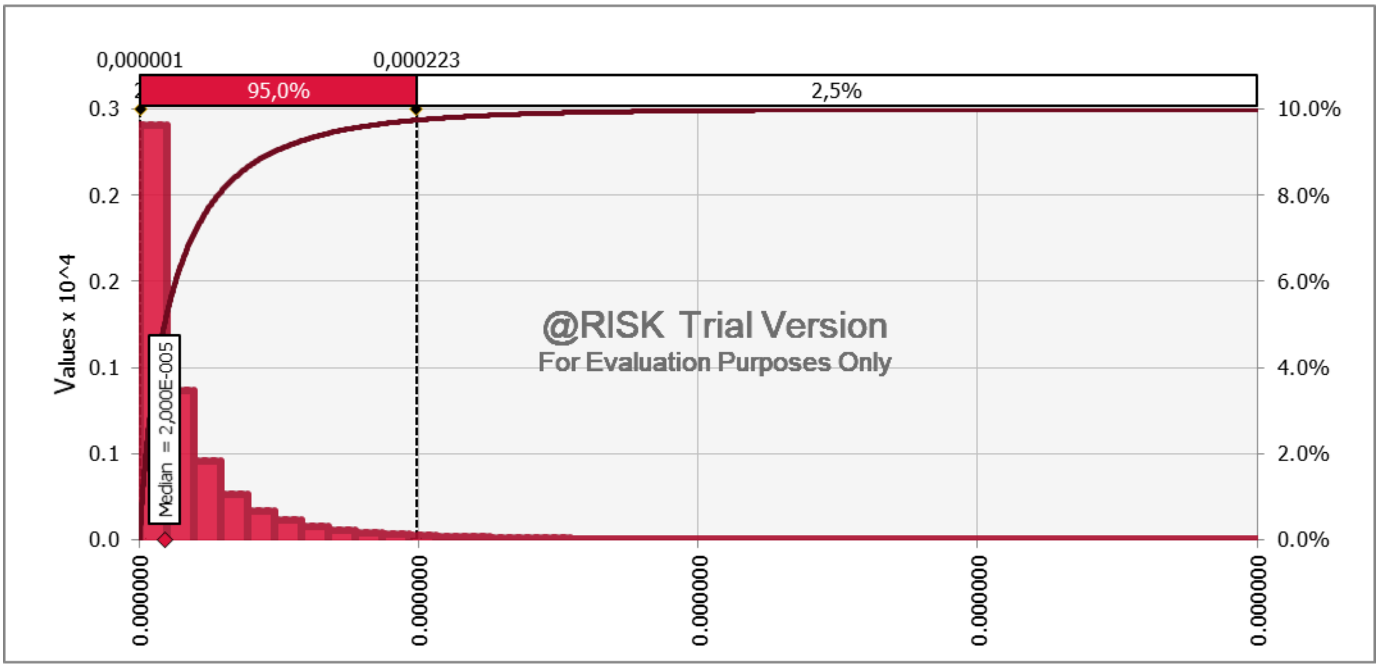

Figure 4.6 The likelihood of foot and mouth disease virus contamination of fresh beef products when the prevalence of the disease is increased to 3.4× 10^{-3}

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone was determined as 2.0×10^{-5} (mean: 4.2 x10^{-5}, SD: 6.4 x 10^{-5}) **(Figure 4.6; Table 4.1).**

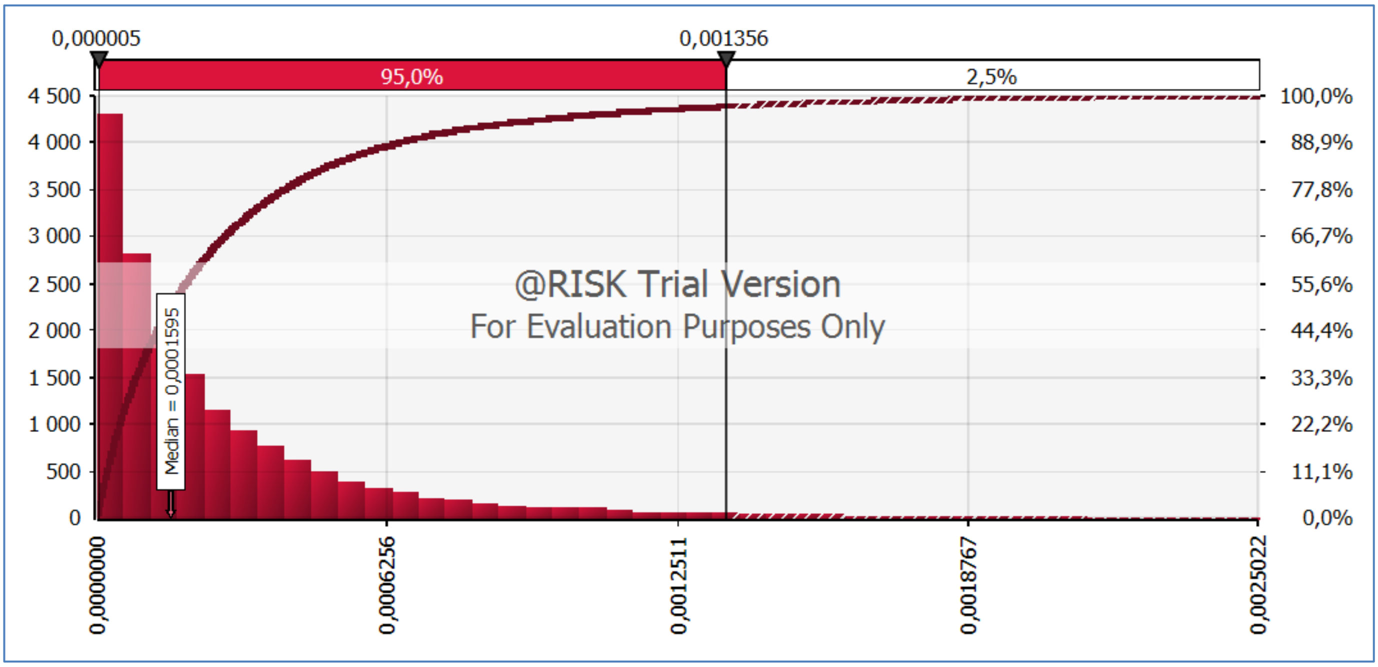

Figure 4.7 The likelihood of foot and mouth disease virus contamination of fresh beef products when the prevalence of the disease is increased to 3.4×10^{-2}

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products if the prevalence for FMD in the FMD free zone is multiplied by 100000: 1.6×10^{-4} (mean: 2.8 x10^{-4}, SD: 3.5 x10^{-4}) **(Figure 4.7; Table 4.1).**

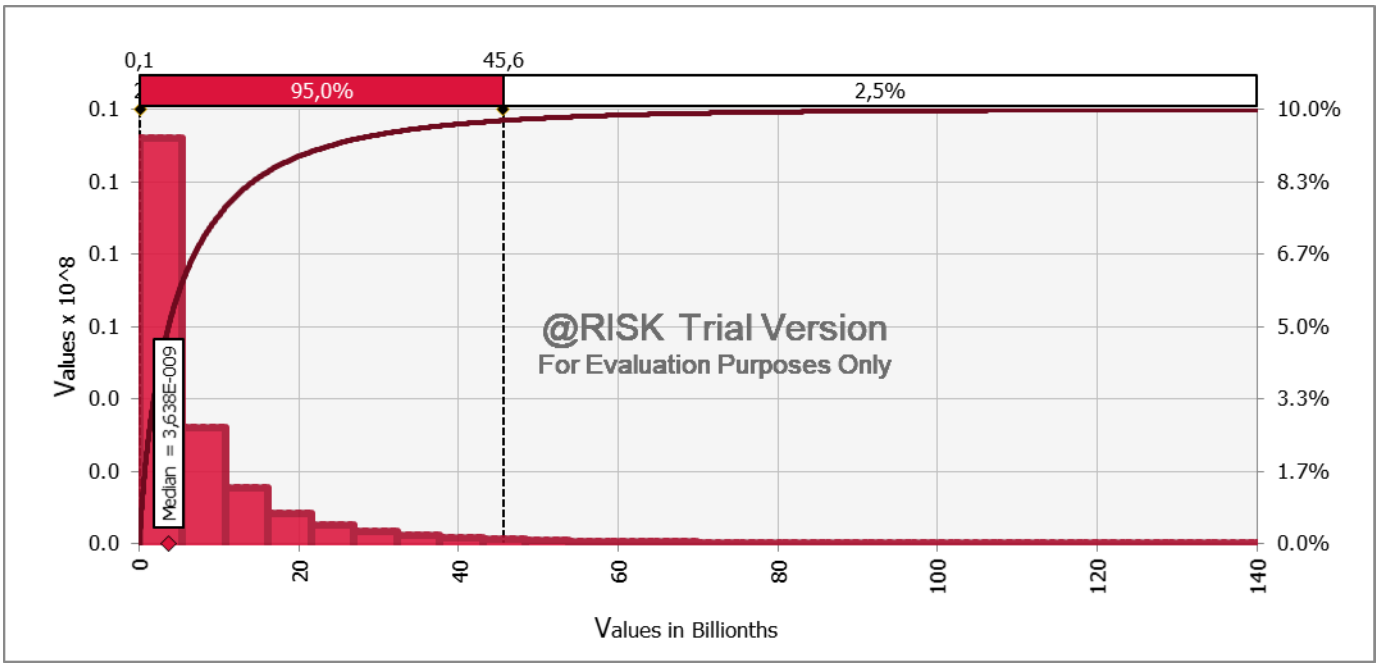

Figure 4.8 The likelihood of introducing foot and mouth disease virus when the probability of subclinical carriers is doubled to 0.4.

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone in the event that the probability of subclinical FMD carriers is doubled was determined as 3.6 $\times 10^{-9}$ (mean: 8.3 x 10^{-9}, SD: 1.3 x10^{-8}) **(Figure 4.8; Table 4.1).**

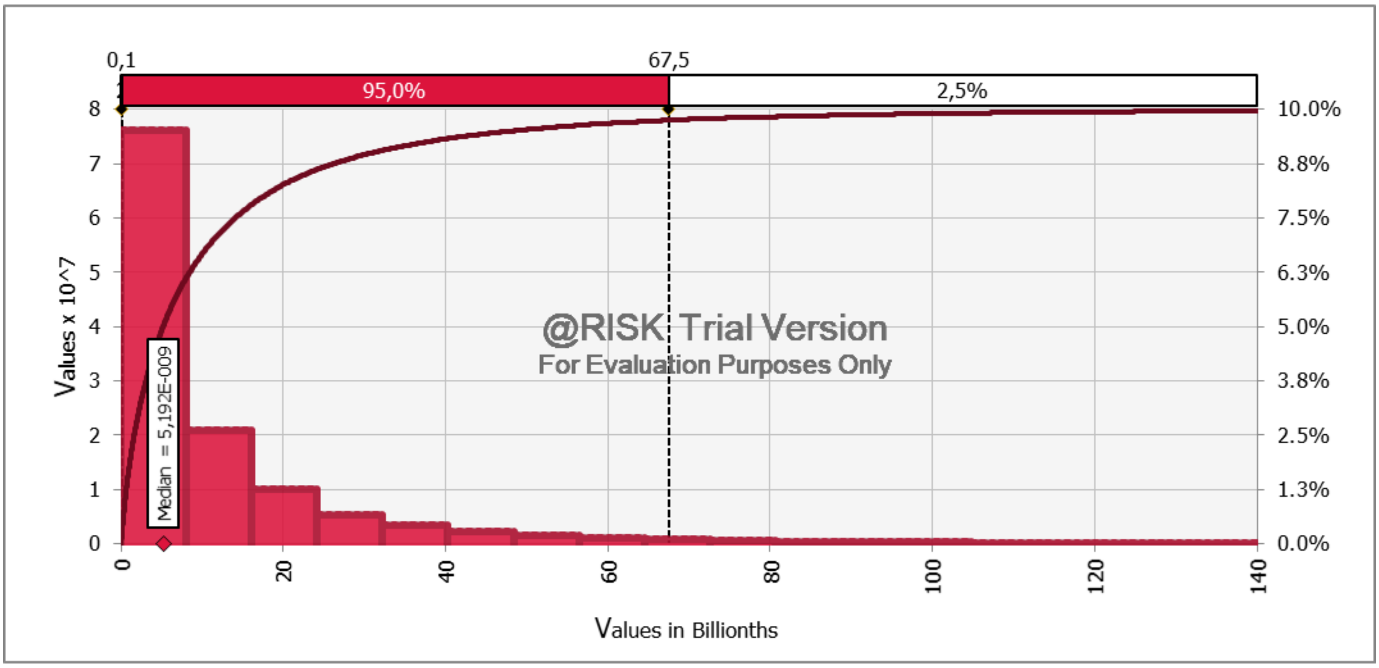

Figure 4.9 The likelihood of foot and mouth disease virus contamination of fresh beef products when the probability of subclinical carriers is tripled to 0.6.

The overall likelihood of foot and mouth disease virus surviving throughout the value chain in beef and beef products in the FMD free zone in the event that the probability of subclinical FMD carriers is tripled was determined as 5.2×10^{-9} (mean: 1.2 x 10^{-8}, SD: 1.9 x 10^{-8},) **(Figure 4.9; Table 4.1).**

CHAPTER 5

5.1 Discussion

Presence of FMD in an area acts as a trade barrier, yet the eradication of the disease in South Africa is not feasible due to the presence of wildlife species (Lebea, PJ; Bhoora, RV; Maree, 2014). The latter is known to be a reservoir for the FMD virus (Lebea, PJ; Bhoora, RV; Maree, 2014). Should an FMD outbreak occur in the FMD free zone in South Africa, the OIE status of zonal FMD freedom without vaccination will be withdrawn. The financial implications, the responsibility to contain and eradicate the disease as a result of the loss of the FMD free status falls on the state. All exports to FMD free countries of beef, pork and lamb cease thereby affecting the revenue of the various industries involved such as farmers and producers. In countries where FMD cannot be eradicated, it is thus feasible to implement zoning or compartmentalisation for areas or facilities that are able to meet the requirements for FMD free status, in order to facilitate trade (World Organisation for Animal Health, 2017). Therefore, zoning remains the most valuable method of controlling the disease to open trade opportunities for the export of fresh beef products to FMD free countries or zones. During the 2011 FMD outbreak, South Africa lost its FMD freedom status resulting in decreased export of fresh beef products. After the outbreak, the declaration of freedom by the OIE exports of fresh beef products increased (Department of Agriculture Forestry and Fisheries, 2017). In this study, a quantitative risk assessment methodology was used to assess the probability of FMD in the FMD free zone in the presence of current mitigation strategies throughout the value chain. The results of this study show that the likelihood of FMD virus in the fresh beef products with the current mitigation measures in the FMD free zone was negligible (2.1×10^{-9}). This is similar to what Moutou et al. (2011) observed regarding the likelihood of introducing foot and mouth disease into Russia and Europe from Georgia, Armenia and Azerbaijan in the presence of a number of mitigation factors. They attributed their conclusions to the fact that the prevalence of disease and capacity of the virus to survive was negligible.

The initial prevalence of FMD disease in the country was strongly associated with the increased likelihood of FMD virus contamination of fresh beef products in the FMD free zone. The prevalence of a disease in the area being linked to the likelihood of exporting the disease has also been proved in studies involving other diseases besides FMD. For example, in the study by Woube et al. (2015) in Ethiopia, the prevalence of contagious bovine pleuropneumonia in the country was associated with the likelihood of exporting infected live cattle.

In the present study, the results of the computational model show that as the overall prevalence of disease in the country increases, likelihood of FMD virus contamination of fresh beef products in the FMD free zone also increases. Similarly, Yu et al. (1997) reported an increase in the likelihood of introduction of FMD as the prevalence of infected herds increases. In view of this, it implies that reducing the prevalence of disease in the country plays an important role in reducing the likelihood of the disease spreading to FMD free countries. Therefore, current efforts to mitigate the likelihood of FMD outbreaks in the country must be continued and strengthened to reduce the likelihood of exposure of the susceptible population to foot and mouth disease. These efforts include but not limited to maintenance of fencing, movements and movement control, vaccination and active surveillance in infected zones.

Vosloo et al. (2002) reported that FMD virus serotypes (SAT types) found in Africa cause milder clinical signs compared to those in other countries and the researchers attributed this to the extensive nature of livestock production system in most areas in Africa. In addition, Garland and Clercq (2011) reported that carrier status can occur in up to 50% of cattle and this may be related to the FMD serotypes. Therefore, depending on the serotype a large number of infected animals may be asymptomatic, therefore, a source of infection for susceptible animals. these reports are supported by findings of this study, that shows that the asymptomatic status of FMD infected cattle was positively associated with the likelihood of FMD virus contamination of fresh beef products in the FMD free zone. This is not surprising as asymptomatic FMD carriers SAT type 1 and 3 were associated with the most recent 2011 FMD outbreak in KwaZulu Natal, South Africa. Serological testing was positive on liquid phase ELISA and the virus was confirmed with PCR (Department of Agriculture Forestry and Fisheries, 2011). Similarly, Sutmoller (2001) reported that the probability of importing FMD into the Caribbean and the United States of America was associated failure to detect FMD clinical signs during ante- and post-mortem examinations.

According to this study, ante and post-mortem had a minor effect on the overall likelihood of FMD virus contamination of fresh beef products in the FMD free zone. This contrasts findings by Yu et al. (1997) who reported that failure to detect FMD at the farm, feedlot, and abattoir increases the likelihood of importing FMD in a country. It also contrasts findings by Garland and Clercq (2011), Sutmoller (2001) and Paton et al. (2010) who also reported that pre and post-slaughter control measures including antemortem and post-mortem inspections were important in reducing the likelihood of FMD occurance.

According to Sutmoller (2001) despite the possibility of asymptomatic animals being missed during clinical examination, the overall likelihood of FMD in exporting countries where disease surveillance is practised at farm, feedlot and abattoir level tends to be negligible. Therefore, the results of this study underscore the role inspection services in the mitigation the likelihood of FMD from exporting countries. However, it is important to note that clinical examination or looking for presenting clinical signs alone is not enough to mitigate the likelihood of FMD as animals may be asymptomatic. Serological and diagnostic surveillance is therefore important in early detection for FMD outbreaks

The protocol currently in the FMD free zone allows only for suspect cases to be screened for FMD. Serological surveillance is not routinely practised in the FMD free zone on the FMD susceptible population. As a result, the detection of FMD using screening and confirmatory tests for

FMD played no significant role in reducing the likelihood of FMD virus contamination of fresh beef products in the FMD free zone.

Findings reported here showed that there were no correlations between maturation, deboning and removal of blood vessels, and lymph nodes and the likelihood of FMD virus contamination of fresh beef products in the FMD free zone in this study. This in contrast to what Paton, et al. (2010) who observed that the combination of maturation, deboning and removal of blood vessels, and lymph nodes reduce the likelihood of contamination of beef with FMD virus. Similarly, no correlations between the ELISA testing and the likelihood of FMD virus contamination of fresh beef products in the FMD free zone was observed in this study. Which also contrasts with what Jori et al. (2009) who reported a reduction in the likelihood of an infected animal going undetected when an additional ELISA test was implemented. Failure to observe similar correlations as has been reported in another study (Jori *et al.*, 2009). Nonetheless, the researcher is of the view that all efforts including bleeding, maturation, deboning and lymph node and blood vessel removal must still be implemented to enhance further reduction of the likelihood of FMD virus being exported (Sutmoller, 2001).

Thornley and France (2009) reported that the rate of FMD virus discharged increases during the exponential stage of the FMD outbreak and once control or eradication measures are implemented within farm infectivity decreases. This has a reciprocal effect on the decrease in infectious strength. Furthermore, the highly infectious character of the FMD virus further necessitates the need for movement control during the outbreak. Therefore, it is not surprising the rate of transmission in this study was associated with the likelihood of FMD virus in the FMD free zone.

5.2 The limitations of the study

The unavailability of pertinent data was a limitation for this study, this necessitated the use of estimates provided by experienced and expert state veterinarians. Therefore, it is possible that the respondents might have suffered from recall bias which will have introduced a systematic error in the study. In addition, information regarding the pathogenesis of SAT types in South Africa was limited therefore data from other SAT types had to be used. It is possible that this could have influenced the level of likelihood of FMD virus contamination of fresh beef products observed in this study. Thrushfield et al. (2005) suggest that personnel, vehicles and equipment's, airborne transmission of cattle, and transportation are important in the FMD transmission, but these were not included in the computation of FMD virus in the FMD free zone as the likelihood for each measure could not be quantified.

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CHAPTER 6

6.1 Conclusion and recommendations

The overall likelihood of FMD virus contamination of fresh beef products in the FMD free zone was negligible, but the prevalence status of the country was an important determinant of the likelihood of FMD virus contamination of fresh beef products. Moreover, an increase in the prevalence of FMD increased the likelihood of FMD virus contamination. Therefore, it is important for regulators and farmers to realise that the FMD free status must be maintained always and not only during an FMD outbreak or when applying for FMD freedom. Educating farmers and training of employees is crucial in preventing FMD introduction and spread.

Information regarding the pathogenesis and clinical presentation of FMD SAT types in South Africa is limited. It is known that the African SAT types are likely to be milder compared to those from other continents. Therefore, more research needs to be done to investigate the South African SAT FMD types as it impacts on clinical presentation and early diagnosis of FMD virus outbreak. The importance of this is underscored by the fact that the asymptomatic status of the FMD infected cattle and transmission rate and ante and post mortem examination were correlated with the likelihood of FMD virus contamination in fresh beef products in the free zone. These factors are influenced by the characteristics of the FMD SAT type involved in the outbreak.

The absence of lesions was the second most important factor contributing to the likelihood of FMD virus contamination of fresh beef products suggesting that clinical examination alone is not the most effective surveillance tool for the FMD virus. Therefore, active laboratory surveillance must be implemented at farm and feedlot to reduce the likelihood of FMD virus contamination of fresh beef products in the FMD free zone. Serological and PCR tests have been reported to have a significant impact on detection of subclinical cases and early response to FMD outbreaks within compartment or establishments that participate in international trade.

In addition, strict biosecurity, movement control, maintenance of fences, traceability, training and education of all stakeholders in the food value chain in line with the OIE guidelines and country protocols are also important in reducing the likelihood of FMD virus contamination of fresh beef products in the FMD free zone. Government and beef industry partners must work together to build capacity in FMD control at national, provincial and community levels. In this way, the likelihood of an FMD outbreak will be kept to the minimum.

CHAPTER 7

7.1 Addendum A

Introduction

South Africa uses zoning for FMD. The control measures differ in each zone according to the Veterinary Procedural Notice for Foot and Mouth Disease control in South Africa in June 2012.

Infected zone is a clearly defined geographical area within RSA in which FMD is endemic due to the presence of FMD carrier buffalo.

i. Routine FMD vaccination of cattle is practised.
ii. Strict movement control of live animals and products is applicable.
iii. Intensive FMD clinical, serological and virological surveillance is conducted.

Protection zone is a clearly defined geographical area between the infected and FMD free zones. The protection zone in South Africa is not part of the FMD free zone. It is subdivided into two subzones:

a). Protection Zone with Vaccination:

The protection zone with vaccination is a clearly defined geographical area adjacent to the infected zone.

i. Routine FMD vaccination of cattle is practised.
ii. No buffalo should be allowed in the protection zone with vaccination in order to maintain a buffalo free zone between the FMD infected and free zones.
iii. Strict movement control of live animals and products is applicable.
iv. Intensive FMD clinical, serological and virological surveillance is conducted.

b). Protection Zone without Vaccination:

The protection zone without vaccination is a clearly defined geographical area adjacent to the FMD free zone and some international boundaries.

i. No FMD vaccination is practised.
ii. Only FMD free buffalo are allowed to be kept in the protection zone without vaccination. Keeping and movement of FMD free buffalo in the Protection Zone without vaccination is subject to the specific requirements for fencing and regular testing at the cost of the owner, or manager, of such buffalo (details in the Buffalo Procedural Manual).
iii. Strict movement control of live animals and products is applicable.
iv. Frequent FMD clinical, serological and virological surveillance is conducted.

FMD **Free zone** is a clearly defined geographical area comprising the entire RSA, excluding the infected and protection zones. It includes the inspection area of the FMD free zone. No FMD vaccination is practised.

a). Inspection Area of the FMD **free zone (High surveillance zone):**

The **inspection area of the** FMD **free zone** is a clearly defined geographical area within the FMD free zone, adjacent to the protection zone and some international boundaries. It forms part of the controlled area as legislated.

i. Movement control of the live game is applicable.
ii. Regular FMD clinical, serological and virological surveillance is conducted.

This study will include a likelihood assessment along the beef value chain in the FMD free zone. Surveillance is only conducted in the inspection area of the FMD free zone and no vaccination and surveillance occur in the rest of the FMD free zone. Animals in the FMD free zone are therefore considered to be naïve since they are unvaccinated. In the event of an FMD outbreak, the likelihood to the National herd and the health status of the herd would be compromised. In addition, no active surveillance occurs in the FMD free zone, we rely on effective passive surveillance to detect the presence of FMD. The questionnaire aims to determine the likelihood of FMD survival throughout the value chain based on the current risk reduction system. The questionnaire was directed to state veterinarians at the provincial and national level throughout the country. The aim is to determine the likelihood that a beef commodity poses to a country that is FMD free of FMD. The likelihood is calculated according to the epidemiology of FMD, level of surveillance and detection and processing procedures in the abattoir. Since the OIE has approved the FMD free zone status, how much emphasis is placed on monitoring and surveillance of FMD. Secondly how effective is the current processing procedures that are currently in place at mitigating the likelihood of FMD survival in a commodity that is destined to be exported to an FMD free country.

7.2 Expert opinion: Foot and Mouth Disease Questionnaire

7.2.1 Farm and feedlot

According to the FMD VPN, no active surveillance is practised in the FMD free zone. Therefore, passive surveillance is important when detecting FMD. It was important to determine how effective and thorough clinical or passive surveillance for FMD is conducted in the FMD free zone of South Africa at farm and feedlot level. Since this is a passive surveillance system it relies on the farmer or trained staff to report suspects cases to the veterinarian. There are few commercial farms and feedlots that have access to a veterinarian; therefore, clinical surveillance is conducted every day by the farm staff

How many farms among 100 are doing clinical surveillance FOR FMD in the free zone?

Minimum	Maximum	Most likely	Confidence

How many feedlots among 100 are doing clinical surveillance for FMD in the free zone?

Minimum	Maximum	Most likely	Confidence

Detection of the diseases relies on clinical observation by farm staff and routine visits by the veterinarian. Farm staff in the controlled zones must at all time be aware and must keep alert for FD clinical signs. However, in the FMD free zone where FMD is a lower likelihood, might give a false sense of complacency toward FMD. How likely would farm staff be aware or trained to look for FMD clinical signs in the event that FMD moves into the FMD free zone. Especially along the borders of the FMD controlled areas and borders of neighbouring countries.

How many animals will be detected for FMD if 100 FMD positive animals in a herd were observed in the FMD free zone at the farm level?

Minimum	Maximum	Most likely	Confidence

How many animals will be detected for FMD if 100 FMD positive animals in a herd were observed in the FMD free zone at feedlot level?

Minimum	Maximum	Most likely	Confidence

FMD virus has 7 serotypes. Each serotype presents differently clinically. In South Africa there are only 3 sat types that are currently present, namely Sat 1, Sat 2 and Sat 3. However, in September 2000, there was an outbreak of serotype O was diagnosed in KwaZulu Natal. Since it was introduced with gally waste from a bypassing ship at Durban harbour and fed to pigs in an untreated swirl, serotype O can therefore not be regarded as a serotype in South Africa. It is therefore important to establish the likelihood that an animal will show clinical signs taking into account that the sat types present differently.

In case of an outbreak in the FMD free zone among 100 animals how many will show clinical signs?

Minimum	Maximum	Most likely	Confidence

7.2.2 Abattoir

According to the Red Meat Safety Act, 2000 (Act no. 40 of 2000) a meat inspector must conduct the ante mortem inspection. The ante mortem inspection must be conducted less than 24 hours after arrival. The ante mortem inspection may also be conducted by a meat examiner. However, in some instances, the abattoir does not have enough meat inspectors to do the post mortem and ante mortem inspections. There is a likelihood that diseases are not detected in the lairages before entering the slaughter line.

Among 100 FMD infected animals that arrived at the abattoirs how many animals with FMD lesions will be detected during the ante mortem inspection?

Minimum	Maximum	Most likely	Confidence

According to the Red Meat Safety Act, 2000 (Act no. 40 of 2000) Inspection of cattle heads and feet must be inspected by observation, the registered inspector must observe and palpate the tongue, observe lips, gums, hard and soft palates. No carcass, part thereof, rough or red offal may be sold or dispatched from an abattoir unless inspected and approved by a registered inspector. Depending on the number of meat inspectors and the number of carcass are assessed will depend on how well the post mortem inspection is conducted and whether disease lesions are detected.

Among 100 animals presenting FMD lesions at Head and hoof inspection, how many will be detected?

Minimum	Maximum	Most likely	Confidence

Since most disease sequester in lymph nodes, most if not all have to be removed at some stage of processing of the carcass. The likelihood of FMD surviving in the carcass may be influenced by the presence of the lymph nodes.