Use of a modified Hazard analysis and critical control points (HACCP) approach for the evaluation of bovine brucellosis control programmes

By

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Declaration

I, Tapiwa Makwavarara, do hereby declare that the research presented in this dissertation, was conceived and executed by myself, and apart from the normal guidance from my supervisors, I have received no assistance.

Neither the substance, nor any part of this dissertation has been submitted in the past, or is to be submitted for a degree at this University or any other University.

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Tapiwa Makwavarara

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Date

Dedication

I dedicate this dissertation to my late mother Charity Agnes Makwavarara and my son Zvikomborero Ryan Mukarati. They are the reason why I never give up.

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Firstly my gratitude goes to the Almighty God who sustains me.

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APHIS	Animal and Plant Health Inspection Service
CCPs	Critical Control Points
CFT	Complement Fixation Test
DAFF	Department of Agriculture Forestry and Fisheries
DEFRA	Department for Environment, Food and Rural Affairs
ELISA	enzyme-linked immunosorbent assay
c ELISA	compétitive ELISA
i ELISA	indirect ELISA
HACCP	Hazard Analysis and Critical Control Points
HIV	Human Immuno-Deficiency Virus
OIE	World Organisation for Animal Health
POPAs	Points of particular attention
MRT	Milk Ring Test
RES	Reticulo-endothelial System
RT-PCR	Real Time-Polymerase Chain Reaction
RBT	Rose Bengal Test
RB51	Strain RB51
SAT	Serum Agglutination Test SSA Sub-Saharan Africa
S19	Strain 19
S-LPS	Smooth Lipopolysaccharide
TB	Tuberculosis
USDA	U.S. Department of Agriculture's

Abstract

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Degree : **MSc (Animal/Human/Ecosystem Health)**

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Brucellosis is a zoonotic disease caused by bacteria of the genus *Brucella*. It is essentially a disease of animals with humans as an accidental host. Brucellosis has a negative socio-economic impact through its effect on bovine reproductive performance, its restriction on international trade of animals and their products and debilitating disease in humans (Corbel, 2006). Livestock and milk production are important contributors to food security and incomes. In humans it causes disease characterised by equivocal diagnosis and multisystem involvement that can progress to a chronic debilitating infection and possibly death. Six species are mainly responsible for brucellosis in animals and humans which are *B. abortus, B. melitensis, B. canis, B. ovis, B. suis* and *B. neotomae*. Other isolates have been found in marine animals including *B. pinnipediae, B. maris* and *B. cetaceae* (Cloeckaert, 2007; Corbel, 2006). Most developing countries experience a high prevalence of brucellosis and it is regarded as a neglected zoonosis by the World Health Organization (WHO, 2018).

A 2015 survey of ten SADC countries identified only rudimentary programmes in operation and no formal method of assessing their value or effectiveness (Abernethy, pers. comm.) These countries would benefit from an evaluation tool that can assess the effectiveness of their current brucellosis control programmes.

Hazard Analysis and Critical Control Points (HACCP) has been used for many years as a monitoring tool in food production, pharmaceuticals and engineering industries. Recently it has also been utilised to assist disease control programmes (Dupont, 2007; McAloon *et al.*, 2015; Noordhuizen & Welpelo, 1996; Van Gelderen, 2015).

This project utilised the basic principles of HACCP to develop an evaluation tool for bovine brucellosis programmes at local, regional or international level, in a hope that the end result can be adopted as a standard framework for evaluating brucellosis disease control programmes. A process flow of a brucellosis programme was developed and Critical Control Point (CCP) equivalents identified that permit brucellosis organisms to persist or escape the system. A system of evaluating these CCPs was created and reviewed by selected brucellosis experts using a modified Delphi technique. The project produced a feasible evaluation tool (qualitative checklist) that can be used at different scales to evaluate brucellosis programmes.

Chapter 1: Introduction

Bovine brucellosis is a zoonotic disease caused by bacteria of the genus *Brucella*. It affects multiple species and has profound negative health effects through human, wildlife and livestock disease (McDermott, 2003). It adversely affects reproductive performance in animals and causes debilitating disease in humans. Brucellosis also has negative economic effects through trade restrictions imposed on live animals and their products in endemic areas (Corbel, 2006). Worldwide, it is estimated that over 300 million cattle are infected with brucellosis (De Figueiredo, 2015).

However, the major reason for controlling the disease in animals is due to its impact on human health, where it is characterised by equivocal diagnosis and multisystem involvement that can progress to chronic debilitating disease and possibly death (Wojno, 2016; Franco *et al.*, 2007). Most developed countries have managed to eradicate bovine brucellosis but with substantial costs, whilst many developing countries still encounter high disease prevalence. Financial constraints in developing countries make control difficult and eradication rather elusive (Fensterbank, 1986).

The negative economic consequences associated with bovine brucellosis can be significant, arising from a reduction in productivity, loss of local and international trade and disability adjustable life years (DALYS) in humans (Franc *et al*., 2018). On average, cattle with brucellosis experience a 10% - 25% reduction in milk production and depending on the number of abortions that occur, a 6% - 10% loss of income per animal. There are also other indirect losses through costs from management of the disease in both humans and animals (McDermott *et al*., 2013). There are long term economic benefits from the control and eventual eradication of brucellosis, however, these should be quantified to motivate for funding, especially in developing and/or low income countries. There is not much recent and reliable data available for South Africa but a study by Hesterberg showed for 1990 in South Africa, losses to brucellosis were estimated at R 300 million per annum (Hesterberg *et al.*, 2008).

In South Africa, livestock and milk production are important contributors to food security and household incomes through employment in the livestock industry. The Department of Agriculture, Forestry and Fisheries (DAFF) South African Veterinary Strategy (2016-2026) reported that milk production in 2012 contributed approximately 6.6% of the total agricultural income and predicts that milk consumption between the years of 2012 and 2022 will increase by an average of 2.1% per annum.

The economic impact of brucellosis in regions or countries will depend on the livestock species farmed, their management systems and also the capacity of the medical and veterinary services within the region or country. In South Africa, outbreaks are common in both cattle and privately owned buffalo and these pose a threat to the contribution of revenue from both the livestock and wildlife industry (Manombe, pers. comm.). The effect on the wildlife industry may be more deleterious as vaccination is not practiced and control in these species is based exclusively on a test and slaughter policy.

Whilst there are no data available on the economic effects of brucellosis in South Africa, some meaningful inferences can be made from its effects in other African countries as animal husbandry practices are quite similar between African countries (McDermott *et al*., 2013) In situation where resources are constrained a targeted approach is advised, where the few available resources are channelled to critical areas within the control programme in an effort to still achieve control.

Many developing countries do not have sufficient financial or labour resources for brucellosis control (Franc *et al.*, 2018; Marcotty *et al.*, 2009) and political will towards eradication may be difficult as the economic impact of the disease has not been well documented or quantified. Resources may be preferentially allocated to other diseases such as Foot and Mouth Disease (FMD), Tuberculosis (TB) and Rabies. By contrast, bovine brucellosis has been prioritised and successfully eradicated in many high income countries such as Australia, New Zealand, Norway and most of Europe (Godfroid, 2002; McDermott *et al*., 2013). In the United States, a study demonstrated that an $ 8.3 million investment in mass vaccination against brucellosis would yield a $ 26.6 million return. This shows it may generally be worthwhile effort to invest in brucellosis control (Franc *et al*., 2018).

In the case of brucellosis, an effective control programme will consequently reduce economic losses, enhance human and animal health and improve livelihoods. If resources are limited for disease control it is vital that resource allocation give priority to critical areas or deficient areas within control programmes in order to achieve the best possible outcome. This means that disease control programmes should be continuously evaluated in order to derive information on whether they are achieving set objectives and to identify critical areas and gaps. Decisions can then be made from an informed position and hence avoiding wasteful expenditure.

There have been other evaluation tools designed, especially for animal surveillance systems, for example, Surveillance Evaluation Framework (SERVAL; Drewe *et al*; 2015) and Surveillance Framework (SurF; Muellner *et al*; 2018). SurF was a generic tool that could be utilized by the MPIs to evaluate biosecurity and animal health surveillance in the animal, aquatic and environmental sectors. The European Union funded a 3-year research project known as Risksur. The research yielded a set of web based tools for animal surveillance that could be utilized by policy makers, veterinary authorities and decision makers (Leger *et al*., 2017). The purpose of this study was also aimed at producing a tool that could be adopted by policy makes and veterinary authorities.

The Hazard Analysis and Critical Control Points System (HACCP), a tool originally developed for use in the engineering and food production industry, was adopted for disease control at farm level (DuPont, 2007; Soon & Baines, 2012; Noordhuizen & Welpelo, 1996) and at national level (Van Gelderen, 2015). This has shown that HACCP can be used for basically any process with a flow. This study sought to use a modified HACCP approach to create an evaluation tool for bovine brucellosis disease control programmes.

Chapter 2: Literature Review

2.1 Aetiology of bovine brucellosis

Brucellosis is an infectious bacterial disease with traditionally, six species responsible for most disease in terrestrial animals and humans; more recently, isolates have been identified in marine animals, namely *B. pinnipedialis* and *B. maris* (Table 1). Bovine brucellosis is zoonotic and caused largely by *B. melitensis* and *B. abortus*. Bovine brucellosis from *B. melitensis* is common in regions where cattle are kept in close proximity to small ruminants mainly sheep and goats. Occasionally, *B. suis* has been reported to cause chronic mammary gland infections in cattle (Boukary, 2013; Lopes, 2010; Cloeckaert, A., 2007; Whatmore, 2014).

Table 1 *Brucella* organisms and primary/preferred hosts

Species	Primary hosts	Secondary hosts	Zoonotic
B. melitensis	Small ruminants (Sheep, goats), Camels, Wildlife (Sable antelope)	Cattle, Dogs	Yes
B. abortus (Biovars 1-9)	Cattle, Bison, Buffalo	Dogs	Yes
B. suis (Biovars 1-5)	Pigs, Reindeer, Caribou (Biovar 4), Rodents (Biovar 5)	Dogs, European hare, Moose, Grizzly bears	Yes except Biovar 5
B. canis	Dogs		Yes
B. ovis	Small ruminants (particularly sheep), Wildlife (Red deer)		No
B. neotomae	Rodents (Desert rats)		No
B. pinnipedialis	Marine species (pinnipeds and cetaceans)		Not well documented
B. ceti	Marine species (cetaceans)		Yes (strain *B. ceti Hum*)
B. microti	Common vole	Wild boar, Red foxes	Potentially
B. inopinata	Humans	None documented	Not well documented
B. papionis	Baboon	None documented	Not well documented

(Cloeckaert, 2007; Corbel, 2006; Foster, 2007; María P. Jiménez de Bagüés, 2010; Sohn *et al.*, 2007; Theron, 2014; Whatmore, 2014)

2.2 Epidemiology

Bovine brucellosis has a worldwide distribution, being most prevalent in developing countries such as those in the Middle East, Central Asia, South America, the Mediterranean, the Caribbean and Africa. Most of Europe has been declared brucellosis free as have Japan, Australia and New Zealand (Boral *et al*. 2009; More *et al*; 2017). Of the countries with the highest incidence of brucellosis, 50% of them are in the Middle East with Iran ranking second in the world (Mirnejad, 2017; Shahzad, 2017). In sub-Saharan Africa (SSA) the predominantly isolated strain is Biovar 3a. There is serological evidence of brucellosis in Africa but specific information with regards to its distribution and prevalence in different geographical locations and farming systems is scarce and limited to a few studies. One study showed a prevalence ranging from 1.5-40% between different farming systems (McDermott & Arimi, 2002).

In South Africa, most reported cases are in the Central and North Western and parts of the country, namely North West and Gauteng provinces (Appendix C). Between 1977 and 1978, 41.5% of the nation's herds were tested and yielded a 6.6% prevalence (Mbizeni, 2015). Hesterberg *et al.* (2008) reported a prevalence of 2.4% - 15.5% in the north-eastern parts of Kwa-Zulu Natal (KZN).

Brucella abortus organisms are shed in secretions such as milk, uterine discharges and semen. Other sources of infection include aborted foetuses, foetal membranes and vaginal discharges (Akinseye, 2016; Theron, 2014). Transmission between animals is mainly through direct contact (e.g. cattle present when a cow aborts) or through pastures and drinking water contaminated by abortion-related products e.g. fluids and tissues. Inhalation, conjunctival inoculation, artificial insemination and skin contamination are also other known forms of transmission.

Brucella abortus has been isolated in urine, faeces and ocular secretions but these seem to play no important role in transmission. Infected but sero-negative animals can occur in a herd and these may serve as a source of infection (Iowa State University, 2009; Poester, 2013).

Some risk factors associated with bovine brucellosis infection include animal production/ grazing systems, breed of cattle and farming methods such as transhumance and pastoralism. In transhumance and pastoralist systems, intermingling occurs between different herds of cattle greatly increasing exposure between individuals and herds.

In these scenarios biosecurity and surveillance are also limited, making it difficult to detect and implement disease control measures. Transhumance and pastoralist systems are the predominant type of systems found in Sub-Saharan Africa, including South Africa (Boukary *et al*. 2013; Akinseye *et al*. 2016; Al-Majali *et al*. 2009).

Speculative buying of cattle as a stock replacement method has also been documented to increase the spread of brucellosis. Speculators tend to buy animals from multiple sources, with little disease history, and this makes them prone to purchasing infected animals.

It is common practice for farmers to sell off "problem cattle", for example, animals that are old, sick or with poor reproductive performance. It is likely that some animals with poor reproductive performance may have brucellosis (Akinseye *et al.* 2016).

Sex, age, breed, herd size, replacement of stock and socio-economic factors have been shown to be risk factors at animal level, whilst herd size, abortion and artificial insemination are documented risk factors at herd level (Shahzad *et al.* 2017). In endemic situations, older female animals are at a higher risk of sero-positivity for brucellosis (Silva, 2000). Larger herd sizes tend to have increased contact and comingling increasing risk of transmission between individuals and herds (Boukary *et al.* 2013). Abortions greatly increase risk of exposure due to contamination of the environment with aborted material and lochia.

The presence of wildlife maintenance hosts such as the African buffalo (*Syncerus caffer*) is a potential risk factor in areas where livestock/wildlife interfaces are common. The disease has also occurred in other wildlife such as zebra (*Equus burchelli*), wildebeest (*Connchaetes vardonii*) and eland (*Taurotragus oryx*) and these animals may serve as a potential source of infection (Godfroid, 2004; Sagamiko *et al.* 2018). Having knowledge of risk factors in disease transmission provides guidelines on how and where to implement control measures. A disease control programme must be able to identify these risks, prioritise them and provide effective risk mitigation methods.

The long incubation of brucellosis and the presence of latently infected animals also pose a major risk for infection as extended periods may pass without any overt signs of infection within a herd. The incubation period is dependent on the age of the animal and the stage of gestation at which infection occurs and this usually varies between 50 and 225 days. Heifers born to seropositive cows may be serologically negative and latently infected up until their first abortion. Latency may extend for two years (Godfroid, 2004), but a case report in the USA documented nine years (Lapraik, 1982).

2.3 Pathogenesis

The organism enters the host through the mucous membranes, skin, respiratory or digestive tract. Once in the host the organisms are phagocytised and establish themselves in the neutrophils, macrophages, trophoblasts and dendritic cells. After the organism is internalised it inhibits fusion of *Brucella*-containing phagosomes with lysosome markers preventing its clearance by the host's immune system (Poester *et al.* 2013; De Figueiredo, 2015). The organism also acidifies its environment in the host cell leading to bacterial gene expressions that favour its survival and further multiplication within the host.

Within the phagocytes and neutrophils the microbes are distributed to the regional lymph nodes where multiplication occurs with consequent lymphadenitis. A bacteraemia ensues and the organisms are carried free in plasma and inside macrophages and neutrophils. They localize themselves in various organs such as the spleen and udder but their main predilection sites are the gravid uterus and foetus. In males they localize in the testes and accessory glands.

It has been proposed that the high levels of the sugar erythritol and steroid hormones found in the placenta of pregnant sheep, cows, goats and pigs explains the tropism of *Brucella* spp organisms for the reproductive tract. High concentrations of erythritol in the trophoblast cells have been experimentally shown to favour growth of *Brucella* spp. (Petersen *et al.* 2013; Barbier *et al.* 2014). The presence of vast amounts of bacteria in the gravid uterus incites tissue damage through inducing the hosts' inflammatory responses. The aftermath is placentitis, placental necrosis and compromised oxygen delivery that lead to abortion, premature birth or the birth of non-viable calves.

Placental retention and infertility are a common sequelae to abortion (Godfroid, 2004; Megid, 2010; Neta *et al.* 2010; Samartino, 1993).

2.4 Clinical and symptoms and pathology

Bovine brucellosis infection causes reproductive losses in affected animals with a clinical presentation of abortion storms, infertility and reduced milk yield. In males it can present as orchitis and epididymitis (Iowa State University, 2009; Simpson *et al.* 2017; Poester *et al.* 2013).

The organism's affinity and localisation in the reproductive organs is responsible for its clinical manifestation. In pregnant cows it replicates in the chorioallantoic trophoblasts resulting in placentitis and diminished oxygen delivery to the foetus. The main consequences are foetal death, abortion or delivery of weak calves (Neta *et al.* 2010). Abortions usually occur during the last trimester (5^{th} to 8^{th} month of gestation). Subsequent pregnancies may reach full term but the afterbirth and milk remains infectious. In males the most common clinical presentation is orchitis, epididymitis and chronic inflammation that eventually leads to partial/permanent sterility (OIE). Other clinical signs that may be observed in the herd include retained placentae, reduced fertility and reduced milk yield. Cattle infected with *B. abortus* serovar 3 commonly present with hygromas and abscesses (Corbel, 2006). The hygroma fluid is normally infected with organisms. Post mortem lesions include a necrotising placentitis with multifocal haemorrhages and pneumonia and diffuse fibrinous pleuritis in aborted foetuses (Poester, *et al.* 2013).

2.5 Human brucellosis

Approximately half a million cases of human brucellosis are reported annually but this might be an underestimate due to under-reporting (Godfroid, 2013). In humans the disease is also known as Undulant fever or Malta fever and has long been recognized as mostly an occupation related disease with certain occupations associated with a high risk of infection. Transmission is broadly classified as occupational or environmental and occurs through the oral, respiratory and conjunctival routes. Contact with aborted material, ingestion of unpasteurised dairy products and undercooked meat or meat products may lead to infection.

Persons at high risk include veterinarians, farm and abattoir workers that may handle infected carcasses or aborted foetuses. Laboratory personnel are at increased risk due to exposure to aerosols whilst handling live cultures or potentially contaminated material (Wojno, 2016; Theron 2014; Franco, 2007; Mirnejad, 2017). With *B. abortus*, human disease often only presents as sub-clinical infection. The main cause of human disease is *B. melitensis* and is associated with virulent clinical signs.

Symptoms in humans are not pathognomonic and laboratory testing for confirmation is paramount in making a diagnosis. Common clinical signs and symptoms include fever, myalgia, night sweats, abdominal pains, sleep disturbances and weight loss. The severe forms of clinical disease in humans are caused by *B. melitensis* and *B. suis* followed by *B. abortus* and *B. canis* (Baldi, 2013; Nematollahi *et al.* 2017; Wojno *et al.* 2016; Franco *et al.* 2007). A novel isolate named *B. inopinata* was isolated from a human lung and human breast implant infection (Scholz *et al.* 2010). Human to human transmission is rare and the documented modes of transmission are sexual intercourse, bone marrow transplantation, blood transfusion and trans-placental transmission (WHO, 2016).

2.6 Diagnosis in animals

Brucellosis can be diagnosed via direct or indirect methods (Table 2). Direct methods demonstrate the presence of the organism whilst indirect methods detect the hosts' immune response to the organisms' antigens. Isolation of the organism is the definitive way of proving infection but is more expensive and often associated with a low sensitivity. The organism can be identified by microscopic examination using Modified Ziehl Neelsen stain, culture or DNA detection (Saxena *et al.* 2018; Godfroid *et al.* 2010). Indirect methods make use of serological assays for antibody detection. They are more cost effective and hence are the most favoured method for use in control programmes. They however only offer a provisional diagnosis.

Diagnosis in animals should be done at herd level and the detection of one or more infected individuals is sufficient to determine the infection status of the herd. It needs to be noted that the disease has a long incubation period and animals may be sero-negative for months or even years. Latently infected animals may not be diagnosed by serological assays.

The World Organisation of Animal Health (OIE) prescribes the use of the Buffered *Brucella* Antigen Tests (BBAT), the Complement Fixation Test (CFT), Enzyme-linked Immunosorbent Assays (ELISA) and the Flourescence Polarization Assay (FSA) for their use in international trade as these tests are highly sensitive and specific. The FPA is further able to distinguish between infected animals and those have been vaccinated by *Brucella abortus* strain 19 or infected with cross reacting organisms (Gall & Nielsen, 2004). The BBAT group consists of the Rose Bengal Test (RBT) and Buffered Plate Antigen Test (BPAT). The Serum Agglutination Test (SAT) is also used but it is not recommended for trade purposes. To improve sensitivity, serological tests may be used in parallel. Primary binding assays such as the indirect enzyme linked-immunosorbent assay (iELISA) and competitive enzyme linked immunosorbent assay (cELISA) are superior in performance to tests such as RBT and CFT. The iELISA makes use of Smooth-Lipopolysaccharide (S-LPS) antigen coated on a matrix. A combination of diluted serum and antiglobulin reagants are added where these antiglobulin reagants are conjugated to an enzyme and are specific to the species antibodies being tested for. The cELISA is similar to the iELISA but in addition makes use of competing monoclonal antibodies. These monoclonal antibodies have a higher affinity for antigen than vaccinal or crossreacting antibodies but with a lower affinity for antigen than that of antibodies produced in response to infection. This subsequently reduces cross reactions with microbes such as *Yersinia enterocolitica*, *Escherichia coli*, *Pseudomonas* and *Salmonella* and vaccinal antibodies (Adone & Pasquali, 2013; Nielsen, 2002).

A study carried out in Northern KwaZulu-Natal showed there was no statistically significant difference between the performance of the primary binding assays and the conventional tests, thus supporting the use of RBT and CFT as appropriate tests for diagnosis in South Africa (Chisi *et al.*, 2017). Other tests such as the Milk Ring Test (MRT) also have their limitations; for example, when it is used in dairy herds as the numbers increase (> 100 lactating cattle) the sensitivity decreases. The sensitivity of recent molecular tests such as the Real Time-Polymerase Chain Reaction (RT-PCR) and DNA tests are not well validated (Chisi *et al.* 2017).

Table 2 Direct and Indirect test methods for diagnosis of infection with *B. abortus* in animals

DIRECT METHODS		INDIRECT METHODS	
Test	**Specimen required**	**Test**	**Specimen required**
Staining Stamps modification of Ziehl-Neelsen	Foetal organs Cotyledons Uterine discharge	Rose Bengal Test (RBT)	Serum
Culture	Foetus Placenta Uterine discharge Milk Semen Lymph nodes	Serum Agglutination Test (SAT)	Serum
PCR	Blood Serum Milk	Complement Fixation Test (CFT)	Serum
Immunohistochemistry	Tissues	Enzyme Linked Immunosorbent Assays (I-ELISA) (C-ELISA)	Serum
		Milk Ring Test (MRT) Milk I-ELISA	Milk
		Brucellin Skin Test (BST)	Host

(Ducrotoy *et al*. 2018; Geresu & Kassa, 2016; OIE)

The RBT, SAT and CFT are common tests serological tests used for brucellosis diagnosis. They make up part of the group of conventional or classic tests used for brucellosis diagnosis. These tests coupled with bacteriology remain the most used tests in South Africa.

2.6.1 Rose Bengal Agglutination Test (RBT)

The RBT uses *Brucella* antigen stained with Rose Bengal. An equal volume of antigen and serum (25-30 µl) are mixed together, agitated and afterwards observed for agglutination. Any visible signs of agglutination are considered positive. However, it tends to give false positive results for animals that have been vaccinated with Strain 19 (S19) (OIE). The RBT antigen tends to deteriorate when it is continuously placed between the refrigerator and room temperature during use and this is a potential cause for false negative reactions.

The sensitivity of the RBT depends on the antigen used during testing (Muñoz *et al*., 2012). One review documented an RBT sensitivity of 98.1% and a specificity of 99.8% (Ducrotoy et al., 2017) and another study showed a sensitivity of 68% (Ducrotoy *et al*; 2018). Even with these limitations it still remains quite useful as a screening test in herds (Weiner *et al.* 2010; Saxena *et al.* 2018).

2.6.2 Serum Agglutination Test (SAT)

This test is not approved by the OIE for international trade. It has less specificity as compared to the CFT. Its specificity is improved after addition of EDTA to the antigen.

2.6.3 Complement Fixation Test (CFT)

The CFT, which is also referred to as the "serology gold standard" is a complex test that requires experienced personnel and good laboratory facilities (Zamri-Saad & Kamarudin, 2016). It is very specific and is an OIE approved test for international trade (Geresu & Kassa 2016). In South Africa it is used as a confirmatory test for samples that test positive on RBT. The CFT can produce positive test results where animals have been vaccinated with Strain 19 or if they have been exposed to antigenically related organisms such as *Yersinia* and *Salmonella.* Hence it may need to be used with other complementary tests such as culture or PCR for a more definitive diagnosis (Nielsen, 2002; OIE). Its sensitivity is reduced when used as a confirmatory test.

2.6.4 Culture

Bacteriological culture is considered to be the gold standard and maybe used alongside serological tests to confirm diagnosis (Chisi *et al.* 2017; Wang *et al.* 2016; Godfroid *et al.* 2010; Nielsen 2002).

2.6.5 Complementary tests

DNA detection tests such as RT- PCR are also available and have also shown to be quite useful in *B. abortus* detection (Kaden *et al.* 2017; Newby *et al,* 2003). These tests are mostly used in cases of abortions where there is an availability of aborted material to collect as samples. Preferred samples include foetal membranes, aborted foetuses (abomasal contents,

lung and spleen) and from carcasses mammary and genital lymph nodes may be collected (OIE; Dehkordi *et al*. 2012; Godfroid *et al.* 2010).

2.7 Control and eradication strategies

Prevention and control are based on a sound knowledge of the epidemiology of brucellosis. A sound knowledge of disease patterns allows for targeted prevention and control measures which in turn will prove cost effective. A brucellosis control programme usually includes surveillance, vaccination, movement control, biosecurity and a testing, isolation and slaughter policy (Zamri-Saad & Kamarudin, 2016; AU-IBAR, 2014; European Commission, 2009; Lopetegui, 2004; Corbel, 2006). The availability of an organised veterinary services with good diagnostic capacity, sufficient resource allocation and good regional and national networks, are paramount to the successful prevention, control and eradication of brucellosis (Truszczyński, 1998; European Commission, 2009).

2.7.1 Surveillance

Surveillance of brucellosis may be passive or active. The former relies mainly on reports and investigation of abortions. Active surveillance involves initiatives to detect disease through sampling activities such as abattoir surveillance and designed herd surveillance programmes (Corbel, 2006). Different combinations of serological tests either in series or parallel can be used to influence sensitivity or specificity. Parallel testing increases sensitivity with lower specificity whilst serial testing does the reverse, therefore the method used depends on the objectives of the test procedure.

Serological surveillance should be coupled with bacteriological investigations from tissue samples or secretions in suspect or infected animals (Adone & Pasquali, 2013). Surveillance in animals requires time, financial and human resources. Its success also relies upon thorough epidemiological investigations and an effective animal identification and movement control system especially given the long incubation period that permits an insidious spread of the disease (Asanishvili *et al*. 2016).

2.7.2 Vaccination

Vaccination is used to reduce clinical disease and develop herd immunity. The most common vaccines used for brucellosis are attenuated strains of *B. melitensis* strain Rev 1 (for use in small ruminants), *B. abortus* S19and *B. abortus* Strain RB51 (RB51) in cattle. These vaccines reduce the risk of abortion and transmission but do not provide sterile immunity (Zamri-Saad & Kamarudin, 2016). S19 was discovered in 1923 after being isolated from the milk of a Jersey cow. Over the years it has proven to be highly efficacious and helpful in the reduction and eradication of brucellosis globally (Crasta *et al*. 2008; Olsen & Stoffregen, 2005). Its efficacy does however come with disadvantages. It is highly immunogenic and associated with post vaccination abortions and interference with serologic testing (Nicoletti, 1990; Schurig *et al.* 2002). Because of these side effects, vaccination is limited to sexually immature animals (< 8 months) (Bardenstein *et al.* 2002). S19 is also associated with orchitis and infertility in bulls and is pathogenic to humans (Schurig *et al.* 2002; Poester *et al.* 2006).

Another vaccine Strain 45/20 was introduced to circumvent the persistent antibodies that are associated with S19 vaccine. It is an attenuated vaccine manufactured from passages in guinea pigs but once in vivo it would revert to the virulent smooth form and it was not able to confer the same immunity as the live vaccines (Dorneles et al. 2015; Chukwu et al. 1985; Schurig et al. 2002). As a consequence, it has not been a favourite for use in vaccination protocols. Generally inactivated vaccines are considered unable to provide long lasting immunity when compared to live vaccines such as S19 and RB51 (Sancho et al. 2015).

RB51 lacks the LPS-O antigen found in S19 and hence does not induce antibodies post vaccination. It is preferred for booster vaccinations or vaccinations in adult females (Poster *et al*. 2006) but is also associated with post vaccination abortions and premature births. (Dougherty *et al*. 2013) reported reproductive losses in two RB51 vaccinated herds of 5.3% and 0.6% respectively. However it is less of an abortifacient as compared to S19 and still remains the preferred vaccine by some (Miranda *et al.* 2016). The efficacy of RB51 and S19 are similar in their prevention of both abortion and fetal transmission. However, there have been suggested variations in its efficacy that are age related and also that RB51 seems more effective when the prevalence is low. (Pascual *et al.*, 2017). RB51 is also pathogenic to humans and resistant to rifampicin, the antibiotic of choice in brucellosis treatment. To avoid these pitfalls, there have been suggestions to use subunit vaccines as an alternative. These

vaccines do not contain infectious material and cannot induce clinical disease making them safer than the current live vaccines in use. There is debate though on their ability to induce solid immunity (Pascual *et al.* 2017; Zakia & Pascual, 2016).

For countries or regions with a high animal prevalence e.g. > 5%, effective control requires a vaccination coverage of > 80% for at least 10 years (Zamri-Saad & Kamarudin, 2016; Boral *et al.,* 2009; European Commission, 2009). The age of vaccination is a critical factor, RB51 is more efficacious when given to cattle between the ages of 5-6 months (Olsen & Stoffregen, 2005; Cheville *et al.* 1996). In South Africa, vaccination is restricted to heifers between the ages of four and eight months. Repeat or booster vaccinations with Strain 19 is illegal and vaccinations should be done only with RB51 (DAFF, 2013).

2.7.3 Biosecurity

Biosecurity refers to hygienic practices that minimise exposure of susceptible animals to *Brucella* pathogens to limit the spread of disease. This can either be implemented at national, regional or farm level (Dargatz *et al.* 2002; Corbel, 2006).

In an outbreak situation, isolation of peri-parturient or parturient animals, proper disposal of placentae and aborted foetuses and disinfection of premises all reduce risk of transmission. Personal hygiene amongst farm personnel aids in preventing transmission between farms via fomites. One of the key factors that contribute to the spread of brucellosis is the movement of infected animals. Movement restrictions must be placed on infected farms and animals within infected herds should be identified individually to allow for traceability. Any movement of animals should either be permitted for direct slaughter or after negative serological test results (European Commission, 2009; Zamri-Saad & Kamarudin, 2016).

Replacement stock must be sourced from brucellosis free herds to avoid re-introducing infection. Quarantine or retention should be imposed on newly introduced animals. Farmers are also encouraged to test animals before movement. Biosecurity is essential but may not always be feasible especially in areas where transhumance and nomadism is practiced (Sancho *et al.* 2015).

2.7.4 Test and slaughter

Prevalence should be low and range between 2% - 5% for test and slaughter to be economically viable (Zamri-Saad & Kamarudin, 2016; Corbel, 2006; WHO, 2016). Even though it is a useful tool in eradication, it is not easy to implement. Cultural and religious beliefs may be restrictive to test and slaughter policies. For instance, in India culling of cattle is a taboo and has been banned (Franc *et al.* 2018; Tejani, 2008). A close cooperation between veterinary services and farmer compliance is paramount to success at eradication. Competitive compensation may be used as an incentive for farmer compliance. This also makes it an expensive tool to utilize. Test and slaughter will not work effectively in isolation but in combination with other control measures (Zhou, 2018).

2.7.4.1 Vaccination with test and slaughter

In areas with high prevalence, test and slaughter can be coupled with mass vaccination (Blasco *et al*. 2010; Sancho *et al.*, 2015). Mass vaccination reduces prevalence first then followed by testing and slaughter (Caetano *et al*. 2013; Ragan, 2002). Areas with moderate prevalence can practice vaccination in young replacement stock coupled with test and slaughter in adult animals. Vaccinations should be carried out using RB51 to minimise interference with serological tests. Mass vaccination should be carried out over long periods e.g. > 10 years or between 6-12 years (European Commission, 2009; Blasco, 2010).

2.7.4.2 Stamping out

When disease prevalence is very low (close to zero), veterinary infrastructure is good as well as compliance with regulatory and/or biosecurity measures, stamping out can be applied as a means to eradication. In this case all infected, exposed or potentially infected animals are removed (European Commission, 2009; Blasco, 2010). As discussed before, this relies heavily on availability of financial resources and farmer compliance.

2.8 Evaluation of disease control programmes

The Center of Disease Control and Prevention (CDC) in their evaluation manual define evaluation as “The systematic collection of information about the activities, characteristics, and outcomes of programs to make judgments about the program, improve program effectiveness, and/or inform decisions about future program development.” Evaluation

assists to assess whether control programmes meet their objectives; to account for resources and to identify any strengths and gaps of a programme over time. This is even more so for in cases where resources are limited. In any case resources must always be utilized efficiently and appropriately allocated.

Evaluation aids to identify which aspects of a control programme to prioritize, in an effort to improve on programme performance and for monitoring of progress. It is essential for identification of strengths and weaknesses within a programme and implementing corrective actions where required.

Disease control programmes are multi-faceted and have multiple stakeholder involvement. To evaluate a control program would require all these aspects to be considered and this makes the evaluation process rather cumbersome. A comprehensive evaluation checklist can simplify this task. The OIE tool for the evaluation of performance of veterinary services is a good example of an evaluation checklist (OIE, 2013). However, it was not designed to intimately evaluate disease control programmes but rather to evaluate performance of veterinary services as a whole. One can only use it to draw inferences on disease control programme performance.

According to the OIE disease control measures need to follow standard operation procedures (SOPs) that include:

i) Implementation
ii) Monitoring of control measures
iii) Evaluation and verification of control measures
iv) Application of corrective actions and
v) Record keeping

Evaluation of disease control programmes, or the recommended SOPs, is time-consuming and subjective, as control programmes have a diverse number of activities with multiple stake holder involvement. The use of a standard framework for evaluation would simplify this task for policy makers and auditors.

2.8.1 Hazard Analysis Critical Control Points

Hazard Analysis Critical Control Points (HACCP) was developed around the 1960s as a concept/risk management tool for use by the Pillsbury Company in collaboration with the US National Aeronautics and Space Administration (NASA) to manufacture safe foods for space flights. It was formulated as a quality assurance tool in the interest of military and space personnel. By coincidence it addressed the issue of foodstuff contamination with *Salmonella* spp. There was difficulty in detecting samples with salmonellosis and end-product testing was proving to be impractical and expensive as large quantities of samples had to be tested to detect a positive sample. HACCP offered a preventative approach through reduced risk of contamination and minimal end product testing. After this milestone, there were considerable efforts to harmonise the use of HACCP in food industries globally and it expanded into all realms of the food industry (Sperber *et al.* 2009). HACCP has been used as a systematic approach for the identification, evaluation and control of hazards, mainly in food operations and these hazards can be physical, biological or chemical. It is used for risk mitigation through the identification of Critical Control Points (CCPs). At these CCPs control or risk mitigation can be implemented in order to eliminate or reduce the risk of hazard occurrence to an acceptable level (Codex Alimentarius Commission, 2003). HACCP is recognised by the Codex Alimentarius Commission and therefore forms a good basis for any organisation, farm or individual to provide assurance of good practices. It has been used by multiple governments in different sectors to facilitate trade giving it credibility (Sperber, 2013).

Over the years HACCP has extended beyond the food industry into the pharmaceutical and motor industries. Essentially HACCP can be utilised in any process with a systematic flow. However, it does become difficult to apply where there are many objectively immeasurable activities and in such cases, a modified HACCP approach can be applied.

HACCP has been used as a risk management tool at farm level for disease prevention to improve animal health and production. It operates on seven principles (Table 3).

Table 3 HACCP Principles (in food production)

Principle	Associated activity/objective
1	Identify the potential hazard associated with food production at all stages from growth until the point of consumption. Assess the likelihood of occurrence of the hazards and identify the preventative measures for control.
2	Determine the points/procedures/operational steps in the production process that can be controlled to eliminate the hazard(s) or minimize its occurrence. These points are termed Critical Control Points (CCP).
3	Establish target levels and tolerances which must be met to ensure the CCP is under control.
4	Establish a monitoring system to ensure control of the CCP either by scheduled testing or observations.
5	Establish corrective actions to be taken when monitoring indicates that a particular CCP is not under control.
6	Establish procedures for verification which includes supplementary tests and procedures to confirm that HACCP is working effectively.
7	Establish documentation concerning all procedures and records appropriate to these principles and their applications.

(Lievaart *et al.* 2005; Boersema *et al*. 2008; Noordhuizen & Welpelo, 1996; Codex Alimentarius, 2003):

In 2006 the European Union (EU) mandated primary producers to conduct risk assessments so as to ensure their end product had a low risk of biological or chemical contamination. This created a need for producers to create disease risk assessment tools that were applicable at production level. There was a need for a quality assurance tool that extended from production through to processing (from farm to fork). A number of pilot projects then extrapolated HACCP for use in disease control. For example, Casgoine and Crilly (2014) used HACCP to identify proactive control measures for cestodiasis. A survey carried out in the United Kingdom (UK) by the AHDB Beef and Trade Marketing hub revealed that *T. hydatigena* cestode infections were a significant contributor of liver condemnation at abattoirs. Of late there are no reliable estimates for losses through morbidity and meat rejections that can be associated with cestode infections but they are projected to be much more than those gathered through the survey. Stemming from these findings and also from the economical complexities around cestode control on sheep farms in the UK, Casgoine and Crilly formulated a risk based approach to control cestode infections. This approach adopted HACCP principles to formulate proactive control measures for cestode infections on sheep farms.

HACCP has also been used at dairy farm level to manage animal production during milk harvesting and cow treatment. Management of animals in production is generally reactive, meaning treatment is instituted after a disease is diagnosed. HACCP can be used to perform risk identification and disease prevention and hence reduce costs associated with treatment or losses associated with observation of drug withdrawal periods and culling. Lievaart *et al.* (2005) adopted a HACCP model for the dairy farm production process. It was used to identify milk residues (physical or chemical) and zoonotic microbiological hazards during milk collection and treatment of dairy cows. Once the CCPs and the risks associated with hazard occurrence had been identified the control or preventative measures were prescribed. The outcome of such an approach would be a product (milk) that has a very little chance of containing contaminants before processing (Lievaart *et al*. 2005). HACCP was also used in the control of bovine paratuberculosis on infected dairy farms (McAloon, 2015).

Van Gelderen *et al*. (2015) used HACCP for Foot and Mouth Disease (FMD) control programmes and the model was successfully adopted by several countries. Disease control programmes are a mandate of veterinary services (VS) but different components often rely on other sectors that are not fully under control of VS. In this case, Van Gelderen adopted an all-inclusive quality assurance tool for an FMD control programme for a FMD-free country that practises vaccination. This also covered other sectors besides veterinary services that are involved in disease control. The programme had three main elements of vaccine production, vaccination of animals and post vaccination activities (surveillance).

At each of these stages the CCPs were identified with their associated hazards (Principle 1 & 2). For each element, expectations and tolerances were established for the identified CCPs. Reference was made from OIE guidelines with standard operating procedures and detection methods provided to detect hazard occurrence (Principle 3 & 4). With use of detection methods, contingency plans could be implemented relative to where a breach had occurred (Principle 5). The tool required that the processes of vaccine production, vaccination of susceptible animals and surveillance have documentation in place to allow for monitoring and auditing purposes (Principle 6 & 7).

This is the first documented attempt of the use of HACCP as an evaluation tool for a disease control programme.

Atlantic Salmon (*Salmo salar*) is a very popular seafood product in the United Kingdom. To help safeguard its market and to ensure public health and in adherence to EU legislation a document was drafted to formulate an Aquaculture Farm Food Safety and Disease Risk Assessment (AquaFRAM). This risk assessment tool adopted some HACCP principles in its model. Biological and chemical hazards and critical factors along the production line were identified together with the risks associated with each point The risks were quantified and corrective actions devised and the tool was also validated by testing it out on farms and seeking end user feedback (Baines & Soon, 2012).

Generally, the use of HACCP is beneficial as it provides a systematic approach to risk assessment. It is for this reason that a (modified) HACCP approach was used in this study in an effort to produce a systematic evaluation tool that targets the critical areas in disease control.

HACCP comes with documentation and record keeping making it less cumbersome for auditors to audit programmes or processes. It also provides a handy monitoring tool that is based on sound science. HACCP, CCPs make it easier to identify problem areas. This provides a cost effective way for risk mitigation or problem solving as solutions are targeted to specific sections or problems. It also provides a standardized approach that can be repeated either by internal or external auditors or other interested stakeholders.

However being a tool that is commonly used in food safety it is more tailored for quantitative rather than qualitative data. Hence some modifications are required in order to use it for qualitative assessments which may or may not be successful. This is probably the biggest challenge encountered when HACCP is adopted for disease control systems.

Chapter 3: Materials and Methods

An extensive literature review was conducted to explore HACCP principles with its diverse applications e.g. in the food, engineering and animal health and production industry, thereafter brucellosis as a disease and its various control and eradication strategies. This was carried out through the web-based databases Web of Science and Science Direct, and websites for recognised organisations e.g. APHIS, DEFRA, DAFF and OIE. At least 267 papers on Brucellosis, HACCP and Brucellosis control were retrieved for use. Key phrases used in the search criteria included "Brucellosis control programmes", "HACCP", "Use of HACCP in disease control" and "HACCP in Brucellosis control". The policies and legislation on brucellosis in South Africa were studied, mainly through documentation produced by the DAFF Brucellosis Cattle Manual for the Veterinarian and The Animal Diseases Act 35 of 1984.

The main components of a brucellosis control programme were identified as surveillance, vaccination, movement control, biosecurity, test and slaughter. Other auxiliary activities or components that feed into the control programme were identified e.g. farmer awareness and education, human resources contribution.

An approach similar to that done by Van Gelderen *et al*. (2015) was adopted as a foundation for the study. A process flow of a typical brucellosis programme was created. After that a HACCP process as depicted in Table 4 was then applied to this process flow to identify a hazard/s and critical programme aspects.

The hazard was identified as "the spread or persistence of *B. abortus* pathogen within or between herds". Contrary to HACCP in which the hazard is entry of a pathogen into the system, the hazard in this case was "escape" of the pathogen from the system consequently facilitating spread of disease. This can be through non-detection of the pathogen or loss of control within the programme through failure to contain and eliminate the pathogen in and between herds.

The identification of the critical programme aspects which were then termed "controlled programme stages" led to the next stage of Principle 2. These controlled programme stages were synonymous with HACCP CCPs and were aspects of the programme were hazard occurrence was most likely to occur and implementation of corrective or preventative measures would either eliminate or mitigate risk of hazard occurrence.

Table 4 HACCP concept application on brucellosis control programme

HACCP Principle	Application
Principle 1 Hazard identification	The hazard was identified as the spread or persistence of *B. abortus* pathogen within or between herds".
Principle 2 Determine the points/procedures/operational steps in the production process that can be controlled to eliminate the hazard(s) or minimize its occurrence. These points are termed Critical Control Points (CCP).	Controlled programme stages . These controlled programme stages were synonymous with CCPs. These were stages of the programme where there is a risk of hazard occurrence
Principle 3 Establish "target levels" which must be met to ensure the CCP is under control.	The "targets levels" defined as the expected performance or standards at each controlled programme stage. These standards are the actions that are expected to be performed to ensure a successful brucellosis programme. They were derived from international guidelines, policies and literature.
Principle 4 Establish a monitoring system to ensure control of the CCP either by scheduled testing or observations	Against each controlled programme stage, evaluation questions were structured with scores ranging from one (1) to four (4). Four was the highest disease-control status with the most desirable outcome and one being the least desirable outcome. These scores could be used to monitor performance.
Principle 5, 6 and 7	The last three HACCP principles were covered by the final checklist which was the final outcome of the research. From this checklist one can assess the current performance of the programme against the expected standards. This would help inform of any required corrective actions. The checklist would enable auditing and monitoring of the control programme and subsequently provide records for these processes.

A further review of literature was carried out through web-based search criteria to gather more data. Key search words were “transmission”, “epidemiology” and “control” of Brucellosis. This was done to identify the risk factors associated with transmission of brucellosis and to find documented best practices for control of Brucellosis.

From the search results, best practices for Brucellosis control were identified e.g. surveillance strategies, vaccination coverage and test procedures. From this information the expected standards for brucellosis control were derived. These expected standards were synonymous with HACCPs critical limits and termed as “target levels”. Most of these target levels were derived from international guidelines, policies and literature available for brucellosis control and management such as those produced by the OIE, DEFRA, DAFF and the U.S. Department of Agriculture’s (USDA) Animal and Plant Health Inspection Service (APHIS)

These guidelines or policies clearly define the actions that are required for successful brucellosis control either from practice or through research. European countries that have successfully eradicated brucellosis have done so through a combination of surveillance, vaccination and testing and slaughter policies. Though strategies for success may differ between regions or countries there are practices that have proven to be standard across the board such as, mass vaccination at >80% in endemic areas and testing and slaughter when prevalence is lower than 5% (Blasco, 2010). These kind of practices were used to make part of the expected performances or standards (target levels) of a successful brucellosis programme.

The next stage was to establish a monitoring system. Based again on literature and what has been documented to be successful, a scoring matrix was established. The scores ranged from one to four. Each score defined a combination of different actions or performances with four indicating the most desirable actions for the programme and one representing the minimal or the least desirable performances.

The first result of the HACCP concept application to evaluate brucellosis control program was a document or checklist that had potential use for evaluation, monitoring and record keeping. After deliberations with the study leader and editing which mainly comprised of correction of grammatical errors and rephrasing of questions, an intermediate checklist was produced. This checklist was termed an intermediate checklist as it was not the final product and was still meant to go through an expert review using the Delphi method.

A modified Delphi method was used for expert review of the intermediate checklist. It consisted of two rounds used to source expert opinion from a group of ten brucellosis experts.

The experts were selected from a range of backgrounds, including academia, policy formulation and disease control. Government experts included those involved in central (national) policy formulation as well as field managers. In the first round, the checklist was emailed to each expert who was given a two week period to peruse the checklist, make comments and return it. The feedback was collated and amendments or modifications made based on inputs from the respondents in the first round.

All experts' comments were anonymized and added to the checklist in a separate column to allow them to see the extent to which their recommendations were used in the modified document for the second round.

The amended intermediate checklist (Appendix D) was then re-sent to the respondents who were given ten days to further comment on the document. The final checklist that included a scoring system was produced based on consolidated inputs from both Round One and Two.

Chapter 4: Results

The end product of this study was the development of a checklist that can be used as an evaluation tool for Bovine brucellosis control programmes. The checklist can be applied at different scales, at national, regional or provincial level.

Eight out of the ten experts responded for Round one, and for Round two, five of the ten experts responded. The intermediate checklist generally received very positive reviews from the experts, who commended it as a relevant tool that could be utilized by authorities for auditing purposes as it was able to cover most of the relevant aspects of a successful brucellosis programme. However, four of the respondents indicated that the checklist seemingly assumed that Brucellosis control was confined to the state and it needed to incorporate the role of the private sector in Brucellosis control by inclusion of evaluation of industry organizations. Two respondents mentioned the need to further break the categories and evaluate them separately e.g. under human resources it was advised that performance and motivation be evaluated separately.

There was also suggested that certain parameters were better off consolidated into others e.g. communication and awareness be reviewed under policy and legislation. Some suggested additional controlled programme stages to allow for a more in-depth evaluation. Two respondents suggested the inclusion for evaluation of databases or information management. There were debates over the level at which the checklist would be more beneficial (e.g. national/provincial) and who would be the appropriate target group or end user. However, there was a general eagerness for the checklist to be further refined and tested in the field. by the provincial programme managers.

All the suggested amendments were incorporated into the modified checklist and circulated to all experts for Round 2. None of those who responded at this time conceded their own views and all accepted the proposed changes. Most of the inputs and suggestions were accepted and used to construct the final checklist. The role of information management was included into the checklist to evaluate the management of databases. Measurable or potentially measurable parameters were allocated percentages or figures in order to give

further justification for score allocation e.g. vaccination coverage, resources and sampling sizes under disease surveillance.

Suggestions that were rejected were only rejected because they had a potential to extend beyond the scope of the study and required more input in terms of time to consolidate them into the checklist. There is obvious room for their inclusion in another study.

A final checklist (Table 5) was produced after consolidation of the chosen inputs from the expert reviews given from Round one and two. The final checklist comes with a scoring matrix that can be used to evaluate programme performance. From this scoring system the end user can monitor the programme or point out the aspects of the programme that require corrective actions or intervention. It also has a section that can identify whether there are adequate resources available for programme implementation.

Table 5 Checklist: Final bovine brucellosis control programme assessment

(1) This checklist is designed to be used by a programme manager to assess the presence and severity of gaps in the brucellosis programme. Please score each aspect ("parameter") on a four-point scale, according to the definitions provided. In some cases, this can be semi-quantified but is much more difficult in others! The goal is to provide a standardized format that can be used by the same manager repeatedly (to evaluate progress) or to allow comparisons between different regions.
(2) The checklist is designed to be used at different scales (e.g. national, regional, provincial, municipal), different production types (e.g. commercial herds, subsistence herds, dairy herds etc.) and in different countries. If, within a region, different sectors of the production system behave differently e.g. commercial vs non-commercial producers, then separate checklists must be used for each sector.

Date of assessment	

Scope of assessment *(indicate where applicable):*

Regional: name of country, province, municipality etc.	
Herd type: dairy, beef, mixed etc.	
Production type: commercial, pastoral, subsistence etc.	
Other (indicate):	

Assessor details:

Name and surname	
Email address	
Telephone number	

Programme component	Controlled programme stage	Definitions (4=Fully sufficient; 1=minimal)		Score (√)
Policy and legislation	Central policy and legislation	National policy is in place, underpinned by adequate legislation for effective implementation. Policy and regulatory documents accessible to all responsible officials with appropriate guidelines/instructions and awareness training provided to all relevant personnel.	4	
		National policy is in place, underpinned by adequate legislation for effective implementation but guidelines/ instructions and awareness training not provided to all relevant personnel.	3	
		National policy and legislation is in place, but weaknesses or gaps evident. Guidelines/instructions and awareness training may or may not be provided to all relevant personnel.	2	
		National policy and/or legislation is absent or insufficient to support programme in a meaningful way.	1	
	Law enforcement by veterinary services	Enforcement is strong farmers are regularly and actively monitored to ensure quarantine, isolation, branding and removal of infected animals; post-outbreak testing and vaccination.	4	
		Enforcement strong but not applied equally across all areas.	3	
		Enforcement implemented where possible but gaps evident.	2	
		Enforcement is weak/absent	1	

Comment if necessary:

Programme component	Controlled programme stage	Definitions (4=Fully sufficient; 1=minimal)		Score (√)
Financial and material resources	Resources for surveillance	Available funding permits surveillance that will meet all epidemiological objectives i.e. sero-surveillance, abattoir surveillance, post-abortion sampling to detect disease, establish disease freedom or *ad hoc* sampling and testing.	4	
		Available funding permits surveillance to meet most (> 50%) epidemiological objectives.	3	
		Available funding permits some surveillance but only meets limited (25% - 50%) epidemiological objectives.	2	
		Little to no funding to carry out active surveillance.	1	
	Resources for control measures	Available resources permit comprehensive control measures to resolve outbreaks i.e. post-outbreak serological testing and/or vaccination, follow-up initiatives, epidemiological investigations, compensation (if included).	4	
		Available resources permit most (> 50%) control measures.	3	
		Available resources permit some (25% - 50%) control measures but epidemiologically significant gaps evident.	2	
		Minimal to no resources for control measures.	1	

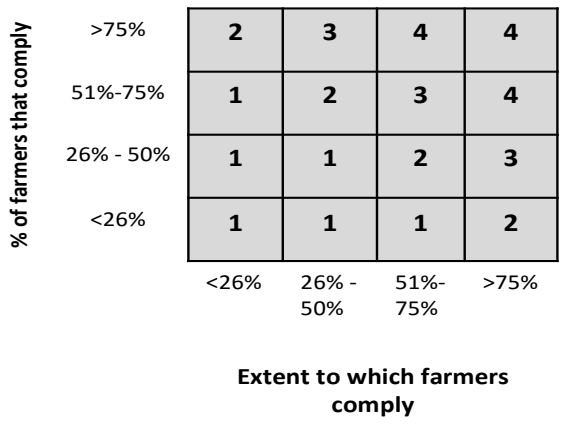
	Resources for routine vaccination	Resources available to procure required quantities of vaccines.	4	
		Resources available to procure > 50% of the required quantities of vaccines.	3	
		Resources are available but can only procure 25% - 50% of required quantities of vaccines.	2	
		No resources available.	1	

Comment if necessary:

Programme component	**Controlled programme stage**	**Definitions (4=Fully sufficient; 1=minimal)**		Score (√)
Human Resources and Management	Personnel complement	There is sufficient human resource capacity (veterinary, para-veterinary, administrative) to implement the programme effectively. If private sector involved, there are sufficient human and financial resources to implement the programme.	4	
		Most (> 75%) of human resource capacity available and if private sector involved most (> 75%) human and financial resources available to implement programme.	3	
		Some 25% - 50% of human resource capacity available and if private sector involved some (25% - 50%) human and financial resources are available to implement the programme.	2	
		< 25% of human resource capacity available and if private sector involved < 25% of human and financial resources are available to implement the programme.	1	
	Personnel motivation	Personnel highly motivated i.e. perform all delegated activities with due diligence, address problems comprehensively, excellent work attendance, very good performance assessments scores.	4	
		Personnel somewhat motivated i.e. they leave out some of their delegated control activities, can address some problems, show some enthusiasm with reasonable work attendance and performance assessment scores.	3	
		Personnel poorly motivated i.e. undertake limited delegated control activities, little enthusiasm, struggle to address problems, periods of absenteeism, performance assessment scores are fair to poor.	2	
		Personnel demotivated i.e. No delegated duties are done, personnel show no interest in control activities, fail to tackle problems, absenteeism is high and performance assessment scores are poor.	1	

	Personnel training	Personnel sufficiently trained i.e. training offered on a regular basis to relevant personnel to optimise awareness, knowledge and skills.	4	
		Training offered on a regular basis but not to all relevant personnel.	3	
		Limited training offered and knowledge/skills/awareness gaps are evident.	2	
		No training is offered.	1	
	Communication on programme strategy	Communication is excellent i.e. all personnel have access to a range of information on programme strategy and feedback is facilitated; evidence exists of excellent communication (e.g. external reviews, personnel feedback etc.).	4	
		Communication is good i.e. wide range of information is provided but feedback mechanisms and evidence is lacking.	3	
		Communication is fair i.e. some information is provided but gaps are clearly evident.	2	
		Poor or no communication is evident.	1	
	Performance assessment and management	Excellent performance management i.e. strong evidence of active performance assessment; explicit audits of programme management; incentivisation programme in place.	4	
		Good performance management i.e. performance actively assessed and managed but limited auditing and/or incentivisation.	3	
		Fair performance management: i.e. some performance assessment takes place but not actively managed; very limited auditing.	2	
		Little evidence of performance assessment and/or management.	1	

Comment if necessary:

Programme component	**Controlled programme stage**	**Definitions (4=Fully sufficient; 1=minimal)**		Score (√)
Farmer behaviour and awareness	Compliance with programme requirements			

	Biosecurity practices	Where applicable farmers practice excellent biosecurity measures, irrespective of state regulation i.e. isolation of calving/aborting animals; appropriate responses to placentae, aborted foetuses; risk-averse livestock movements and grazing practices; comprehensive testing and/or vaccination for brucellosis. Quarantine/retention of newly introduced animals.	4	
		Where applicable farmers practice good biosecurity e.g. few gaps are present.	3	
		Where applicable farmers practice fair biosecurity e.g. there are considerable gaps.	2	
		Farmers practice poor/no biosecurity.	1	
	Reporting of abortions	Most abortions (visualised or suspected) are reported to the relevant authorities; aborting animals isolated and tested.	4	
		Most abortions reported and followed up, but only by limited sector of industry e.g. dairy/commercial herds.	3	
		Abortions rarely reported or limited evidence of follow-up testing.	2	
		Abortions not reported and/or no evidence of follow-up testing.	1	
	Outbreak resolution	Farmers actively assist regulatory authorities and comply with regulations by showing personal initiative in resolving outbreaks. They comply fully with testing/vaccination schedules, biosecurity advice, livestock movement regulations and provision of epidemiological information.	4	
		Farmers comply with regulations but show limited personal initiative in resolving outbreaks or protecting their/others' herds.	3	
		Farmers comply with most instructions.	2	
		Compliance limited or absent.	1	
	Awareness and Training	Active consultation with farmer representative groups and explicit, formal programme of raising farmer awareness through appropriate media i.e. farming press, training or extension programmes, social media.	4	
		Programmes in place to raise farmer awareness through appropriate media undertaken i.e. farming press, training or extension programmes, and social media. Consultations with representative groups may be weak or does not occur.	3	
		Some efforts made at raising farmer awareness through appropriate media.	2	
		Awareness, training, consultation negligible or absent.	1	

Comment if necessary:

Programme component	**Controlled programme stage**	**Definitions (4=Fully sufficient; 1=minimal)**		Score (√)
Vaccination	Vaccine availability	Vaccines are used that comply with international standards are always available from manufacturer with a timeous procurement process to ensure availability when it is required for use.	4	
		Vaccines are used that comply with international standards, are usually available from the manufacturer and a reasonable procurement process is in place to ensure availability when required.	3	
		Vaccines are used that comply with international standards, are usually available from manufacturer but with a slow, inefficient procurement process OR vaccine is unavailable from manufacturer even though a timeous and efficient procurement process is in place.	2	
		No vaccine available or do not comply with international standards or no procurement process is evident.	1	
	Vaccination coverage and implementation	Vaccination coverage sufficient (> 80% of relevant herds/cattle) and appropriate (i.e. according to manufacturer guidelines: heifers between 4-8 months; adults with RB51), in both routine and post-outbreak vaccination.	4	
		Vaccination coverage 60% - 80% and appropriate.	3	
		Vaccination coverage 40% - 60% and/or no assessment if appropriately implemented.	2	
		Vaccination coverage < 40% and/or no assessment if appropriately implemented.	1	
	Vaccine handling/ administration and equipment	Field personnel are adequately trained and know how to administer vaccines and have appropriate, functional equipment and in sufficient quantities.	4	
		Field personnel are adequately trained and know how to use administer vaccines and have appropriate and functional equipment which may or may not be in sufficient quantities.	3	
		Personnel are not well versed with vaccine administration even though equipment is functional, appropriate and in sufficient quantities.	2	
		Personnel may or may not be well versed with vaccine administration and there is no equipment available for vaccine administration.	1	
	Maintenance of cold chain	Cold chain maintained throughout the whole supply chain and in the field, with appropriate audits (i.e. temperature range maintained at delivery, storage and handling and personnel are trained on cold chain; Cold chain guidelines available and contingency plans in place for cold chain violations and equipment failure.	4	
		Cold chain maintained throughout the whole supply chain and in the field, but evidence of audits lacking.	3	
		Cold chain maintained but potential gaps evident and/or no guidelines or contingency plans/audits.	2	
		Poor to absent cold chain and/or no record of cold chain implementation.	1	

Comment if necessary:

Programme component	**Controlled programme stage**	**Definitions (4=Fully sufficient; 1=minimal)**		Score (√)
Surveillance	Screening	All herds/cattle tested (serology, milk etc.) in accordance with programme aims and/or to achieve programme effectiveness	4	
		> 50% of eligible (i.e. cattle herds with Brucella-susceptible cattle) tested	3	
		25% - 50% of eligible herds/cattle tested	2	
		< 25% of eligible herds/cattle tested	1	
	Serological test strategy	Appropriate internationally recognised tests employed with appropriate test strategies (e.g. parallel or serial testing when required) and relevant follow-up testing (i.e. for inconclusive results or where multiple, consecutive testing required).	4	
		Appropriate internationally recognised tests and test strategies employed but follow-up testing not complete.	3	
		Inappropriate tests and test strategies employed and/or no follow-up testing.	2	
		No serological testing.	1	
	Laboratory personnel training	Laboratory personnel are qualified, trained and well experienced with testing methods. They keep abreast with recent advances in brucellosis tests and test methods.	4	
		Laboratory personnel qualified and trained but may not be well acquainted with regards to test methods and recent advances in testing.	3	
		Laboratory personnel qualified but deficiencies in training, experience and competence are evident.	2	
		No qualified laboratory personnel available.	1	
	Information management	A central database is available and test-related data/results are entered immediately and are thus accessible to relevant personnel and the Central Veterinary Authority.	4	
		No central database but test-related data/results are captured, collated and stored in such a way that allows for analysis and extraction and prompt dissemination of result to relevant personnel and the Central Veterinary Authority.	3	
		Data are not digitized and dissemination is either inefficient and/or very slow.	2	
		Test-related data/results are inadequately produced and disseminated.	1	

Comment if necessary:

Programme component	Controlled programme stage	Definitions (4=Fully sufficient; 1=minimal)		Score (√)
Sampling/ Laboratory Practices	Collection and management of field samples	All samples (serology, milk, tissues) collected and managed appropriately i.e. guidelines are in place for sample collection and management with quality assurance measures) and records i.e. relevant field and clinical data captured fully, accurately and stored.	4	
		All samples (serology, milk, tissues) collected and managed appropriately but deficiencies detected in data capture, quality assurance or records.	3	
		Deficiencies in sample (serology, milk, tissues) collection and, quality assurance or records are poor.	2	
		No appropriate sample management or quality assurance processes in place.	1	
	Laboratory procedures	Quality assurance and guidelines in laboratories are explicit and implemented, appropriate accreditation in place and samples managed appropriately.	4	
		Quality assurance, guidelines and accreditation in place but inadequate, or sample management deficient.	3	
		Limited quality assurance, accreditation and sample management.	2	
		No quality assurance processes in place.	1	
	Reporting of Results	Results made available within pre-agreed time < 10 days of submission to relevant authorities; with electronic back-up copies retained in laboratory.	4	
		Results made available < 14 days of submission; back-up copies may be retained but not digitized or easily available.	3	
		Results made available between 14 and 30 days of submission.	2	
		Feedback poor (> 30 days) or absent.	1	

Comment if necessary:

Programme component	Controlled programme stage	Definitions (4=Fully sufficient; 1=minimal)		Score (√)
Outbreak resolution by veterinary services	Farmer notification after receipt of results	Prompt and comprehensive notification to farmer of positive result i.e. farmer notified within 3 working days by technical personnel; comprehensive zoonotic and biosecurity advice provided.	4	
		Notification to farmer < 1 week with some information on outbreak management.	3	
		Notification provided > 1 week with some information on outbreak management.	2	
		Notification not provided.	1	
	Epidemiological investigations	Comprehensive epidemiological investigation undertaken, including formal investigation report; forward and backward tracing initiated < 72 hours of notification; contact or suspect herds/animals identified and relevant testing arranged; zoonotic advice provided.	4	
		Epidemiological investigation undertaken; forward and backward tracing implemented within two weeks; contact or suspect herds/animals identified and relevant testing arranged; zoonotic advice provided.	3	
		Some forward and backward tracing, and identification of contact herds/animals, but significant gaps evident.	2	
		No forward or backward tracing or testing of suspect herds	1	
	Response vaccination	Vaccination of all susceptible cattle on affected farm and of in-contact cattle undertaken within three weeks of positive result notification.	4	
		Vaccination undertaken within one month of positive result notification; > 80% of susceptible cattle vaccinated.	3	
		Vaccination undertaken of some or eligible cattle.	2	
		No response vaccination.	1	
	Re-testing of infected herds	All infected herds re-tested according to policy guidelines (with respect to coverage and timelines) until they are declared free of brucellosis and issued with the relevant disease-free status certificate.	4	
		Infected herds are tested until the herd is declared free of brucellosis, but may be longer than policy guidelines suggest.	3	
		Re-testing may be done to identify and remove infected animals but is not followed through till the herd is declared free.	2	
		No retesting is carried out.	1	
	Removal and sampling of reactors	All test positive reactors removed within one month of test positive result with appropriate isolation, identification and supervision. Sent to an abattoir for slaughter and samples taken for bacteriological examination. Compensation is provided.	4	
		All test positive reactors removed within three months of test positive result with appropriate isolation, identification and supervision. Follow ups may or may not be done at abattoirs.	3	
		Removal of reactors is partially enforced, gaps evident and supervision lacking. Evidence of slaughter at abattoirs is lacking.	2	
		No removal of reactors is enforced or supervised.	1	

	Quarantine and movement control	A written quarantine notice is served on the affected premises and all susceptible animals individually identified and prohibited from moving except for direct slaughter. Compliance with the notice is checked and/or enforced.	4	
		A written quarantine notice is served on the affected premises but not all susceptible animals individually identified. Compliance with the notice is checked and/or enforced.	3	
		Quarantine is applied written or verbally on the affected premises but identification of cattle and/or movement control is insufficient.	2	
		There is no quarantine and / or movement control on affected premises.	1	

Comment if necessary:

Chapter 5: Discussion

This study was a novel concept but reference was made to similar previous studies done by other authors such as the use of HACCP in FMD control programmes by Van Gelderen *et al*. and its use in dairy herd health management (McAloon *et al*. 2015; Lievaart *et al*. 2005; Noordhuizen, 2008; Noordhuizen 1996). One of the closest studies of HACCP in brucellosis control was by Sandrou *et al*. (2000) on the use of HACCP in prevention of brucellosis and tuberculosis in milk. This study built on the approach by Van Geldren *et al*. but went further to provide a checklist that attempted a more thorough evaluation of brucellosis control. The produced format can also be tailor made to evaluate any other disease control programme.

The intention of this final checklist was to provide a tool that can assess the performance if brucellosis control programmes at provincial, national or even regional level. This would aid programme managers, auditors, policy makers and other interested parties to audit or monitor the level of implementation of brucellosis control programmes. It would aid in identification of gaps and where improvements are required. This checklist would assist countries that would like to know where they are with regards to brucellosis control.

Hence it can either be used to improve, maintain or remove certain aspects of the control programme depending on what is required.

The use of HACCP did however come with limitations and HACCP did not prove to be applicable in its entirety. As this was a novel concept there was no supporting literature to make comparisons especially regarding the establishment of quantitative target levels. It is also difficult to adopt HACCP when one is working with semi-quantitative or qualitative data. Which unfortunately was the case in this study most of the data for the tool was mainly qualitative and HACCP's main use has been with measurable parameters.

There is need for more research on how critical limits can be established for semi-quantitative data when using HACCP. Most data that aided in the scoring criteria was derived from literature, policies and what has been documented as successful in brucellosis control for different countries and scenarios. Regardless, a modified HACCP approach was still useful as the it provided a systematic method of identifying the critical aspects of brucellosis control and the required performances associated with it. The Delphi method was the preferred and selected method used to analyse the checklist.

The Delphi method consists of obtaining opinions from experts and providing repeat feedback to allow the participants the opportunity to see others' views and thereby move to consensus It is a method that can also be used to remotely source expert opinion without direct confrontation (Okoli, 2004). For this study this kind of approach came with the convenience that expert opinion could be sourced without having to gather all experts into one forum. A task that can prove to be difficult as availability varies between people. The Delphi has commonly been used to consult for policy formulation and resource allocation and utilization (Hsu *et al*. 2007). The experts were anonymized to reduce bias and to avoid individuals having an inclination towards opinions associated with one group member. In this project, two rounds were used to source expert opinions. As discussed prior, for logistical reasons experts did not meet but had the opportunity to view others' comments, confirm or amend their own views and see what amendments were made following Round One.

The response rate declined between rounds with five experts responding for the 2nd round. This was unlikely to have had a significant effect as those who did respond did not recommend any further changes. The positive responses from the experts confirmed that the checklist is a good platform to build from. If applied to programmes, it will provide a good evaluation tool, assist to identify deficiencies and monitor progress over time. Its strength lies in its flexibility in that it can be used at different geographic scales e.g. by a local veterinary manager for a district or can be used to aid in comparison of performances between regions. Such evaluations should then provide a basis to motivate for political will and subsequent funding towards further enhancement of the programme.

To the author's knowledge, no such checklist has been used for brucellosis programmes before. However, it will need to be validated as a next step and this will be done through applying it in different countries with differing programmes and at different regional scales. Provisional agreement has already been reached to test the checklist in the following manner:

(a) At national level, it will be tested in a country that has successfully eradicated Brucellosis, in one with an ongoing programme of control with vaccination and in one where there is little structured control.
(b) At regional level, it will be tested in two African countries, in several provinces within the countries.
(c) At local level it will be utilised by selected local state veterinarians in their districts in South Africa.

Brucellosis is an ongoing concern for the veterinary authorities in South Africa and threatens both human and animal health. The state carries the financial cost of control-related vaccination in the country for the national herd which should be costly as this includes vaccine costs and human resources. Farmers lose out due to slaughter without compensation in infected herds and through abortions and infertility. Registered abattoirs also purchase infected animals at lower prices. A study by Hesterberg in 1990 estimated losses of R300 million per annum from Brucellosis and DAFF estimates an annual loss of R600 000 plus to the dairy farmer and R240 000 plus to the commercial beef farmer at a 10% abortion rate. During the author's tenure as a State Veterinarian under Limpopo province's Mopani district the animal health section faced challenges in effective implementation of brucellosis control. It was difficult to make adjustments as one could not formally identify which areas were deficient and required immediate intervention to re-establish control. Such a checklist would have simplified the task as the critical or high priority areas pre-identified.

Conclusion

The checklist has strong potential for use as a Brucellosis control programme evaluation tool that allows end users to monitor progress and inform for effective resource allocation. It would be beneficial for programme managers, policy makers and auditors, offering a simplified but comprehensive approach to Brucellosis disease control evaluation. In South Africa it will help evaluate the gaps within the country's current brucellosis control programme. It can be made more generic to be applied for other disease control programmes as well. It would also be more beneficial if it is used alongside a quantitative assessment of the economic burden the disease poses in the region under evaluation.

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Appendix A:
Research Committee Protocol Approval

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

FACULTY OF VETERINARY SCIENCE

RESEARCH ADMINISTRATION

PROTOCOL COVER PAGE 2016

PROJECT (please type)		
Title	An assessment of HACCP as a monitoring tool for the Bovine Brucellosis control programme in Limpopo Province, South Africa	NUMBER

APPLICANTS	Student # : 13398866			
	NAME	QUALIFI-CATIONS	EMAIL ADDRESS	SIGNATURE
RESEARCHER	Dr Tapiwa Makwavarara	BVSc	tash.ie@live.com	
SUPERVISOR	Prof Darrell Abernethy	BVSc, MSSc, PhD	darrell.abernethy@up.ac.za	
Co-SUPERVISOR(s)				

TYPE OF RESEARCH				
MSc ✓	~~MMedVet~~	~~PhD~~	~~Contract~~	~~Other~~

RESEARCH THEMES		Tick ✓
FOOD	Veterinary aspects of food safety and food security	✓
WEH	Wildlife and Environmental Health	
MIPD	Molecular studies on infectious and parasitic diseases of animals	
PEVM	Phytomedicine and ethno-veterinary medicine	
ECA	Equine and companion animal health and welfare	
ANPH	Anatomical and physiological studies on animals	

CONSENT TO PROVIDE SERVICES		
Type of Service	Personnel	Signature
1.		
2.		
3.		

APPROVAL	
NAME OF HOST DEPARTMENT	
(acting)	22/3/2017
SIGNED: HEAD OF DEPARTMENT	DATE

Appendix B:
Animal Ethics approval

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Veterinary Science
Animal Ethics Committee

Ref: V046-17

13 June 2017

Prof. D Abernethy
Dean
Faculty of Veterinary Science
(Darrell.abernethy@up.ac.za)

Dear Prof. Abernethy

Project V046-17
An assessment of HACCP as a monitoring tool for the *Bovine Brucelliosis* Control Programme in Limpopo, South Africa (TMT Makwavarara)

The application was discussed by the Animal Ethics Committee of the University of Pretoria at the May 2017 meeting. The committee did not have any concern with the project as no animals were involved. However, since the application is a questionnaire it is incumbent on the researcher to apply for ethical approval from the Humanities or Health Sciences Ethics Committees, as the case may be

If you have any questions, please feel free to contact the committee.

Yours sincerely

Prof V Naidoo
CHAIRMAN: UP-Animal Ethics Committee

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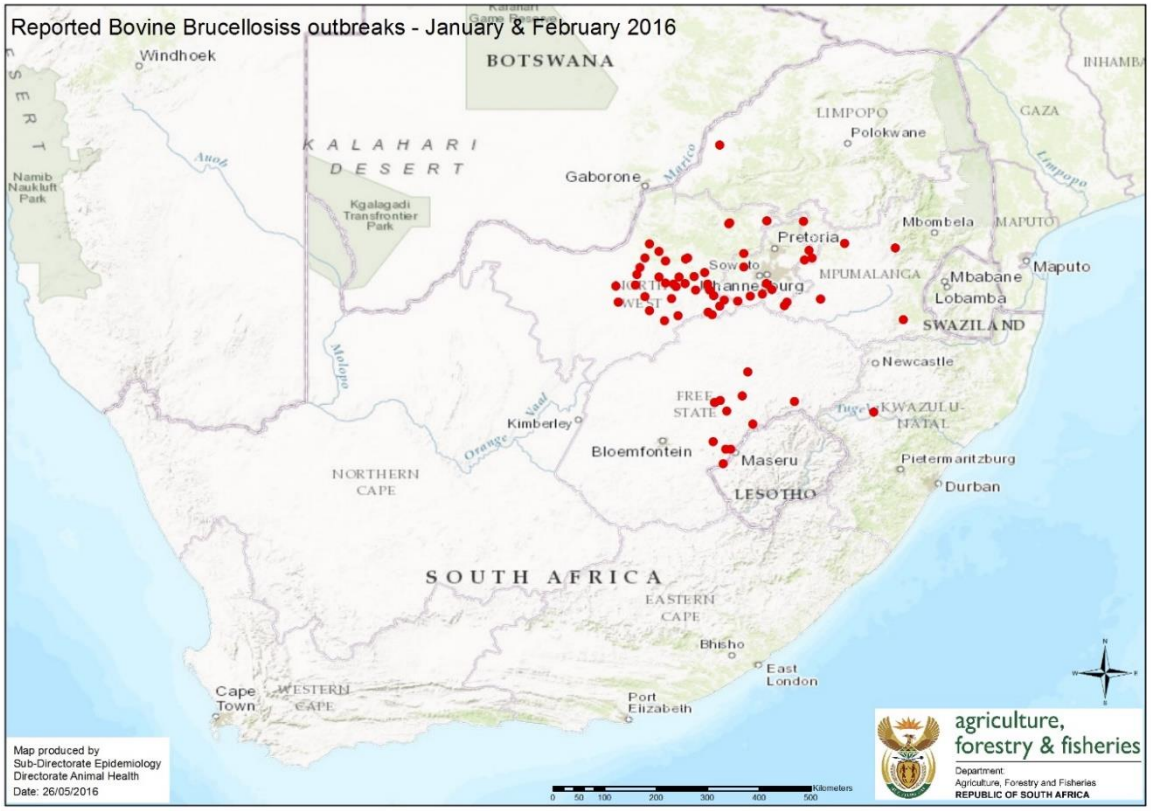
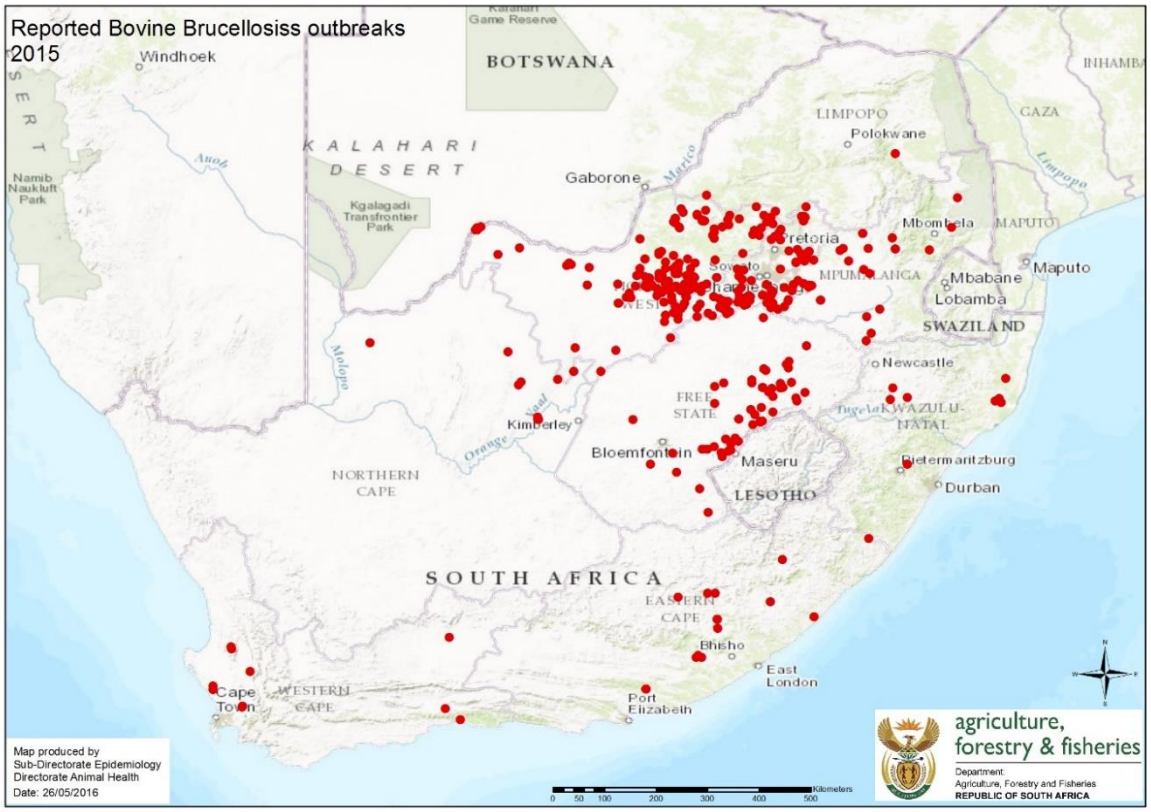
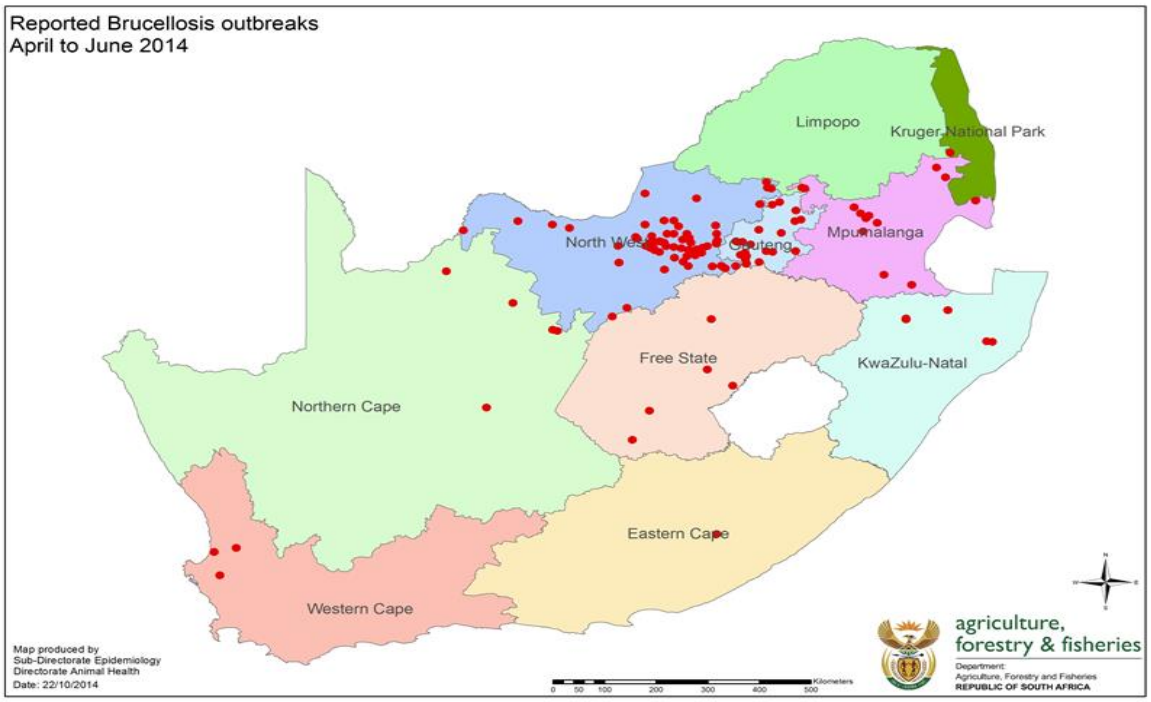
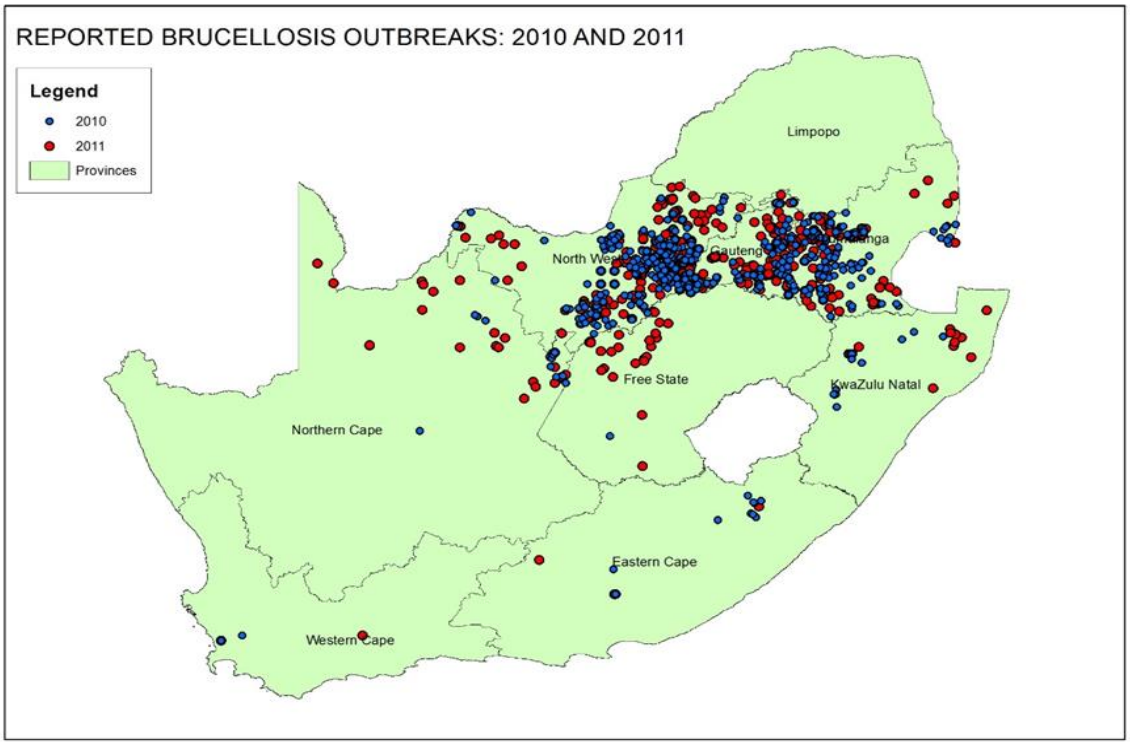
Fakulteit Veeartsenykunde
Lefapha la Diseanse tša Bongakadiruiwa

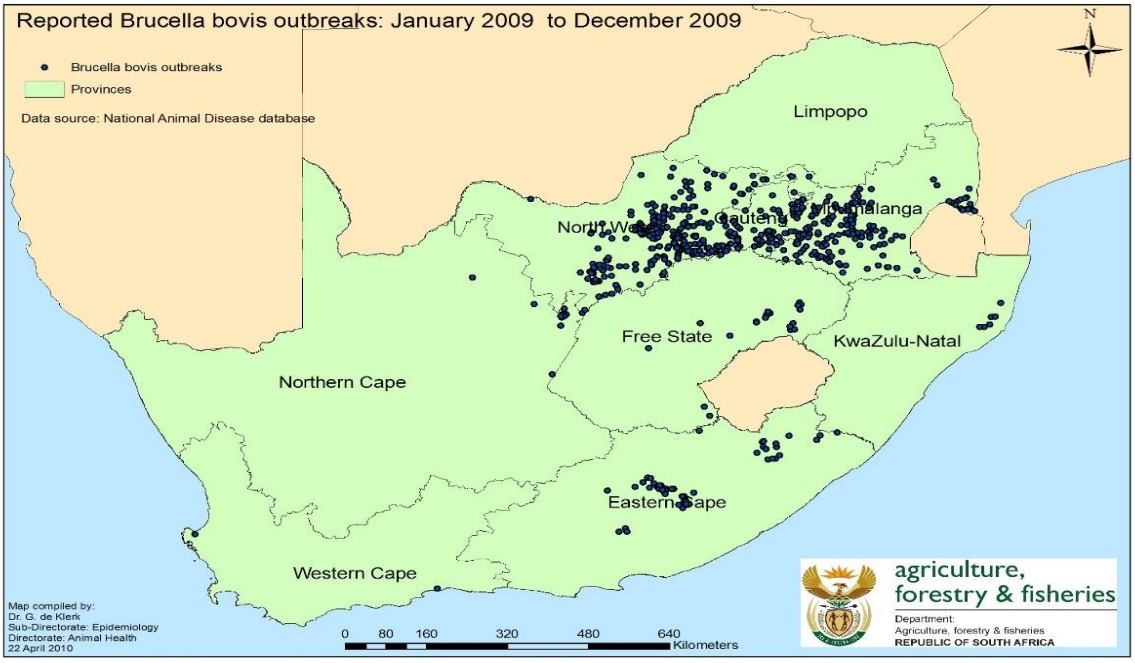
Appendix C:
Reported *Brucella abortus* outbreaks 2008-2016 (South Africa)

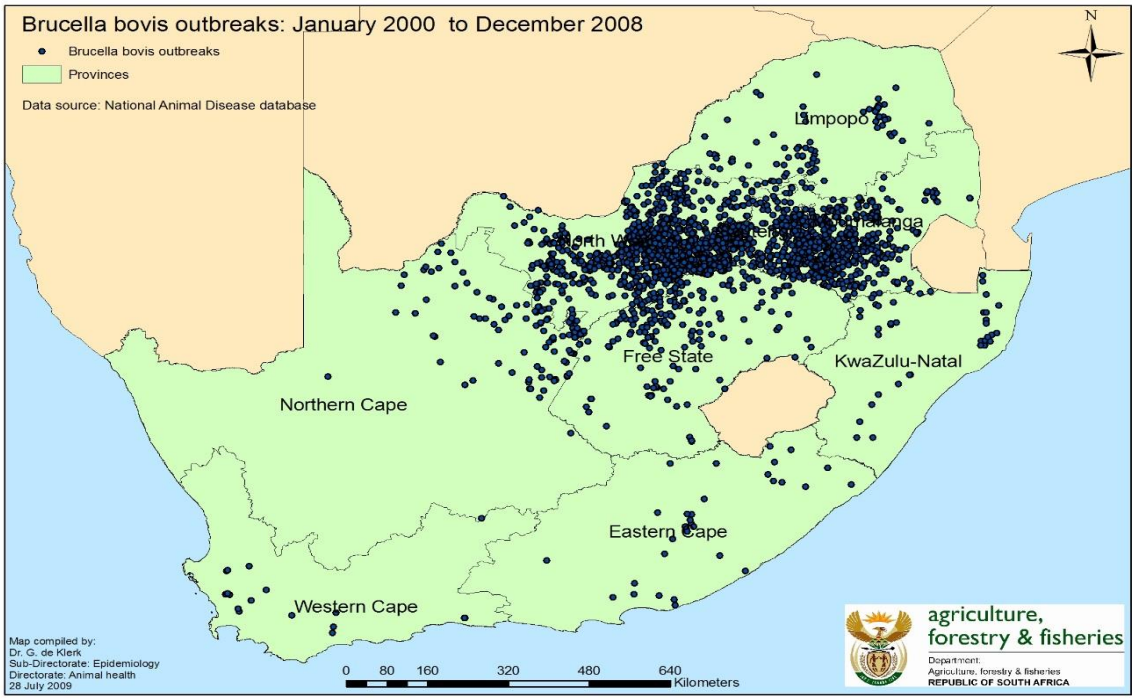



Reported Bovine Brucellosiss outbreaks
2015
Windhoek
BOTSWANA
KALAHARI
DESERT
Gaborone
LIMPOPO
Polokwane
GAZA
Pretoria
Mbombela
MAPUTO
Maputo
Mbabane
Lobamba
SWAZILAND
Newcastle
KWAZULU-
NATAL
Kimberley
Bloemfontein
Maseru
LESOTHO
Pietermaritzburg
Durban
NORTHERN
CAPE
SOUTH AFRICA
EASTERN
CAPE
Bhisho
East
London
Cape
Town
WESTERN
CAPE
Port
Elizabeth
Map produced by
Sub-Directorate Epidemiology
Directorate Animal Health
Date: 26/05/2016
agriculture,
forestry & fisheries
Department:
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA


Reported Brucellosis outbreaks
April to June 2014
Limpopo
Kruger National Park
Mpumalanga
Free State
KwaZulu-Natal
Northern Cape
Eastern Cape
Western Cape
Map produced by
Sub-Directorate Epidemiology
Directorate Animal Health
Date: 22/10/2014
agriculture,
forestry & fisheries
Department:
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA


REPORTED BRUCELLOSIS OUTBREAKS: 2010 AND 2011
Legend
2010
2011
Provinces
Limpopo
Gauteng
Free State
KwaZulu Natal
Northern Cape
Eastern Cape
Western Cape


Reported Brucella bovis outbreaks: January 2009 to December 2009
Brucella bovis outbreaks
Provinces
Data source: National Animal Disease database
N
Limpopo
Gauteng
Free State
KwaZulu-Natal
Northern Cape
Eastern Cape
Western Cape
Map compiled by:
Dr. G. de Klerk
Sub-Directorate: Epidemiology
Directorate: Animal Health
22 April 2010
0 80 160 320 480 640
Kilometers
agriculture, forestry & fisheries
Department:
Agriculture, forestry & fisheries
REPUBLIC OF SOUTH AFRICA


Brucella bovis outbreaks: January 2000 to December 2008
Brucella bovis outbreaks
Provinces
Data source: National Animal Disease database
N
Limpopo
Mpumalanga
Free State
KwaZulu-Natal
Northern Cape
Eastern Cape
Western Cape
Map compiled by:
Dr. G. de Klerk
Sub-Directorate: Epidemiology
Directorate: Animal health
28 July 2009
0 80 160 320 480 640
Kilometers
agriculture, forestry & fisheries
Department:
Agriculture, forestry & fisheries
REPUBLIC OF SOUTH AFRICA

Appendix D:
Amended intermediate checklist

Table 6 Checklist: Intermediate (Amended)

Programme component	Controlled programme stage	Risk	Expected standard/most desirable outcome
Policy and Legislation	Central policy and legislation	Lack of sufficient national policy legislation guidelines for effective implementation	National policy is in place, underpinned by adequate legislation for effective implementation. Policy and regulatory documents accessible to all responsible officials with appropriate guidelines/instructions and awareness training provided to all relevant personnel.
	Law Enforcement by veterinary services	Non-compliance	Enforcement is strong farmers are regularly and actively monitored to ensure quarantine, isolation, branding and removal of infected animals; post-outbreak testing and vaccination.
Financial and material resources	Resources for surveillance	Non detection	Available funding permits surveillance that will meet all epidemiological objectives i.e. serosurveillance, abattoir surveillance, post-abortion sampling to detect disease, establish disease freedom or *ad hoc* sampling and testing
	Resources for control measures	No resources for programme implementation	Available resources permit comprehensive control measures to resolve outbreaks i.e. post-outbreak serological testing and/or vaccination, follow-up initiatives, epidemiological investigations, compensation (if included).
	Resources for routine vaccination	No resources for vaccination	Resources available to procure required quantities of vaccines

Programme component	Controlled programme stage	Risk	Expected standard/most desirable outcome
Human Resources and Management	Personnel complement	Lack of effective programme implementation	There is sufficient human resource capacity (veterinary, para-veterinary, administrative) to implement the programme effectively. If private sector involved, there are sufficient human and financial resources to implement the programme.
	Personnel motivation	Lack of effective programme implementation	Personnel highly motivated i.e. perform all delegated activities with due diligence, address problems comprehensively, excellent work attendance, very good performance assessments scores.
	Personnel training	Lack of effective programme implementation	Personnel sufficiently trained i.e. training offered on a regular basis to relevant personnel to optimise awareness, knowledge and skills.
	Communication on programme strategy	Lack of effective programme implementation	Communication is excellent i.e. all personnel have access to a range of information on programme strategy and feedback is facilitated; evidence exists of excellent communication (e.g. external reviews, personnel feedback etc.).
	Performance assessment and management	Lack of effective programme implementation	Excellent performance management i.e. strong evidence of active performance assessment; explicit audits of programme management; incentivisation programme in place.
Farmer behaviour and awareness	Compliance with programme requirements	Non-compliance	An acceptable proportion of farmers should attempt to meet at least the minimum to full programme requirements.
	Biosecurity practices	Lack of effective biosecurity practices	Where applicable farmers practice excellent biosecurity measures, irrespective of state regulation i.e. isolation of calving/aborting animals; appropriate responses to placentae, aborted foetuses; risk-averse livestock movements and grazing practices; comprehensive testing and/or vaccination for brucellosis. Quarantine/retention of newly introduced animals.
	Reporting of abortions	Non-reporting of abortions	Most abortions (visualised or suspected) are reported to the relevant authorities; aborting animals isolated and tested.
	Outbreak resolution	Spread of pathogen between and within herds due to inadequate outbreak management	Farmers actively assist regulatory authorities and comply with regulations by showing personal initiative in resolving outbreaks. They comply fully with testing/vaccination schedules, biosecurity advice, livestock movement regulations and provision of epidemiological information.
	Awareness and Training	Lack of knowledge and awareness to facilitate effective programme implementation	Active consultation with farmer representative groups and explicit, formal programme of raising farmer awareness through appropriate media i.e. farming press, training or extension programmes, social media.

Programme component	Controlled programme stage	Risk	Expected standard/most desirable outcome
Vaccination	Vaccine availability	Poor to no vaccination, Insufficient herd immunity	Vaccines are used that comply with international standards are always available from manufacturer with a timeous procurement process to ensure availability when it is required for use.
	Vaccination coverage and implementation	Low vaccination coverage, insufficient herd immunity	Vaccination coverage sufficient (> 80% of relevant herds/cattle) and appropriate (i.e. according to manufacturer guidelines: heifers between 4-8 months; adults with RB51), in both routine and post-outbreak vaccination.
	Vaccine handling/ administration and equipment	Improper equipment and vaccination administration	Field personnel are adequately trained and know how to administer vaccines and have appropriate, functional equipment and in sufficient quantities.
	Maintenance of cold chain	Loss of cold chain and subsequent loss of vaccine potency	Cold chain maintained throughout the whole supply chain and in the field, with appropriate audits (i.e. temperature range maintained at delivery, storage and handling and personnel are trained on cold chain; cold chain guidelines available and contingency plans in place for cold chain violations and equipment failure.
Surveillance	Screening	Non-detection	All herds/cattle tested (serology, milk etc.) in accordance with programme aims and/or to achieve programme effectiveness.
	Serological test strategy	Inappropriate test strategy	Appropriate internationally recognised tests employed with appropriate test strategies (e.g. parallel or serial testing when required) and relevant follow-up testing (i.e. for inconclusive results or where multiple, consecutive testing required).
	Laboratory personnel training	Improper testing	Laboratory personnel are qualified, trained and well experienced with testing methods. They keep abreast with recent advances in brucellosis tests and test methods.
	Information management	No records available for outbreak management	A central database is available and test-related data/results are entered immediately and are thus accessible to relevant personnel and the Central Veterinary Authority.
Sampling/ Laboratory Practices	Collection and management of field samples	Sample mismanagement	All samples (serology, milk, tissues) collected and managed appropriately i.e. guidelines are in place for sample collection and management with quality assurance measures and records i.e. relevant field and clinical data captured fully, accurately and stored.
	Laboratory procedures	Improper laboratory procedures	Quality assurance and guidelines in laboratories are explicit and implemented, appropriate accreditation in place and samples managed appropriately.
	Reporting of results	Non-reporting, subsequent non-detection	Results made available within pre-agreed time < 10 days of submission to relevant authorities; with electronic back-up copies retained in laboratory.

Programme component	Controlled programme stage	Risk	Expected standard/most desirable outcome
Outbreak resolution by veterinary services	Farmer notification after receipt of results	No notification/reporting	Prompt and comprehensive notification to farmer of positive result i.e. farmer notified within 3 working days by technical personnel; comprehensive zoonotic and biosecurity advice provided.
	Epidemiological investigations	Non-detection, environmental contamination and spread within and between herds	Comprehensive epidemiological investigation undertaken, including formal investigation report; forward and backward tracing initiated < 72 hours of notification; contact or suspect herds/animals identified and relevant testing arranged; zoonotic advice provided.
	Response vaccination	Poor vaccination response and consequent spread within and between herds	Vaccination of all susceptible cattle on affected farm and of in-contact cattle undertaken within three weeks of positive result notification.
	Re-testing of infected herds	Non-detection and consequent spread within and between herds	All infected herds re-tested according to policy guidelines (with respect to coverage and timelines) until they are declared free of brucellosis and issued with the relevant disease-free status certificate.
	Removal and sampling of reactors	Environmental contamination and spread within and between herds	All test positive reactors removed within one month of test positive result with appropriate isolation, identification and supervision. Sent to an abattoir for slaughter and samples taken for bacteriological examination. Compensation is provided.
	Quarantine and movement control	Environmental contamination and spread within and between herds	A written quarantine notice is served on the affected premises and all susceptible animals individually identified and prohibited from moving except for direct slaughter. Compliance with the notice is checked and/or enforced.