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GAP ANALYSIS: SMALL RUMINANTS BRUCELLOSIS CONTROL AND ERADICATION PROGRAM IN BOSNIA AND HERZEGOVINA

BY

Mersiha Torlak
Degree to be awarded: M.P.H.
Career MPH

Susan Butler, EdD, MCHES	Date
Grant Baldwin, PhD, MPH	Date
Melissa Alperin, MPH, CHES Chair, Career MPH Program	Date

GAP ANALYSIS: SMALL RUMINANTS BRUCELLOSIS CONTROL AND ERADICATION PROGRAM IN BOSNIA AND HERZEGOVINA

BY

Mersiha Torlak
M.P.H., Emory University, 2012
B.S., Emory University, 2007
A.S., Martin Luther University, 2000

Thesis Committee Chair: Susan Butler, EdD, MCHES

An abstract of
A Thesis submitted to the Faculty of the
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Abstract

GAP ANALYSIS: SMALL RUMINANTS BRUCELLOSIS
CONTROL AND ERADICATION PROGRAM
IN BOSNIA AND HERZEGOVINA

BY
Mersiha Torlak

Brucellosis is a global zoonosis caused by the Brucella bacteria. It is a very contagious disease, accompanied by great economic loss, of various ruminant animals that can be transmitted to humans and cause debilitating illness. The disease is well controlled in developed countries due to implementation of sustainable vaccination and surveillance programs. Nevertheless, brucellosis is endemic in many developing countries around the world, especially in the Mediterranean region with recent epidemic outbreaks of Brucella melitensis infection in sheep and goats, and subsequently in humans, in Bosnia and Herzegovina.

The purpose of this project was to analyze and evaluate the recent changes in the brucellosis prevention program in sheep and goats in Bosnia and Herzegovina with the aim to discover and address any gaps in the new program, as well as to make specific recommendations for program improvement based on the Socio-Ecological framework for prevention. After an extensive literature review and numerous expert key informant interviews, it can be concluded that the newly implemented small ruminants vaccination

program is very successful and has accomplished its initial aim to control brucellosis outbreaks in Bosnia and Herzegovina. Despite its overall success, there are many gaps that exist in the new program and country specific recommendations can be made to further strengthen the program and improve the chance of a long long-term brucellosis control and eradication in the entire Bosnia and Herzegovina. Specific recommendations target the five essential benchmarks for the overall program success and include the following: 1) Animal Registration, Identification, and Movement Control, 2) Strategic Brucellosis Vaccination Process, 3) Accurate and Timely Brucellosis Testing/Routine Surveillance, 4) Quality Assurance/Quality Control Program, and 5) Continuous and Targeted Brucellosis Education.

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LIST OF ABBREVIATIONS

BIH- Bosnia and Herzegovina

CDC- Center for Disease Control

GDP- Gross Domestic Product

ELISA-Enzyme Linked Immunosorbent Assay

EU-European Union

FAO-Food and Drug Administration of United States

FBIH- Federation of Bosnia and Herzegovina

FVE- Federation of Veterinarians of Europe

OIA-World Organization for Animal Health

PPE-Personal Protective Equipment

QA-Quality Assurance

QC-Quality Control

RBT- Bose Bengal Test

RS- Republic Srpska

SAA-Stabilization and Association Agreement

SEE-South Eastern Europe

SEEHN- South Eastern Europe Health Network

SIDA- Swedish International Development Agency

SVO – State Veterinary Office

USDA- United States Department of Agriculture

WHO-World Health Organization

CHAPTER I: INTRODUCTION

Rationale

Brucellosis remains the commonest zoonotic disease worldwide despite various reventive efforts in place. Worldwide, more than 500 000 new cases emerge each year (P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006). The disease is well controlled in developed countries due to implementation of sustainable vaccination and surveillance programs; however it is endemic in many developing countries around the world, especially in the Mediterranean region with recent increase in the number of new cases reported in Bosnia and Herzegovina (BIH) (P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006). The primary source for human infection in Bosnia and Herzegovina is sheep and goat meat and dairy products and therefore prevention programs primarily concentrate on small ruminant population (Z. Mulabdic, personal communication, March 30, 2011).

Prior to the war in Bosnia and Herzegovina that took place from April 6, 1992 to December 14, 1995, brucellosis was well controlled. BIH had a well-developed public health capacity and infrastructure; however, war caused chaos in all aspects of the public health sector, as well as migration and great displacement of the population within the country (Michael J.Toole, 1993). As a result of the war, brucellosis control and surveillance became very difficult and epidemic outbreaks were inevitable.

Reports of first confirmed human cases started to appear sporadically in year 2000. However, the number of confirmed cases of brucellosis has been steadily increasing since 2001(P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006). The incidence of human brucellosis has risen from 0.6/100,000 during 2002 to 6.49/100,000 in 2006 in the Federation of Bosnia and Herzegovina (FBIH), while very few cases have been reported by the Republic

of Srpska (RS) (Kahn, 2007). In 2007, as brucellosis became epidemic, the Prime Minister of Bosnia and Herzegovina recognized the public health problem and invited a group of Center for Disease Control (CDC) experts to launch an investigation of the current situation in the country. A group of four CDC experts were able to assess the situation and make country specific recommendations for disease prevention and control; however they recognized the level of difficulty and challenges associated with execution of their suggestions (Kahn, 2007).

The ongoing challenges with the public health infrastructure and capacity, as well as ongoing migration of the animal and human population make it very difficult to determine true incidence rates for the entire country. Social and economic burden of brucellosis infection in animal and human sector in the entire country is evident and experts agree that prevention is the most suitable approach for disease control and eradication (M. Guerra, W. Nicolson, personal communication, June 17, 2011).

Until recently Bosnia and Herzegovina relied on the test and slaughter method for disease control in the animal population (Seric-Haracic S, 2008). Even though public health officials were able to control epidemic outbreaks with the test and slaughter method in short term, timely and more efficient strategies are needed for long term disease control. The number of euthanized animals grew significantly over the years contributing to significant economic loss in the entire country. “The number of euthanized animals has increased severely from 8,788 to approximately 32,000 animals in 2008 (mostly sheep)”, (Kahn, 2007). Initially, officials were reluctant to start the vaccination programs due to individual believes, lack of education, lack of funding and government support (M. Guerra, W. Nicolson, personal communication, June 17, 2011). However, in 2009 after realization of the

unsatisfactory conditions in the current brucellosis prevention program in the entire country, officials recognized the need to implement animal vaccination as a more efficient strategy for disease control and prevention. The Swedish Embassy provided the needed financial support for implementation of the “mass vaccination” program in sheep and goats in hopes to provide better disease control and possible brucellosis eradication in the entire Bosnia and Herzegovina ("State Veterinary Office: News Conference", 2011).

The success of the recently implemented mass vaccination program is of great economic and public health interest for the entire country (Krkic-Duatovic S, 2006; Zarema Obradovic, 2010). While there is a great need for the success in the initial mass vaccination, continuation of the animal vaccination is of even greater importance. In order to continue with a strategic animal vaccination program, ongoing program evaluation and assessments based on the socio-ecological framework is essential.

Problem Statement

Failure to control brucellosis outbreaks in Bosnia contributes to global reemergence of this debilitating zoonosis. Adaptation of the developed countries brucellosis prevention policy is essential for control of the disease in the animal and human sector ("TV Alfa "In the Mirror" special edition broadcasted on July 19, 2009," 2011). As a result of recent epidemic outbreaks and ongoing public health challenges, as well as the economic gain of increasing the export of animals and animal products into other countries, an immerse need exists for ongoing systematic and effective brucellosis prevention program (Felix Roth, 2003). Establishment and continuity of effective brucellosis programs is essential for Bosnia’s entry into European Union (EU) as well, further validating the need for a successful brucellosis program (Europa.ba, 2011; Fejzic, 2006).

This project seeks to analyze and evaluate the recent changes in the brucellosis prevention policy in sheep and goats in Bosnia and Herzegovina with the purpose to discover and address any gaps in the new program, as well as to make specific recommendations for program improvement based on the Socio-Ecological framework for prevention. In order to provide an efficient assessment of the current state of the brucellosis prevention program in Bosnia and Herzegovina, the following benchmarks need to be addressed in detail: 1) Animal Registration, Identification, and Movement Control, 2) Brucellosis Vaccination Process, 3) Brucellosis Testing/Routine Surveillance, 4) Quality Assurance (QA) / Quality Control Program (QC), and 5) Brucellosis Education.

Research Questions

The purpose of the present project is to answer the following research questions:

1. What are the key strengths and challenges of the new brucellosis prevention program in small ruminants in Bosnia and Herzegovina?

2. What specific improvement suggestions can be made for long term success?

Significance Statement

The significance of this project on the current brucellosis prevention program in Bosnia and Herzegovina is multi-dimensional. One major purpose of this project is to analyze the current prevention program for its key strengths and weaknesses. By evaluating the current state of the prevention program and comparing it to the developed countries/EU standards reasonable and country specific program improvement strategies can be made. A successful brucellosis prevention program is essential not only for public health improvement in Bosnia and Herzegovina, but also for economic improvement in Bosnia and Herzegovina

which can only be accomplished by diminishing political and religious differences by placing the public and veterinary health in the first place.

The need for ongoing public health evaluation, education, and development is inevitable in countries such as Bosnia and Herzegovina and is essential for short and long-term success. Control and eradication of brucellosis in Bosnia and Herzegovina is only possible through ongoing public health education and acclimation to developed countries standards through implementation of continuous animal vaccination programs. The ongoing survival challenges people face on a daily basis and ways to prevent future epidemic outbreaks are important issues to learn. This project seeks to review the current brucellosis vaccination program success in Bosnia and Herzegovina, and to list country specific suggestions for its improvement and need for continuation.

Definition of Terms

1) Brucellosis: Brucellosis is a global zoonosis caused by bacteria of the genus *Brucella.* Brucellosis is transmitted to humans through direct and indirect contact with infected animals. Direct contact with fluid, secretions, or tissue of infected animals is the most common form of acquisition. Indirect form of transmission is mostly caused by ingestion of infected dairy products (unpasteurized dairy products) or raw meat.

2) Infection: Infection is an invasion and multiplication of microorganisms in body tissues, causing local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. An individual is considered to be infected with Brucella species when: 1) for individuals with health insurance, local (USC) serological testing performed using Rose-Bengal agglutination test is positive/reactive, and 2) uninsured individuals present with symptoms clinically compatible with brucellosis. All individuals considered having brucellosis infection are hospitalized for treatment. Brucellosis treatment is comprised of a combination of doxycycline and either gentamicin or streptomycin for six weeks. The effectiveness of the therapy is assessed through Enzyme Linked Immunosorbent Assay (ELISA) testing of human serum. At least two tests are done during the course of treatment.

3) Occupational disease: Occupational disease is defined as an illness that is caused by exposure at the workplace. Although not a lethal disease itself, brucellosis can cause major disability. Brucellosis poses an increased risk of infection in farmers, butchers, slaughter house workers, and veterinarians, thereby meeting the definition of an occupational disease.

4) Postwar era: Post war era refers to the period after December 14th, 1995 when the Dayton Agreement was signed. Dayton agreement is the General Framework Agreement for Peace in Bosnia and Herzegovina, which ended the three and a half year long war in Bosnia.

5) Zoonosis: Any disease or infection that is naturally transmissible from vertebrate animals to humans and vice-versa is classified as a zoonosis.

6) Rose-Bengal Test (RBT): A rapid agglutination slide test for the detection of Brucella specific agglutinins.

CHAPTER II: REVIEW OF THE LITERATURE

Introduction

Knowledge about the country, as well as historical and current studies in brucellosis research is critical in order to understand the development of the brucellosis disease over the years, as well as the need for the development and implementation of successful and sustainable prevention programs. This chapter summarizes the current literature on brucellosis, specifically focusing on etiology and epidemiology, diagnosis, surveillance and prevention in Bosnia and Herzegovina. It also covers the current status, legislative requirements, and available support system in developed and developing countries in Europe, especially focusing on countries with similar socio-economic and geographic background to Bosnia and Herzegovina.

Bosnia and Herzegovina

In order to understand the roots for the ongoing challenges in brucellosis prevention and control in Bosnia and Herzegovina, one must know some basic facts about the country and its recent history. Bosnia and Herzegovina is located in the western part of the Balkan Peninsula and covers 51,197km^2 (Wikipedia, 2011b). The war (1992-1995) created a complex political environment with two administrative entities, Federation of Bosnia and Herzegovina and Republic Srpska, and the district of Brcko (Wikipedia, 2012). Both entities are responsible for their own internal affairs, environmental, economic, social and health sectors. Government segregation causes constant disagreements between the entities, ultimately resulting in slow economic, as well as health system recovery (Z. Mulabdic, personal communication, March 30, 2011). Pre-war population was approximately 4.5 million and estimated population in 2001 was 3.8million (Michael J.Toole, 1993). More than

1.0 million Bosnians were displaced during the war, causing disruption of public health services and rise in communicable and non-communicable diseases.

The first case of brucellosis in Bosnia and Herzegovina was registered in 1952 (J.A. Gaon, 1989). While brucellosis occurred only sporadically in the area of Bosnia and Herzegovina in the pre-war period, it has become endemic since 2007 ranging number nine on the leading reportable infectious diseases list according to the Institute of Public Health data (Ante Ivankovic, 2010). By the middle of 2007 brucellosis became epidemic in the majority of the regions in Bosnia and Herzegovina, involving both entities, causing extensive economic and health consequences for the general population, especially farmers and herdsmen families (Zarema Obradovic, 2010). Despite the availability of safe and effective vaccines against the most common *Bucella* species the economic and political situation, as well as misconception about the public health implications of the disease have hindered implementation of effective and sustainable prevention programs for prevention of future epidemic outbreaks of brucellosis (M. Guerra, W. Nicolson, personal communication, June 17, 2011).

Control of brucellosis in animals is directly linked to the control of disease in human and therefore human and veterinary sectors should be in continuous and real time collaboration (Radovan Cekanac, 2012). Experts believe that only implementation of effective animal vaccination programs, and effective animal and human surveillance systems can lead to control and eradication of brucellosis (Kahn, 2007). Due to post war political and economic instability, as well as weak Public Health infrastructure, Bosnia and Herzegovina continues to be challenged with implementation and maintenance of effective brucellosis surveillance, and control and prevention programs.

Etiology

Brucellosis is a global zoonosis caused by bacteria of the genus *Brucella ("CDC.GOV (Brucellosis: an Overview),").* There are four species of the *Brucella* bacteria that can cause infections in animals and are of immediate concern to humans (Young, 1995). *Brucella melitensis* mainly affects sheep and goats, *brucella abortus* mainly affects cattle, *brucella suis* mainly affects pigs, and *brucella canis* mainly affects the dogs ("Facts about Brucellosis", 2011). The most prevalent brucella infections among animals that are of great concern to humans are caused by *brucella melitensis* and *abortus species*.

Ever since the discovery of *Brucella melitensis* by David Bruce in 1887 (Tan S, 2011) and *Brucella abortus* by Bernhard Bang in 1895 (Wikipedia, 2011c) it has been an emerging disease in many parts of the world. *Brucellae* are slow growing Gram-negaticve cocci, coccobacilli, and short rods. Brucella appears in smooth and rough strain form. It can survive up to 10 weeks in soil, and up to 2 ½ years in liquid manure providing a viable source for re-infection in animals and humans. Mutated strains have been developed as live-attenuated vaccines for controlling brucellosis infection among livestock. Due to small inoculum needed to induce human disease, its propensity for airborne transmission and induction of debilitating disease *Brucella* has been traditionally considered a biological weapon (P. P. G. Pappas, L. Chrisou, N. Akritidis, 2006).

Epidemiology

Brucellosis is a zoonosis that can be transmitted between animal species, and frequently to humans as well. Although incidence and prevalence of the disease vary widely from country to country it still remains a major source of disease in humans and domesticated animals in the Mediterranean region, Asia, and parts of African and Latin America. While the true incidence of human brucellosis is unknown, the reported incidence in endemic-disease areas varies widely from <0.01 to >200 per 100, 000 population ("CDC.GOV (Brucellosis: an Overview),"). Low levels of surveillance and reporting, and higher infection risk of the population may play a big role in the number of reported cases.

Generally the infectious dose of the *brucella* species is relatively small, especially in aerosol form. Brucellosis can be transmitted from infected animals to humans through direct and indirect contact ("Facts about Brucellosis", 2011). Direct contact with fluid, secretions, or tissue of infected animals is the most common form of the direct transmission path. Indirect form of transmission is mostly caused by ingestion of infected dairy products (unpasteurized dairy products) or raw meat. Brucellosis is also considered an occupational disease for farmers, slaughterhouse workers, butchers, veterinarians and laboratory workers. While contamination through skin wounds is most common for individuals working in slaughterhouses, butchers, farmers and veterinarians, inhalation is the most common mode of transmission in laboratory workers. Human-to-human transmission of Brucellosis is very low but nevertheless it has been associated with sexual and/or close contact, transplacental exposure and breast milk, or tissue transplantation ("CDC.GOV (Brucellosis: an Overview),").

In a retrospective study done by Obradovic et al, analysis of official reports from the Institute of Public Health and epidemiological surveys in Bosnia and Herzegovina from 2001 through 2008 revealed the dominant mode of human infection to be consumption of unpasteurized dairy products, followed by occupational exposure through inhalation of infected animal secretion or inoculation of *Brucella* microorganisms through skin cuts and abrasions (Zarema Obradovic, 2010). The increasing number in animal and human seropositivity ultimately led to replacement of the test and slaughter method to mass vaccination. Study findings indicate a strong need for continuing public education, as well as training on personal protective equipment (PPE) in professional settings.

Diagnosis

The isolation and identification of *Brucella* offers the only definitive diagnosis of brucellosis and may be useful for epidemiological purposes, as well as to monitor the progress of vaccination programs in animals (Corbel, 2006). In principal there are two categories of diagnostic tests in humans and in animals: those that directly demonstrate the presence of the microorganism, and those that detect the immune response to its antigens providing indirect diagnosis. Bacteriological diagnosis provides direct recovery of bacteria from biological samples and is the only conclusive and most specific evidence of *Brucella* infection. Blood culture, isolation and identification of *Brucella* species is the direct form of diagnosis and provides 100% sensitivity and specificity. The other indirect form of diagnosis is done through serologic testing of biological samples. While the sensitivity is in the upper 90^{th} percentile, there is a possibility for cross-reaction and false positive results.

At their 2007 visit to Bosnia and Herzegovina, CDC experts stressed out the importance of effective and timely testing of animals and humans in order to prevent further

spread of infection (Kahn, 2007). They questioned the local laboratories ability to perform qualitative and quantitative tests, especially understanding of the results. Therefore, specific recommendations were made to standardize across all entities, as well as to establish a State Public Health Laboratory Reference Network. Many local public health officials are still concerned that the actual numbers of brucellosis cases in animals and humans are under reported and it ultimately will lead to re-infection and ongoing endemic conditions in the region (Z. Mulabdic, personal communication, March 30, 2011). According to Cavaljuga, lack of case definition for brucellosis surveillance and lack of urgency to call out epidemic outbreaks after a significant rise in brucellosis cases in 2007 lead to prolongation and increased severity of the brucellosis outbreaks (Cavaljuga, 2008). This indicates the need for effective surveillance programs in place, as well as timely disease identification and elimination in the animal population.

Diagnosis in Animals

Stained smear method and culture method are the widely used bacteriological methods for the diagnosis of *Brucella* species (Corbel, 2006). Smears of biological placental, vaginal and stomach content material may be stained using modified Ziel-Neelson or Kosters method. Presence of large intracellular aggregates of organisms provides direct evidence of brucellosis. *Brucella* can also be cultured from a wide variety of biological material, including vaginal mucus, placenta, fetal stomach contents and milk.

Serological method of detection of specific antibody in serum or milk is the most practical and cost-effective way to diagnose brucellosis (Corbel, 2006). In practice mostly used test is the RBT test that relies on the principle of antigen-antibody agglutination and is an excellent screening test; however it may be over-sensitive for individual animal diagnosis,

especially for vaccinated animals. ELISA tests on the other hand offer the best sensitivity and specificity, with minimal equipment requirements, even though results may vary between laboratories depending on exact methodology used.

Diagnosis in Humans

RBT is currently the rapid screening test of choice; however results should be confirmed by other serological and bacteriological tests due to possibility of false positive results and cross-reaction. Serum tube agglutination test detects specific antibodies to the smooth lippopolysacharide antigen and are mostly useful for diagnosing human brucellosis. However, the most specific diagnostic test is the direct culture, isolation and identification of *Brucella* species (MR, 1961). The simplest and most commonly used culture is the blood broth culture. Incubation time varies for positive (7 days) and negative culture (45 day).

Surveillance

Brucellosis is a serious livestock disease that significantly impacts not only animal health and public health, but also domestic and international trade. The need for timely and effective surveillance systems is indisputable. In the United States the National Surveillance Program was established in 1934 ("Facts about Brucellosis", 2011). According to the USDA Animal Health Monitoring and Surveillance, United States is free of Brucella melitensis related Brucellosis since 1999.

In contrast to the well-established brucellosis surveillance program in the United States, Bosnia and Herzegovina is still struggling with implementation of a well-developed and country-specific brucellosis surveillance program. In 2007, a group of CDC experts visited Bosnia and Herzegovina and assessed the current surveillance in place. It was concluded that for the entire country there were 814 veterinarian personnel available,

employed in government and private veterinary practices (Kahn, 2007). While some regulations and rules exist for cattle and small ruminants, there are ongoing challenges with enforcement of the same, especially for the animal movement control due to personnel shortage, equipment shortage, insufficient animal health control funds, lack of communication between the veterinary subunits, and lack of compliance by the producers. While there is a national animal identification system in place for the identification of cattle, no such system existed for small ruminants until recently ("State Veterinary Office: Agency for Animal Identification", 2011). The small ruminant's identification database was started with the recent sheep and goat mass vaccination program in May of 2009 (Dz. Hadzovic, personal communication, January 06, 2012). Bosnia and Herzegovina continues to struggle with the inefficient disease reporting system in place. Local veterinary offices report the number of positive disease outbreaks to the entity level veterinary office which then sends monthly reports to the State Veterinary Office (Kahn, 2007). Even though reports are generated, they lack specificity in regards to the number of animals tested, number of flocks/herd tested, as well as municipal level census data further questioning the reliability of the current surveillance program.

The last war devastated the domestic livestock industry as well as the veterinary infrastructure. The international community donated livestock to returnees in part of support of sustainable minority return to ethnically cleansed rural areas. However, sick animals entered the country due to lack of modern veterinary border controls, thereby infecting domestic stock and its consumers (Graham, 2006). According to Fejic et al, Bosnia and Herzegovina has made tremendous effort to enhance its national veterinary infrastructure in order to improve animal and public health, as well as to improve food safety since 1996

(Fejzic, 2006). In December, 2000 the State Veterinary Office (SVO) was established, however it became effective only after a state veterinary law was adopted in October, 2002.

Lack of central level administration and national disease surveillance during the post war era 1995-2003 had a negative effect not only on animal and consequently human health, but also lead to isolation of Bosnia from regional and international markets. Working on efforts to comply with the World Trade Organization Sanitary-Phytosanitary agreement, Bosnia has been collaborating with the Animal Population Health Institute of Colorado State University since 2001 (M. Guerra, W. Nicolson, personal communication, June 17, 2011). Numerous training programs and technical workshops have been organized in Bosnia and Herzegovina since 2001, leading to small but steady improvements in the veterinary infrastructure, as well as disease surveillance and control. In the effort to develop an Animal and Health Surveillance Infrastructure in Bosnia and Herzegovina, Fejzic et al stress out the great challenge transitional and developing countries face in meeting international requirements for animal and public health, as well as overall animal welfare (Fejzic, 2006). The need for further improvements in the animal disease reporting system for the establishment of a surveillance infrastructure is essential in Bosnia and Herzegovina.

Brucella Vaccine

Effective vaccines against brucellosis in animals have been available for many decades. Brucella melitensis REV-1 vaccine is currently the only vaccine used for brucellosis control in goats and sheep (Banai, 2002). Even though there has been a lot of conflict, or at least discrepancies in regards to both safety and efficacy, the vaccine has been used for more than 55 years. Use of REV-1 vaccine is associated with substantial risks that should be overcome through increasing public health awareness, restricting adult vaccination to

lactating and late pregnant animals (Balasco, 1997). There is currently no alternative, safer vaccine for prevention and control of brucellosis in small ruminants and careful use of REV-1 vaccine over long period of time induces a great decrease of the infection prevalence in animals and humans.

While vaccines have the ability to control brucellosis in animals, they do not lead to eradication of brucellosis by itself. Accoring to Donev, “brucellosis control and eradication is not a simple and quick procedure”(Donev, 2010). Only through multi-factorial investment in continuous and long-term control and eradication programs can lead to successful eradication of brucellosis. Those programs should include vaccination, test and slaughter of infected animals, active surveillance, education, and legislative support in order to accomplish the desired outcome. According to the Federation of Veterinarians of Europe, the Community Animal Health Strategy for 2007 to 2013 emphasizes that “Prevention is better than cure”, stressing out their vision “to work in partnership to prevent animal health problems before they happen” (Services, Decembar, 2010).

US Success in Brucellosis Control and Eradication

Animal vaccination programs have proven to be effective in controlling brucellosis primarily in the animal population, and thereby reducing transmission and disease outbreaks in humans. In the United States, efforts to eradicate brucellosis began in 1934 as part of an economic recovery program ("Facts about Brucellosis", 2011). In 1954, the magnitude of the brucellosis problem in the United States prompted establishment of the Cooperative State and Federal Brucellosis Eradication Program. The focus of the program was to prevent the considerable economic impact on cattle production through abortion and low fertility, as well as to reduce the transmission of the disease to humans.

As of 31st December 2000, there were no affected cattle herds in the United States. One of the key conclusions from the effective Brucellosis Eradication Program in United States was that as much as it is important to have tools to eliminate the disease, disease surveillance (Services, Decembar, 2010) is the first and critical step that must be in place in order for successful eradication.

According to Donev, "The methods used in developed countries to control and eradicate brucellosis may not be appropriate for developing countries and those in transition" (Donev, 2010). However, desired outcomes can be achieved if effective long term programs are in place as demonstrated in United States. Similar success in Brucellosis control and eradication has been seen in some European countries.

Brucellosis Status in Europe

Today, brucellosis is a serious concern in many European countries (V.Taleski, 2002). While the European Union declared brucellosis-free status to many Western European countries, many countries in the Mediterranean region are endemic (P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006). However, efficient, but time consuming brucellosis eradication is possible as was demonstrated by no other than France in 2000. It took France over 25 years to eradicate this zoonosis, which shows the level of persistence, compliance, and adequate programs and regulations needed for successful eradication.

Pappas at all reports endemic conditions in Spain, Portugal, southern Italy, Bosnia, Albania, Macedonia and Greece. There is a clear correlation between the socioeconomic status or gross domestic product (GDP) and endemicity of brucellosis in a specific country (P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006). The difference is clearly seen in Italy, where "the human brucellosis has travelled to south" which is clearly explained by the

shift in the socio economic status from rich to poor between north and south. According to International Monetary Fund information for 2010 Bosnia and Herzegovina ranked on the 104th place in the world with 16,530 GDP in US Dollars, which supports the GDP bound hypothesis (Wikipedia, 2010).

According to Pappas et al, brucellosis is not endemic in Eastern Europe. However, while there is little chance for reemergence in western European countries due to existence of adequate surveillance systems in place, same is not true for the rest of Europe. There is great reason to believe that human brucellosis cases are underreported in many endemic countries due to inadequate awareness from medical staff, illegal animal and animal product trafficking due to inadequate control programs and policies, inadequate health education and literacy of general population, as well as the low socio economic status in the specific countries (P. P. G. Pappas, L. Chrisou, N. Akritidis, E. Tsianos, 2006; M.Guerra, W. Nicolson, personal communication, June 17, 2011).

A retrospective study based on reviews of presentations and discussions from the International Scientific Conference on brucellosis in South Eastern Europe (SEE), as well as published papers and review of relevant literature, concluded that "Re-emergence or worsening of the situation with brucellosis in many SEE countries indicated weaknesses in the control programs and insufficient organization and collaboration in their implementation" (Donev, 2010). Donev points out that brucellosis poses a great concern in many SEE countries and only systematic, long-term, strategic and collaborative disease control and eradication programs will lead to disease free status as seen in numerous Western European countries. He further stresses out the importance and need for technical and financial support from the European Commission, as well as other international organizations.

Major constrains of successful Brucellosis control and eradication in SEE are due to weak veterinary infrastructure, insufficient legislation on internal and external food market control, poor quality of vaccines used, insufficient cooperation between farmers and veterinary services, uncontrolled animal movement and animal ownership change, lack of inter-sectorial collaboration, as well as lack of collaboration between neighboring and other regional countries. Until those constrains are eliminated a successful brucellosis control and eradication in SEE will not be possible.

Due to increasing difficulties in disease control, many European countries are shifting from test and slaughter method to implementation of vaccination programs (Donev, 2010;Eleni Jelastopulu, 2008;Zarema Obradovic, 2010). In a retrospective animal data analysis done by Naletoski et al, many gaps in the chain of brucellosis eradication in Macedonia were found in the test and slaughter strategy (Ivanco Naletoski, 2010). Study findings ultimately lead to change in implementation of a vaccination policy for sheep and goats in 2008. While there was a significant disagreement between expected and sampled animals, lack of complete removal of infected animals was one of the most important reasons for campaign failure. In 2005 only 21% and in 2006 only 23% of all infected animals were successfully removed, which led to a clear campaign failure and need for change in strategy (Ivanco Naletoski, 2010).In 2008, Macedonia ultimately switched to animal vaccination as a result of the study.

A similar scenario was seen in Greece as well. The sheep and goat *Rev-1* vaccination of young 3-6 month old replacement animals was started in 1975 and significantly decreased abortion in animals, as well as the incidence in humans (A. Minas, 2004). In 1994 the vaccination program was stopped due to believe that brucellosis was successfully eradicated

resulting in immediate increase in animal prevalence and human incidence. The test and slaughter method was applied from 1994 through 1998. Emergency mass vaccination of young and adult sheep and goat was implemented in 1998. Once over 30% of all animals were vaccinated, steady decrease of incidence and prevalence in animals and respectively humans was observed. The observations in Greece clearly demonstrates that whole-flock vaccination is the best and the only suitable method for effective brucellosis elimination (Balasco, 1997). The whole-flock vaccination should be applied in the endemic European countries in order to effectively eliminate animal and subsequently human brucellosis.

Support System within European Union and beyond

Support for improvements in the veterinary sector, and consequently human health sector is available through European Union to many member and non-member countries. Bosnia is eager to become EU member and is in the process of accomplishing all the short and long term goals before it can officially apply to become an EU member state. The Stabilization and Association Agreement (SAA) was signed on June 16th of 2008 (Wikipedia, 2011a), and one of the major stipulations was improvement, modernizing and restructuring of the agro-industrial sector in order to reach veterinary requirements (Europa.ba, 2011).

Even though Bosnia and Herzegovina still remains a potential candidate country, many promising improvements in the veterinary sector have been accomplished through past EU assistance programs in the country. Past assistance programs with total assistance of over 3.2 million Euros include; Technical Assistance to Implementation of Animal identification Scheme, Supply of Equipment to Veterinary Laboratories for Diagnostics, Twinning Assistance to the State Veterinary Office, as well as Support in implementation of state legislation and ongoing support for export of animal products in the EU (Europa.ba, 2011).

In effort to improve its community animal health and subsequently acquire EU member status, Bosnia and Herzegovina became a member of the Federation of Veterinarians of Europe (FVE). FVE was established in 1975 and represents 46 national veterinary organizations in 38 European countries, including all EU Member States ("Federation of Veterinarians of Europe", 2011). Its vision is to “work in partnership to prevent animal health problems before they happen”. FVE promotes the shift from disease control to prevention, and necessitates the need of adequate disease monitoring and surveillance for prevention of disease outbreaks.

In addition, Bosnia and Herzegovina belongs to the South Eastern Europe Health Network (SEEHN) in order to improve its veterinary and health sector status. SEEHN, established in 2001, is a political and institutional forum set up by nine South-Eastern European governments, including Bosnia and Herzegovina. It is responsible for health development in various areas, especially communicable diseases, food and safety, public health services and health systems. The ten partner countries and five international organizations provide continuous political, technical and financial support to all SEEHN member states ("WHO Europe: South-eastern Europe Health Network (SEEHN)," 2011).

Besides support in Europe, Bosnia and Herzegovina is a member state of the World Organization for Animal Health (OIE), an international organization responsible for worldwide animal health improvement. OIE provides up to date country specific reports on animal disease situation, as well as latest scientific information for disease control. Most importantly it provides technical support to its member states, specifically providing support for Veterinary and Laboratory services for developing and transitioning countries such as Bosnia and Herzegovina.

Legislative Requirements

European Union, biggest importer of food worldwide, has clearly defined rules for import of meet and meet products, as well as trade and import of live animals ("Europa: General Food Law-Principles"). Transparency is the single most important factor for animal health control and food safety. The latest changes in the food law emphasize the need for process control throughout the food chain “from farm to fork”, not only at the end product in order to achieve highest levels of safety, quality and transparency. Competent exporting countries veterinary authority, responsible for inspection and certification of animals, meet and meet products are required for import consideration. Additional requirements include EU animal health standards, and hygiene and public health requirements. Veterinary border control and animal identification are of crucial importance for the control of infectious diseases and are fully applied in the EU ("Europa: Veterinary Border Control,").

Currently existing Food safety legislation in Bosnia and Herzegovina is a mixture of both, old Yugoslav laws and new EU laws and regulations required for EU entry ("B&H LAW ON AGRICULTURE, FOOD AND RURAL DEVELOPMENT," 2008). Ongoing improvements and amendments to earlier adapted laws are in the process of being approved in order to maximally adapt and comply with the EU laws and regulations. Due to recent brucellosis outbreaks, specific laws for brucellosis control have been recently adopted for animal welfare and animal disease control (Sabahudin Bajramovic, 2010). While, positive and systematic changes in the Food Safety and Veterinary laws and regulations are seen in Bosnia and Herzegovina, their implementation is slow and adherence and compliance to same is questionable. According to Dr. Nedic, Director of SVO, Bosnia and Herzegovina lacks manpower in order to follow current laws and regulations in place ("TV Alfa "In the

Mirror" special edition broadcasted on July 19, 2009," 2011). Only through full compliance with current animal health and food and safety laws and regulations will it be possible to control brucellosis outbreaks in Bosnia and Herzegovina. Specific suggestions for legislative enforcement should be developed in order to ensure compliance with laws and regulations.

Progress in Bosnia and Herzegovina

Due to increasing reports of brucellosis cases in Bosnia, in July 2007 CDC experts were invited by the Prime Minister of Bosnia and Herzegovina, Mr. Nikola Spiric, to assist Bosnia and Herzegovina in an investigation of brucellosis along with Q fever and other food-borne illnesses. A request was made for the CDC experts to evaluate the public health monitoring, laboratory capacity, identify institutional deficiencies, and to give specific recommendations for brucellosis Q fever and food-borne illnesses control. CDC Deputy Director of National Center for Zoonotic, Vector-bortne, and Enteric Diseases and five of his colleagues visited Bosnia and Herzegovina from July 9th 2007 through July 21st 2007. During their two week visit they were able to visit many sites throughout the country, evaluate the current situation and provide recommendations for improvement. The following five recommendations were made in order to strengthen communicable disease control and prevention by establishing new capabilities at the state level and strengthening institutions at all levels of government charged with animal and human health;

- Establish an Inter-Sectorial State Commission for Zoonotic and Emerging Infections
- Establish a State Office for Communicable Disease Control and Prevention
- Establish a State Public Health Laboratory Reference Network
- Develop a State Animal Health Strategy

- Create a State Science Based Veterinary Health Program (Kahn, 2007).

Despite the clearly outlined recommendations little to no progress has been made in the recent years. According to two experts from the 2007 trip to Bosnia and Herzegovina, William L. Nicholson, MS, PhD a Microbiologist and Martha Guerra, DVM, PhD Veterinary Epidemiologist there is a lot to be done before Bosnia can establish a sustainable brucellosis surveillance and eradication program (M. Guerra, W. Nicolson, personal communication, June 17, 2011). Both experts emphasized the questioning of the reliability of existing public health data, improper conditions and specimen handling in the diagnostic laboratories, as well as the overall attitude of the public health personnel and the government. Even though the situation has changed for the better since the first CDC post-war visit in 2000, when they visited Bosnia and Herzegovina in order to help set up diagnostic laboratories, it is too little of improvement considering how many years have passed by. The need for ongoing public health education of the general population, especially farmers and herdsmen, as well as medical and government personnel is greatly understated. The ongoing economic chaos and political disagreement make any effort for a large scale change unrealistic. Therefore a small scale change/pilot study is needed in order to convince the public of the benefits of implementation of preventive programs that can be applied across both entities in Bosnia and Herzegovina.

According to Ms. Guerra and Mr. Nicholson, the Veterinary sector of the Federation of Bosnia and Herzegovina is most collaborative and ready for change; however at that time the Veterinary sector is was not interested in animal vaccination due to economic reasons (M. Guerra, W. Nicolson, personal communication, June 17, 2011). From their field trip experience, Ms. Guera and Mr. Nicholson repeatedly stressed out that older people are not

open to change, however younger people are more open and willing to change and should be targeted in any campaigns for systematic long term success.

The healthcare system in Bosnia and Herzegovina is in transition, or a process of reform and premature decentralization based on the European Observatory on Health Care Systems (Richard Coker, 2008). The segregation along all sectors within the country makes any inter entity collaboration impossible and consequently the entire population suffers. According to UNHCR: " It may be simply stated that the health care system in Bosnia and Herzegovina is not capable of meeting the needs of the country's population and that overall state of the health care system is worse than in 1992. More concerning, however, is the finding that persons suffering from many illnesses that might be considered to be of only minimal hindrance to the leading of a "normal: life in a more developed country, may be at serious risk if required to seek treatment in Bosnia and Herzegovina. The unavailability of a number of treatments may be life threatening in certain cases" (Cain, 2002).

The economic burden of brucellosis outbreaks in Bosnia and Herzegovina mostly affects the farmers/herdsmen and their families. Majority of the population lives in the suburban areas and the main income source comes from farming efforts. In case of brucellosis outbreaks on family farms, which is mostly the case, the source of income is lost or diminished immediately. In the past the government has provided some relief to families with infected animals that had to be euthanized, however the timeliness and the amount of indemnity was well below the fair market value of the specific animal (Z. Mulabdic, personal communication, March 30, 2011). Human suffering from the infection is enormous. Brucellosis in not a lethal disease, but it causes major disability in infected individuals, affecting them for the rest of their lives (Young, 1995).

From 2000 until 2008 the animal brucellosis control was done exclusively by applying the test and slaughter method ("Key Informant Interview with Dzeno Hadzovic, DVM," 01/06/2012). However, due to nomadic grazing of sheep the number of infected animals increased severely, resulting in correlative increase in the number of euthanized animals. Compared to 8,788 euthanized animals in 2007, approximately 32,000 animals were euthanized in 2008 of which most were sheep (Kahn, 2007). The initial brucellosis control in animals was further complicated by the different strategies and legislation in the two entities. While all animals from herd were euthanized if 20% tested positive in the RS, same was the case in FBIH if 50% tested positive (Kahn, 2007). Clearly, the test and slaughter method was insufficient and unsatisfactory, and a new method for brucellosis prevention is needed.

Recently, collaborations with the Swedish International Development Cooperation Agency (SIDA) and the Swedish embassy in Bosnia and Herzegovina led to implementation of the first stage of the sheep and goat mass vaccination program (Kahn, 2007). The entire project was funded by SIDA and the initial vaccination should be completed within one year. The initial vaccination was carried out from May until July of 2009 using the OCUREV 1 vaccine. The specific vaccine was used in other EU countries and reported very promising results. According to the director of the SVO, Drago Nedic PhD, the entire project should last for at least eight years in BIH in order to get optimal results. Other countries that have used the same vaccine report that yearly re-occulation with the vaccine is needed for at lest 5 year following the initial vaccination in order to get the desired immunity in animals. The vaccination of cattle is not yet been implemented, however plans for possible evaluation of cattle vaccination will be carried out in the near future according to Dr. Nedic ("TV Alfa "In the Mirror" special edition broadcasted on July 19, 2009," 2011).

Summary of Current Problem and Study Relevance

As demonstrated in the extensive background and literature review of brucellosis status in Bosnia and Herzegovina and other countries, it is clear that brucellosis is one of the most serious livestock diseases and effective prevention is the key to successful disease control and eradication as seen in many developed countries. Scientific evidence demonstrates that the test and slaughter method may be effective and sufficient in non-endemic countries; however preventive vaccination programs are essential in endemic countries such as Bosnia and Herzegovina. Despite the recent implementation of the promising mass vaccination program of sheep and goats in Bosnia and Herzegovina, there are many gaps in the program that need to be filled in order to achieve a brucellosis free status. This project will analyze the fundamental system requirements of the current brucellosis prevention program in sheep and goats and will provide specific suggestions for improvements through development, in order to shift from endemic to brucellosis fee status in entire Bosnia and Herzegovina.

CHAPTER III: METHODOLOGY

Introduction

The following chapter describes in detail the actual steps taken for completion of the gap analysis of the current small ruminants brucellosis control and eradication program in Bosnia and Herzegovina. The recently implemented mass vaccination of sheep and goats is a relatively new concept of prevention for veterinary sector in Bosnia and Herzegovina and its success is of great animal and public health interest for the entire country. In addition, its success would essentially support countries overall economic recovery, as well as lead to a successful association to the European Union. In order to efficiently and effectively control and eradicate brucellosis within the sheep and goat population in Bosnia and Herzegovina, while keeping the program cost at a minimum, other countries success stories can be used for general and country specific guidance. This gap analysis will be based on literature review, key informant interview, and relevant national expert media interviews.

Research Design

The type of research design used in this project was the gap analysis of the current sheep and goat vaccination program in Bosnia and Herzegovina. Gap analysis is “a technique for determining the steps to be taken in moving from a current state to a desired future- state” ("Business Directory: Gap Analysis"). It consists of evaluation of specific factors contributing to the current state, including pointing out of performance strengths and weaknesses, as well as highlighting gaps and opportunities for improvement for achievement of the desired outcome. This gap analysis was a pseudo evaluation of the currently available data for sheep and goat brucellosis mass vaccination program in 2009. It includes comparison of identical/existing programs in countries with similar animal and human brucellosis status.

The specific program evaluation was performed using 1) currently available literature, 2) key informant interviews, and 3) relevant national expert media interviews. The specific literature review was done by using the Google search engine and the US National Library of Medicine National Institute of Health search engine for collection of current and old brucellosis related published article and journals. The literature review provided the necessary information about brucellosis background, specific control and eradication programs, and available support organization. The key informant interviews were done with Dr. Nicholson and Dr. Guerra, CDC experts that were part of the team that visited Bosnia and Herzegovina in 2007. Dr. Nicholson and Dr. Guerra provided me with valuable information about the progress made over the last decade, as well as with their professional judgment of the current situation. I also met with Dr. Zerina Mulabdic, Epidemiologist and Chair of Crisis Committee of the Institute of Public Health in Bihac, Unsko Sanki Canton. Dr. Mulabdic provided me with important information in regards to brucellosis history in Bosnia, as well as issues and difficulties the Public Health officials are facing in trying to implement new prevention programs. In addition to the two in person key informant interviews, I was able to get in contact with the State Veterinary Inspector for Animal Health Protection, Dr. Dzeno Hadzovic. Dr. Hadzovic is the main project manager working on the brucellosis control and eradication program in Bosnia and Herzegovina. He was able to provide me with valuable and up to date information about project logistics that was essential for the gap analysis. In addition to detailed literature review and key informant interviews, I was able to access the media covered interviews done with national experts in the field on the main veterinary office website in Bosnia and Herzegovina ("State Veterinary Office: Brucellosis control in Bosnia and Herzegovina 2009-tertiary phase,"). The official veterinary

office website, including the media covered interviews with local experts provided the best available information on the logistics of the program implementation and execution.

Upon review of all the available materials, including other countries success stories and challenges, specific program gaps and recommendations for program improvement were made and are listed in Chapter 5.

Limitations

As with any project, limitations were present for this particular project as well. The main limitations of this project were doubtfulness of data accuracy, local officials' unwillingness to share information, and untimely literature availability. The doubtfulness of data accuracy was initially presented to me by the key informants Dr. Nicholson and Dr. Guerra. Throughout their two week stay in Bosnia they received contradicting and questionable information about the current brucellosis incidence and prevalence rates within the animal and human population. Due to general infrastructure challenges, as well as states transitional status, local officials' reports were questionable in regards to representing the true picture of the brucellosis status in the country. That trend continued and was reflected in local officials' unwillingness to share specific information, as well as reasoning for their decisions. According to the Dr. Nicholson and Dr. Guerra, it seems that local officials were afraid to share information because they lack authority in making any final decisions. Last but not least, there is a limited number of relevant and program specific literature available on line. Publishing of literature, as well as program updates are not available in real time causing disruption in the flow of information. A small number of academic journal articles are available online, and many portray a contradicting picture of the current status.

Despite all the limitations I was able to perform the gap analysis with the help of the State Veterinary Inspector and Brucellosis Mass Vaccination Project Manager, Dzeno Hadzovic. Dr. Hadzovic was able to provide me with valuable information about project logistics and updates about the current situation on site.

Emory University Institutional Review Board (IRB) Clearance

The following project did not involve human subjects and therefore did not require Emory University Institutional Review Board (IRB) approval.

CHAPTER IV: RESULTS

Introduction

In 2009, Bosnia and Herzegovina changed its brucellosis control and eradication program due to inability to control the disease within small ruminants, and ineffectiveness of its previous test and slaughter program in place. The following gap analysis of the current small ruminant brucellosis control and eradication program in Bosnia and Herzegovina was performed by evaluating specific benchmarks required for the success of the program. Illustrated below are the five essential performance benchmarks of interest which will be addressed in detail in this gap analysis (Figure 1). Individual benchmarks will be assessed for their strengths and challenges.

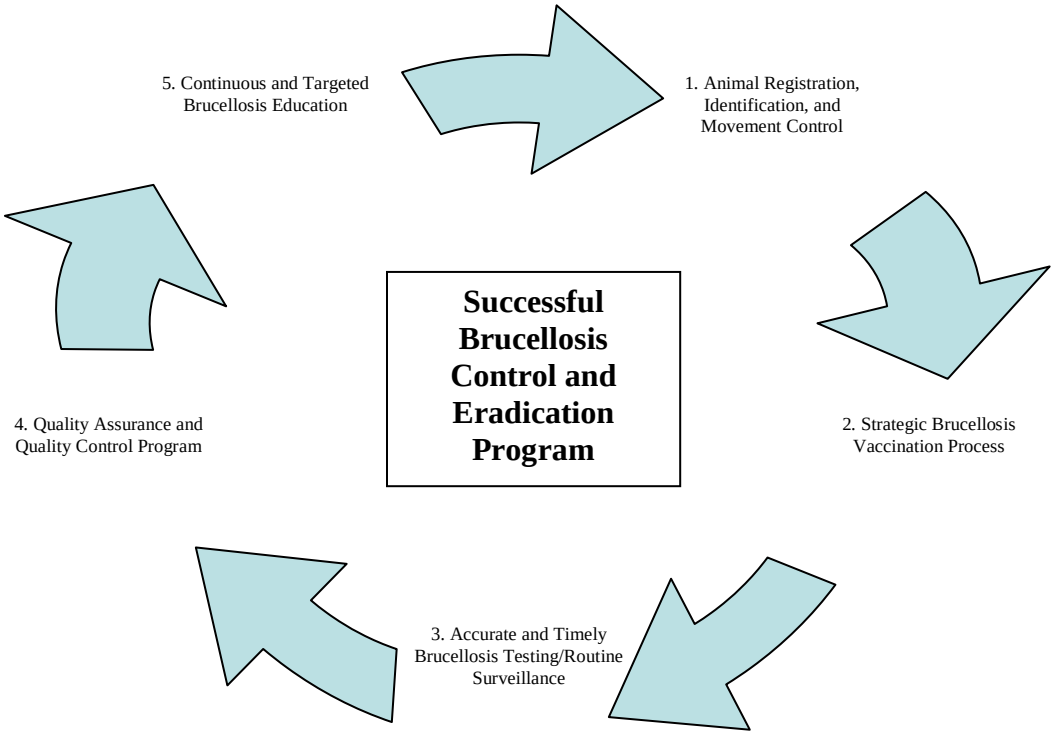

Figure1. Performance benchmarks of interest

Benchmark 1: Animal Registration, Identification, and Movement Control

Background

Most developed countries have standardized and integrated small ruminant registration, identification, and movement control programs in place. It allows for continuous animal traceability, thereby improving disease prevention and control. Animal registration, identification, and movement control is one of the most important steps in the brucellosis control and eradication campaign. Preventive and control programs can only be successful if all animals are accounted for. Failure to register and identify animals ultimately leads to failure of any disease prevention or control programs.

The importance of animal registration, identification, and movement control was best portrayed in a study done by Naletoski et al in the gap analysis in brucellosis eradication campaign in sheep and goats in republic of Macedonia (Ivanco Naletoski, 2010). The retrospective analysis compared the census animal count and the number of sampled animals. There was a significant difference between those two, which ultimately did not provide the needed transparency and lead to change in the strategy to animal vaccination. In that particular setting, the test and slaughter method was not efficient because all animals were not accounted for and therefore were not properly removed which lead to brucellosis endemic and failure of the Brucellosis control program overall.

Status in Bosnia and Herzegovina

Until recently the small ruminant's registration, identification, and movement control in Bosnia and Herzegovina was incomplete and doubtful mainly due to the decentralization of the public and veterinary health offices and application of different procedures between the two entities and the district of Brcko (Z. Mulabdic, personal communication, March 30,

2011). In addition, the small number of veterinary inspectors adds to the difficulty of following and proper execution of the veterinary laws (Kahn, 2007). According to Dr. Dzeno Hadzovic, registration and identification of small ruminants has been practiced since 2007, however data was collected separately for the two entities and District of Brcko and forwarded to the State Veterinary Office.

Concurrently with the newly implemented mass vaccination of small ruminants in 2009, animal registration, identification, and movement control was strongly enforced and completed at the state level by the agency for Animal Identification at the State Veterinary Office ("State Veterinary Office: Agency for Animal Identification", 2011). Currently, in accordance with the Veterinary law, each animal receives a unique identification number and is marked with an ear tag for identification purposes. At the time of the animal registration its owners are presented with passports which are required for animal movements within and outside of the country (Dz. Hadzovic, personal communication, January 06, 2012). Animals are registered into the Animal identification and Movement Control System (AIMCS) and their movement can be easily tracked. All animal movements must be entered into the State Veterinary database, and animal import requires proof of vaccination, as well as mandatory border control animal health status exam("State Veterinary Office: Agency for Animal Identification", 2011).

The border control inspection is a critical element for brucellosis control and eradication in Bosnia and Herzegovina simply because Public Health and Veterinary Officials strongly believe that sick animals were imported in the country due to lack of proper animal paperwork and lack of animal examination by the border control veterinary inspectors (Z. Mulabdic, personal communication, March 30, 2011).

Conclusion

The Veterinary Sector of Bosnia and Herzegovina is currently in a transitional state. As demonstrated with the implementation of the mass vaccination of sheep and goats, only by working together as a whole country, and not as individual entities and the District of Brcko, can we achieve positive outcomes and project success. It is clear that the current animal registration and identification is successful, simply because same rules are applied across the entire country. However, there is currently no quality control in place in order to confirm that all animals are registered and identified. Continuous registration of animals is of great importance, not only for vaccination purposes, but also for identification purposes in case of epidemic outbreaks. Going forward a quality control program/unit should be created in order to account for all animals. As previously mentioned the veterinary office is still short staffed and additional veterinary inspectors should be hired in order to perform a timely animal registration, as well as random and ongoing quality control audits. Through random quality control audits the Veterinary Office will be able to capture and identify any missed or unregistered animals, as well as vaccinate those animals and thereby decrease the risk of future epidemic outbreaks.

Benchmark 2: Strategic Brucellosis Vaccination Process

Background

Success of sheep and goat vaccination with the conjunctival Brucella melitensis REV-1 (OCUREV) vaccine has been proven to be very effective in many counties neighboring Bosnia and Herzegovina. In a study done by Jelastopulu et al, incidence of human brucellosis in Tritaia, western Greece, was assessed before and after implementation of mass vaccination where 99.3% of all sheep and goats were vaccinated with the conjunctival Brucella melitensis REV-1 vaccine. There was a significant decrease in incidence rates among animals and subsequently humans after the vaccination. Between 1997 and 1998 human incidence rate was 10.3 per 1000 population, whereas in the period after the mass vaccination, between 2000 and 2002 the human incidence rate was only 0.3 per 1000 population (Eleni Jelastopulu, 2008). In addition, a decline in human incidence rates was observed in population of not yet vaccinated herds. Experts believe that health education efforts from 1997 and 1998 contributed to the human incidence rate decline as well. It was concluded that decline in human and animal brucellosis incidence can be effectively reduced with combined mass vaccination and health education approach.

The best available vaccine nowadays is the REV-1 vaccine (Balasco, 1997). The ocular administration provides better protection in comparison to the subcutaneous injection as shown in a study done in Israel (Banai, 2002). In addition, a review of the use of B.melitensis Rev-1 vaccine in adult sheep and goats in Spain concludes that the conjunctival vaccination is safer than the subcutaneous vaccination; however it does not provide increased safety in pregnant animals (Balasco, 1997). Even though fewer abortions are reported when pregnant animals are vaccinated with the conjunctival REV-1 vaccine, vaccination of

pregnant animals should be avoided until after delivery. In addition, Blasco et al conclude that in areas with high brucellosis prevalence and low socio-economic status, the only feasible prevention program is the mass vaccination.

There is quite some controversy in regards to how long the animals remain immunogenic after initial vaccination, as well as how long should animals be vaccinated to achieve complete Brucellosis eradication (Balasco, 1997; Banai, 2002). Different countries provide different results in regards to vaccination coverage, however the best indication for the need of continuous vaccination is offered in review of the Brucellosis program in Greece. Prior to stopping the sheep and goat vaccination with REV-1 in 1994, Greece performed vaccination of 3-6 month old sheep and goats since 1975. Great decline in the human and animal Brucellosis incidence was seen as a result of vaccination; however vaccination was stopped completely in 1994 due to the believe that the disease was under control and test and slaughter method was applied from then on. As soon as the vaccination was stopped an increase in the brucellosis prevalence was seen in human and animal population (A. Minas, 2004). The human and animal brucellosis incidence decreased again once the emergency mass vaccination was completed in 1998. The study concluded as well that the vaccination coverage and brucellosis incidence in humans was not linear. Decline in human cases was first seen after >30% of animals were vaccinated.

Status in Bosnia and Herzegovina

Since the outbreak of the first cases of small ruminant brucellosis in 2000 Bosnia and Herzegovina relied on the test and slaughter method for disease control and prevention. Despite all the efforts, major epidemic outbreaks were inevitable in 2007 and 2008. It ultimately led to numerous expert meetings, site visit from CDC experts and general outreach

for help in hopes to develop and implement a sustainable brucellosis control and eradication program. In 2009, Bosnia and Herzegovina changed its strategy from test and slaughter to mass vaccination after the Swedish Embassy and SIDA agreed to donate the needed funds for realization of the new brucellosis control and eradication program.

The program was designed in three stages. The first stage was the “informative campaign” that offered different educational materials for the public, but specifically the farmers in order to gain their trust, active involvement and support in the project realization ("State Veterinary Office: Brucellosis control in Bosnia and Herzegovina 2009-primary and secondary phase"). The second stage was execution of the mass vaccination of sheep and goats across the entire Bosnia and Herzegovina, which involved analogous animal registration. The third stage involves the continuation of the vaccination program up to eight years. After the initial mass vaccination, continuing vaccination of replacement animals will be executed in the following years in order to fully control and eliminate the disease among small ruminants.

According to the Veterinary State Office, the initial mass vaccination was started in May of 2009 and was completed by September of 2009. Mandatory vaccination involved sheep and goats three to six months of age. Vaccinated animals received an ear tag documenting the vaccination. Vaccination of animals older than six months of age was permitted as well, however if the animal was pregnant it was only registered and vaccination was postponed for the following year. Close to 85% of all sheep and goats were vaccinated in Bosnia and Herzegovina in 2009. In the Republic of Srpska 95.4% of all animals were vaccinated, while in the Federation of Bosnia and Herzegovina only 67.4% of all animals were vaccinated (Figure 2).

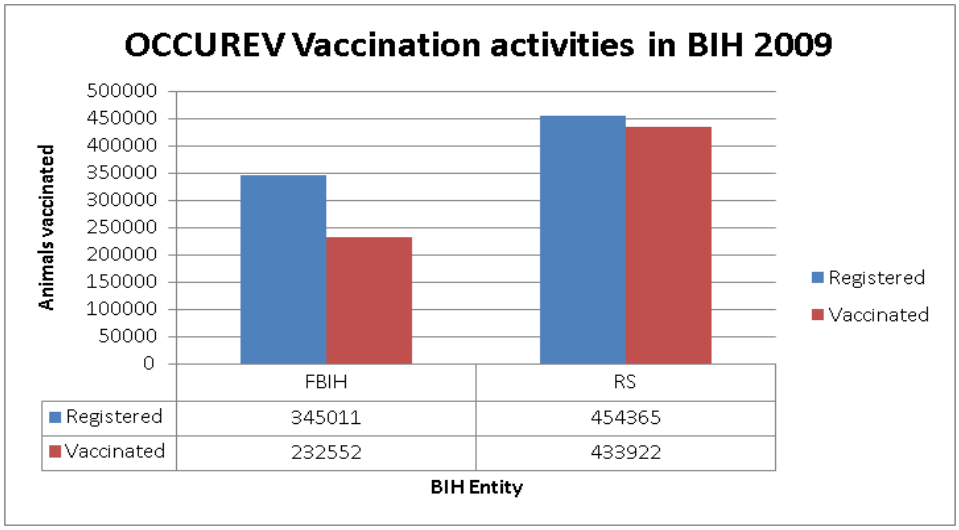

Figure 2. Total number of vaccinated small ruminants in BIH-2009 (SVO, 2011)

In 2010 the OCUREV vaccination program of small ruminants continued and included vaccination of animals younger and older than 6 months. In the Federation of Bosnia and Herzegovina 141 665 small ruminants were vaccinated, and 154 756 in the Republic of Srpska (Figure 3). The total number of vaccinated small ruminants was about 50% less than in 2009.

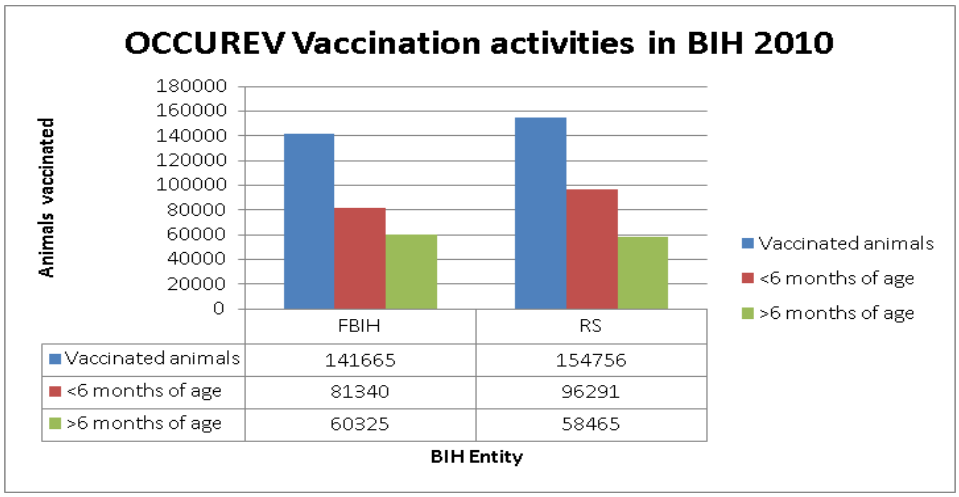

Figure 3. Total number of vaccinated small ruminants in BIH-2010 (SVO, 2011)

In 2011, the total number of vaccinated animals decreased to about 50% from previous year. In the Federation of Bosnia and Herzegovina 68 318 small ruminants were vaccinated with the OCUREV vaccine, while in the Republic of Srpska 88 383 animals were vaccinated in the same year (Figure #4).

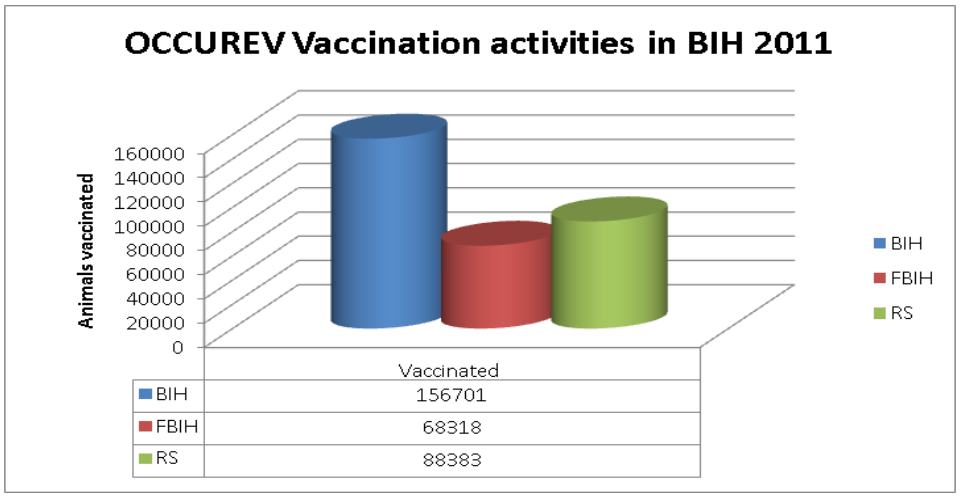

Figure 4. Total number of vaccinated small ruminants in BIH-2011 (SVO, 2011)

Over the years (from 2008 to 2011) there was a consistent difference in the percentage of vaccinated animals between the two entities. FBIH had consistently a smaller number of vaccinated animals than the RS. Even though the reason for such a large difference is unknown and future studies/surveys should be conducted, one of plausible explanations is the ongoing religious discrimination against Bosniaks from the side of Republic of Srpska. According to Dr. Hadzovic there was no prioritization of vaccination for any entity or region in the BIH.

The overall success of the recently implemented small ruminants' vaccination program is visible through the diminishing number of brucellosis cases within the human population (figure 5). However, due to uncontrolled nomadic grazing, ongoing vaccination of replacement animals is essential for continuing program success. Ongoing test and slaughter

method has been applied analogous to the vaccination for all suspected animals (Dr. Hadzovic, personal communication, January 06, 2012).

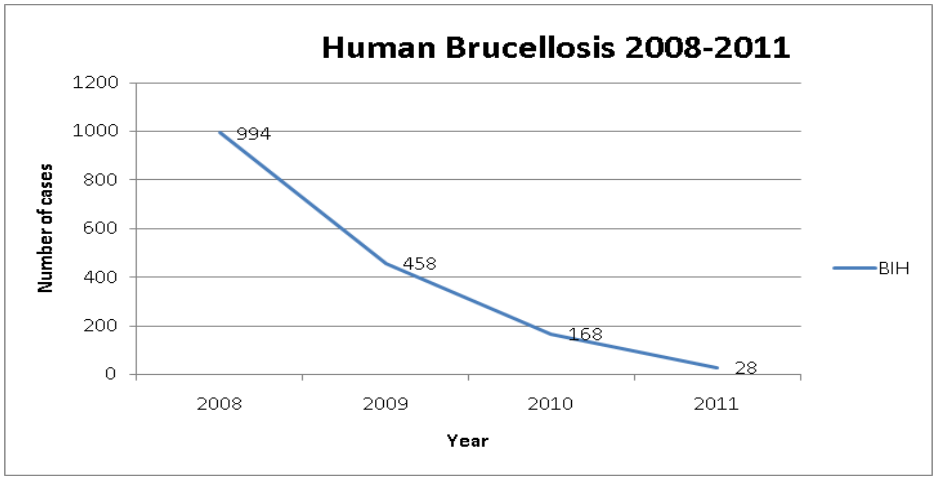

Figure 5. Prevalence of human brucellosis in BIH, 2008-2011 (SVO, 2011)

Conclusion

Endemic countries with similar socio-economic status have provided evidence based suggestions for effective brucellosis control and eradication programs. While Bosnia and Herzegovina has done the first step towards implementation of the mass vaccination of sheep and goats, many suggestions for improvement can be made upon review and comparison to other countries of similar background.

According to Dr. Hadzovic, nomadic grazing is still not controlled in Bosnia and Herzegovina. Therefore, continuous vaccination is the only plausible answer for brucellosis control and eradication. Simultaneous test and slaughter method is and should be applied continuously for suspected Brucella infected animals, leading to increased chance of reactor removal before disease spread. Vaccinations of replacement animals should be ongoing regardless of brucellosis prevalence in the country; therefore the public health and veterinary sector of Bosnia and Herzegovina should secure needed funds for program continuation beyond the initial eight years.

Benchmark #3: Accurate and Timely Brucellosis Surveillance

Background

Besides the lack of the proper control program in place, one of the key reasons of uncontrolled brucellosis outbreaks is the use of an inefficient surveillance system. Three specific requirements must be met for a brucellosis surveillance program to fulfill its intend according to FAO (Robinson, 2003). Those are sensitivity, specificity, and Timeliness. Tests should be sensitive to capture all cases, as well as specific in order to capture true cases, but also timely in order to take immediate action and suppress disease spread. Guidelines for coordinated human and animal brucellosis surveillance from FAO indicate that active surveillance provides a clearer picture of true prevalence/incidence in a region compared to the passive surveillance approach. Therefore active surveillance, including a random sampling program, should be the method of choice for maximum surveillance success.

The importance of adequate surveillance systems in place has been addressed by many scientists and endemic countries, especially in Europe, are improving and standardizing their surveillance systems within and across countries (Ivanco Naletoski, 2010; V, 2010; V.Taleski, 2002). As suggested in the review of the current status and perspective strategies of brucellosis control and eradication in the South Eastern European Countries; ”A baseline sero-prevalence survey with test combination for diagnosis of infection in animals and continuous surveillance and reporting are necessary for animal/herd identification and risk analysis, to monitor the presence/absence of brucellosis in herds/flocks, to monitor the efficacy of the control programs, and to ensure early warning against spread of disease/infection to new areas...” (Donev, 2010). In addition, ongoing personnel education

and process improvement in the veterinary sector, as well as diagnostic laboratories is essential for overall program success.

Status in Bosnia and Herzegovina

Starting in 2000, numerous positive changes have happened in Bosnia and Herzegovina, specifically the Veterinary Health, in effort to meet international standards of Animal Health and Welfare (Fejzic, 2006). However, brucellosis surveillance was still inefficient and needed immediate improvement as suggested by the CDC experts (Kahn, 2007).

Since the implementation of the brucellosis mass vaccination program, Bosnia and Herzegovina has made tremendous improvements in their brucellosis surveillance system. With the start of the new brucellosis control and eradication program positive changes have been adapted in the laboratory field, and animal registration-identification and movement control, including use of electronic data records. According to Dr. Hadzovic, prior to the mass vaccination, 500000 blood samples were taken from sheep and goats in order to establish baseline brucellosis prevalence. The results indicated 4.55% brucellosis prevalence on the individual level, and almost 50% brucellosis prevalence at the flock level. All infected animal were removed by using the test and slaughter method in order to increase the success of the upcoming mass vaccination campaign.

In addition to baseline prevalence assessments and ongoing animal vaccination, test and slaughter of suspect animals is done as well. The supplemental test and slaughter method allows for timely elimination of positive animal reactors and thereby decreases the chance of future major outbreaks. Implementation of electronic animal registration, identification, and movement contributes as well to better disease control, as well as lower prevalence and

incidence rates in the recent years (Dz. Hadzovic, personal communication, January 06, 2012).

Conclusion

While remarkable improvements in the brucellosis surveillance have been made in Bosnia and Herzegovina in recent years, there is still room for improvement. Currently, animals that are suspected to be infected with brucellosis are tested and if positive subsequently removed. That alone is not sufficient for active surveillance needed for a brucellosis endemic country like Bosnia and Herzegovina according to FAO guidelines and recommendations (Robinson, 2003). In order to proactively control and eradicate the disease, active surveillance should be applied in the upcoming years until complete control and eradication of the disease. Bosnia and Herzegovina should secure funds for implementation of active surveillance, applying random sampling in order to avoid bias while collecting blood samples.

Benchmark #4: Quality Assurance and Quality Control Program

Background

One of the essential elements for newly implemented program success is application of quality assurance and quality control activities. Quality assurance refers to the planned and systematic review of activities and processes in order to fulfill the quality requirements (Wikipedia). The first and essential type of Quality Assurance is done during the vaccine production (Mowat, 1991), which is done by the vaccine manufacturer and is not of concern in this project. For the purpose of this project the QA activity includes review of storage and administration of REV1 vaccine, as well as completion of animal registration and identification. Quality control refers to review of the end product meeting the pre-set specifications (Wikipedia). Quality control of the brucellosis vaccination program involves immunogenicity testing following completion of vaccinations in order to confirm desired antibody titers.

In the 2009 OIE Terrestrial Manual, scientists provide a solid review of the caprine and bovine brucellosis, specifically vaccine of choice (REV1) and its immunogenicity. It's advised to handle the vaccine very carefully in order to avoid human infection during vaccination process (J.M. Balasco, 1993). The maintenance of cold chain is extremely important during the vaccine distribution for vaccine viability ("Caprine and Ovine Brucellosis," 2009). Field experience studies suggest that while the conjunctival REV1 vaccine provides good and long lasting immunity, immunity declines over time and re-vaccination may be required (Plommet, 1995). Therefore, vaccine induced antibodies should be checked after vaccination of animals is completed.

Status in Bosnia and Herzegovina

Currently no Quality Assurance activities are conducted on an ongoing basis in the newly implemented brucellosis mass vaccination program in Bosnia and Herzegovina. The need for implementation of effective quality assurance components is indisputable for proper realization of the project. The 2009 statistics from the mass vaccination campaign show a great disproportion of vaccinated animal between the two entities. While 95.5% of all registered sheep and goats were vaccinated in the Republic of Srpska, only 67.4% of all registered sheep and goats were vaccinate in the Federation in Bosnia and Herzegovina ("Current Brucellosis Vaccination Program Statistics," 2012). It is unclear why there is such a big gap between the vaccination coverage in the two entities. If proper Quality Assurance activities were implemented along the way, the vaccination gap could have been reduced.

The program completeness is further compromised by nomadic grazing practice. It is questionable if all animals have been registered in 2009, as well as the following years, because of previously mentioned shortage in manpower. In addition, compliance and maintenance of the cold chain is questionable due to lack of proper storage facilities and tools (Kahn, 2007), which further implicates overall program success. In addition, the mandated proper removal of infected animals is questionable because no quality assurance activities exist within the slaughter houses domain. It is questionable if proper sanitation requirements and personal protective equipment is used.

While there are no clear Quality Assurance activities in the newly implemented brucellosis mass vaccination program in Bosnia and Herzegovina, there is a specific quality control measure that is being conducted on an ongoing basis. The one and only quality control measure involves immunogenicity testing anywhere from 15 days up to four months

post vaccination while the cellular response can be measured (Dz. Hadzovic, personal communication, January 06, 2012). Blood samples are taken from vaccinated animals and sent for antibody titer testing to the Veterinary Faculty, University of Sarajevo. According to Dr. Hadzovic, that provides proof of immunologic response, as well as proper practice control of the veterinary inspectors.

Conclusion

The importance of Quality Assurance and Quality Control measures has been studied extensively and provides grounded reasons for their continuous use. The recently implemented brucellosis control and eradication program encompass many gaps to be filled in regards to implementation of specific QA and QC activities for quality management purposes. Certain QA activities should be implemented in order to ensure proper project completion and accomplishment of desirable end product, mainly eradication of brucellosis within the small ruminants in the entire Bosnia and Herzegovina. The following random Quality Assurance activities should be performed by an independent quality management agency: 1) Comparison of animal registration and identification database records and actual number of animals on farms, 2) Vaccine product storage, preparation, and handling review, and 3) Review of animal removal practices at slaughter houses. There are no additional quality control measures that should be implemented at this time.

Benchmark #5: Continuous and Targeted Brucellosis Education

Background

The last, but not least stage of successful brucellosis control and eradication program involves continuous health education of population. There is a great need for continuous, targeted and culture oriented Brucellosis prevention health education in order to eliminate brucellosis (Corbel, 2006). The occurrence of many neglected and endemic zoonosis can be drastically reduced by simply increasing the public awareness about them (Ian Maudin, 2009).

Comparison of incidence rates between the conjunctival REV1 vaccination periods with and without health education in Western Greece revealed grater decline in brucellosis incidence with practice of concurrent health education (Eleni Jelastopulu, 2008). In addition, a significant decrease in brucellosis incidence was seen in areas where animals were not vaccinated and health education was performed, further indicating the great benefit of continuous health education. Upon review of documents and recorded conferences at the International Scientific Conference on Brucellosis in South Eastern Europe, one of the key recommendations was the implementation of targeted awareness programs and health education in brucellosis control and eradication programs (Donev, 2010).

It is evident from past experience that there is a great benefit of continuous health education. Therefore, health education should be incorporated in development and implementation of brucellosis control and eradication programs.

Status in Bosnia and Herzegovina

The primary phase of the new brucellosis control and eradication program in Bosnia and Herzegovina was started with the Informative Campaign in 2009 ("State Veterinary Office: Brucellosis control in Bosnia and Herzegovina 2009-primary and secondary phase"). The Informative campaign included; “textual information for print media, poster and educational pamphlets for professional and all other institutions, posting of jumbo posters for mass informing, production and presentation of radio and TV reportage, and publication of all mentioned above via telecommunicating and informational media” ("State Veterinary Office: Informative material," 2009).

Three program oriented posters have been developed by the State Veterinary Office for mass dissemination. One poster is of special interest since it addresses specific details about farmer’s-, citizen’s-, and country’s interest of following the new brucellosis control program. It clearly states that Swedish Embassy and SIDA will cover the program cost further eliminating economic instability and down time as a reason for unwillingness for participation. Educational posters for mass informing were written in both Latin and Cyrillic Alphabet in order to reach all target populations. In addition, throughout the initial mass vaccination period numerous TV shows (i.e. In the Mirror) provided updates on accomplished and upcoming program activities, as well as program challenges and their solution strategies. Listeners were able to call into the TV show’s to ask questions or to make comments. Yearly progress and updates are offered via video reportage from the Director of the State Veterinary Office, Dr. Drago Nedic.

Conclusion

The initial effort for population education via different media channels was very successful. According to Dr. Nedic, many farmers were resistant to implementation of the new brucellosis control and eradication program because of lack of knowledge about the disease, as well as the benefits of the vaccination. However, after reading and hearing about it from regional and national experts they started to fully support the new program.

Even though some education was provided and desirable results have been achieved according to Dr. Nedic, many gaps exist in the educational component of the new brucellosis control and eradication program. The initial mass education campaign was primarily indirect and passive in nature. There was no direct and targeted education of farmers and their families. Dr. Nedic implies that all sheep and goats were vaccinated in the initial mass vaccination in 2009; however results confirm a great difference in vaccination coverage between the two entities. Therefore, it is questionable that the educational materials have reached all farmers, and that all farmers have actively participated.

In addition to no direct health education for farmers and their families, there is no ongoing education of the same in place. As previously mentioned, ongoing health education is of great importance for overall project success and compliance, and should be a mandatory part of the program. SVO should organize continuous mandatory farmer's health education, which should include distribution of health education certification. Only then will we be able to reinforce continuous participation of farmers, and thereby achieve brucellosis free status in the entire Bosnia and Herzegovina.

CHAPTER V: CONCLUSIONS, IMPLICATIONS, AND RECOMENDATIONS

Introduction

Brucellosis outbreaks between 2007 and 2008, and current endemic status in Bosnia and Herzegovina clearly emphasize the need for proper prevention programs in order to effectively control and eradicate brucellosis in the entire country. While the initial test and slaughter approach provided some short term disease control among small ruminants and subsequently humans, the economic loss was too high to continue with the passive strategy approach. In order to reduce the economic cost of this emerging zoonosis, as well as to adapt to European Union Veterinary Laws and Regulations, a mass vaccination of small ruminants was implemented in the entire Bosnia and Herzegovina in 2009.

Conclusions and Recommendations

Prior to implementation of the small ruminant vaccination program, the baseline brucellosis prevalence was established through collection of 500000 blood samples from sheep and goats. A state wide animal identification and registration was performed concurrently with the mass vaccination as well. Despite the initial doubt and disbelieve in the new program, through different media channels and country wide public education, the mass vaccination was successfully implemented and carried out according to Dr. Nedic, Director of State Veterinary Office. However, statistical data analysis confirms a great discrepancy in the number of vaccinated small ruminants between the Federation of Bosnia and Herzegovina and Republic of Srpska. While 95.4% of all small ruminants were vaccinated in the RS, only 67.4% were vaccinated in FBIH. It is unknown why there is such a large discrepancy between the two entities and this should be addressed in future studies. It is

however worth mentioning that there are ongoing religious discriminations against the Bosnian Muslim population, and this could be yet another form of it.

The goal of the small ruminant brucellosis vaccination program is to successfully and continuously control and eradicate brucellosis in small ruminants in the entire Bosnia and Herzegovina. Despite successful implementation of the new program, specific recommendations can be made upon completion of this projects gap analysis. Upon review of the recently implemented small ruminants brucellosis vaccination program and the relevant literature, as well as European Union veterinary standards, the following are the recommendations and requirements for successful brucellosis control and eradication in Bosnia and Herzegovina:

1) CONTINUE VACCINATION OF SMALL RUMINANTS

According to previous studies done in neighboring countries with similar brucellosis status, specifically Greece, it is recommended to continue vaccination of small ruminants and not switch back to test and slaughter method after initial vaccination. Until all sources of infection have been addressed and eliminated, including more rigorous border inspection control, vaccination should be the standard approach for the entire Bosnia and Herzegovina. According to Dr. Nedic, vaccination of small ruminants is expected to be performed for 8 years, at which point the strategy would be reassessed an depending on brucellosis prevalence a different strategy would be considered. Continuation of small ruminant vaccination is strongly recommended because of the overall instability of the country which includes weak border control, improper handling and disposal of infected animals, and continuous uncontrolled nomadic grazing, all resulting in a high probability for brucellosis reemergence.

2) INDEPENDENT QUALITY MANAGEMENT PROGRAM

The newly implemented state level animal registration, identification, and movement control program has demonstrated great success. However, it is questionable that all animals are registered in real time and accounted for without any quality control programs in place. An independent quality control unit should be established to perform random quality control audits in order to capture and identify any missed or unregistered animals and thereby ensures timely and continuous animal vaccination. This unit would be able to identify vaccination discrepancies, as seen between the two entities in 2009. In addition, the independent quality control unit would be responsible for collection of blood samples for immunogenicity testing, as well as prevalence testing. This would allow for unbiased sample collection further increasing data accuracy and transparency.

3) CONTINUOUS HEALTH EDUCATION

Continuous Health Education plays an essential role in the brucellosis prevention program. As indicated in the study done in Western Greece, a considerable incidence rate decrease in human brucellosis was seen in individuals whose herds had not yet been vaccinated. This clearly indicates the benefit of continuous health education. The health education should target farmers and their families specifically in use of personal protective equipment (PPE) (Corbel, 2006), as well as proper animal removal strategies. In my key informant interview with Mr. Nicholson and Mrs. Guerra, they both stressed out the significant willingness of younger farmer population in regards to accepting and applying change. Therefore, I recommend that mandatory continuous health education be performed with younger farmers who are willing to adapt to new changes in PPE and hygienic animal removal. A continuous health education certificate should be issued to

farmers as proof of attendance. In addition, farmers should be given a pre and post education test, and specific individual needs should be further addressed if needed.

4) CONTINUOUS COLLABORATIONS

Continuing collaboration between the public health sector and the veterinary sector within Bosnia and Herzegovina is essential for timely and efficient brucellosis prevention and control. In addition, continuous collaborations with EU and neighboring countries with similar endemic brucellosis status should be ongoing at the State level (V.Taleski, 2002). Veterinarians, Scientists and Educators should be given opportunities to attend meetings and seminars held by international brucellosis experts. Continuing Education of staff is extremely important in order for them to learn about novel prevention approaches or obstacles others have faced in the current prevention program.

5) ENFORCEMENT OF VETERINARY LAWS

The most important part of the brucellosis control and eradication campaign is the enforcement of the veterinary laws. As previously seen, due to many reasons many farmers did not and still don't follow the veterinary laws in Bosnia and Herzegovina. Only through legislative enforcement, including monetary penalties for not following the laws, can we expect to see success in the brucellosis control and eradication in the entire Bosnia and Herzegovina.

Public Health Implications

Brucellosis is a globally re-emerging disease and poses a significant public health problem in Bosnia and Herzegovina. While there are many obstacles and challenges in the brucellosis control and eradication program in Bosnia and Herzegovina, great changes have been made in recent years and continue to be made even today. Recommendations made in this Gap Analysis should be considered in the effort to not only improve the current brucellosis control and eradication program, but also help Bosnia get one step closer to becoming part of the European Union by adopting their veterinary and food safety laws and regulations. Continuous improvements in public and veterinary health could open many international doors for Bosnia and Herzegovina and should be one of the top priorities, especially for farmers.

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