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The Role of Veterinary Vaccines in Livestock Production, Animal Health, and Public Health

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1.1 Introduction: The Need for Veterinary Vaccines

The growing human population and rising standards of living in developing countries add to the global demand for meat, eggs, and dairy products. Changes in animal agriculture in recent decades include larger and denser populations of livestock species. Infectious diseases that degrade the health and productivity of livestock herds can be economically devastating and destabilize food supplies. Zoonotic transmission of infectious organisms from food-producing animals to humans is a significant threat to public health. There is an array of strategies used to control infectious diseases of livestock species, including facility sanitation, isolation or culling of infected animals, selection of disease-resistant genetic stock, treatment with antibiotics, and vaccination.

Vaccines are biological products designed to induce immune responses specific to pathogenic microorganisms, in order to prevent or reduce infectious diseases. Veterinary vaccines are a cost-effective method to prevent animal disease, enhance the efficiency of food production, and reduce or prevent transmission of zoonotic and food-borne infections to people. Safe and effective animal vaccines have become essential to modern society. The cost of producing enough animal protein to feed the 7 billion people on Earth would be dramatically higher without vaccines to prevent epizootics in food-producing animals. The lack of vaccines would leave farmers, communities, and countries more vulnerable to economically devastating livestock diseases. Zoonotic diseases such as brucellosis and leptospirosis would be much more prevalent in humans without effective vaccines for use in animals.

Rinderpest is a powerful example of how livestock vaccination, combined with other control measures, can dramatically improve animal health and human well-being. Rinderpest is an acute, highly contagious, viral disease of cattle, domesticated buffalo, and some species of wildlife. In 1889, cattle shipped from India carried the rinderpest virus to Africa, causing an epidemic that established the virus on the continent. Initially, approximately 90% of the cattle in sub-Saharan Africa died as well as many sheep and goats. The loss of draft animals, domestic livestock, and wildlife resulted in mass starvation, killing a third of the human population in Ethiopia and two-thirds of the Maasai people of Tanzania. The reduced number of grazing animals allowed thickets to form in grasslands. These thickets served as breeding grounds for tsetse flies, the vector for trypanosomes, resulting in an outbreak of trypanosomiasis (African sleeping sickness) in humans. This rinderpest epidemic is considered by some to have been the most catastrophic natural disaster ever to affect Africa. The Global Rinderpest Eradication Programme was a large-scale international collaboration involving vaccination, local and international trade restrictions, and surveillance. In 2011, rinderpest infection was declared to be eradicated from the world's livestock and wildlife, marking one of veterinary medicine's greatest achievements (OIE 2011).

Continuing improvement and increased use of livestock vaccines will promote the health and welfare of animals, promote efficient food production, reduce economic losses to producers, and reduce the dangers of zoonotic diseases. For animal vaccines to make a significant impact on animal and public health, they must be widely used, which means they must be affordable. This chapter provides an overview of the benefits and challenges of vaccines for livestock species.

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1.2 Diversity of Veterinary Vaccines

Because a variety of livestock and poultry species are raised around the world and each species is susceptible to an array of bacterial, viral, and parasitic infectious agents, it is not surprising that many diverse vaccines are produced in the world. Livestock vaccines are developed and licensed for a variety of purposes, which are sometimes different from the purposes of human vaccines. Examples would be food safety vaccines to reduce the shedding of *Salmonella* by poultry and *Escherichia coli* 0157/H7 by cattle. Livestock vaccines are primarily used to improve the efficiency of production of food animals. The cost of the vaccine is an important consideration as to whether the vaccine will be used. It must contribute to profitability for the producer in the long run to be widely accepted. Vaccination against zoonotic diseases also can be used to reduce or eliminate the risk of human infection (e.g. rabies, brucellosis). Wildlife vaccines are generally used for zoonotic diseases (e.g. oral bait vaccines for rabies), or in some cases in conjunction with disease control programs in domestic species (e.g. brucellosis vaccine for bison and elk, oral bait vaccines for classic swine fever in feral swine).

Today, in the USA alone, there are about 1280 active licenses for nonautogenous veterinary vaccine products, including vaccines that consist of viruses, bacterins, bacterial extracts, toxoids, and many combinations (USDA-APHIS 2014). Licensed animal vaccines are available for some diseases where vaccines are not available for analogous human diseases, such as brucellosis and bovine respiratory syncytial virus in cattle, and *Mycoplasma hyopneumoniae* in swine. Veterinary vaccines have a distinct advantage in that they can be developed and licensed much more quickly and at much less cost than human vaccines. The ability to conduct safety and efficacy studies, including vaccination/challenge experiments, in the target species greatly facilitates licensing of veterinary vaccines. Liability issues associated with adverse reactions are much less restrictive for manufacturers of veterinary vaccines than for manufacturers of human vaccines. In addition, veterinary vaccines produced in developing countries may undergo less rigorous approval processes than in developed countries.

The equine West Nile virus vaccine is an example of how an animal vaccine can be developed and licensed quickly to meet an emergency situation (Brown et al. 2016). The West Nile virus was discovered in the USA in August 1999. The veterinary vaccine industry, working in cooperation with the US Department of Agriculture (USDA) Center for Veterinary Biologics, quickly developed an effective vaccine to prevent the disease in horses. By August 2001, an equine vaccine for West Nile virus was conditionally licensed by the USDA. West Nile virus vaccine is now considered one of the core equine vaccines in the USA (American Association of Equine Practitioners – Vaccination guidelines). The vaccine has also been used off label to protect some endangered birds, such as California condors (Chang et al. 2007). Porcine circovirus 2 vaccines (Chae 2012) and influenza pandemic H1N1 vaccines (AVMA 2010) for swine are additional examples of newly emerging diseases for which veterinary vaccines were developed and licensed quickly.

1.3 Vaccines and Food Production

Veterinary vaccines are used in livestock to maintain animal health and improve overall production. More efficient animal production and better access to high-quality protein are essential to feed the growing population. According to the United Nations Department of Economic and Social Affairs Population Division, the world population was approximately 7 billion in 2014, and is estimated to increase to just over 8 billion in 2025 and to reach 9.1 billion people in 2050 (Figure 1.1). The United Nations Food and Agriculture Organization (FAO) estimates that 805 million people were undernourished in 2014 (FAO, IFAD, and WFP 2014). There were dramatic increases in world meat and egg production between 1962 and 2006 (Figure 1.2). The FAO projected that feeding a world population of 9.1 billion people will require overall food production to increase by 60% between 2007 and 2050 (FAO 2009; Alexandratos and Bruinsma 2012). The global demand for beef, pork, poultry, and other animal protein sources will increase sharply by the year 2050 (Figure 1.2). Vaccines that preserve animal health and improve production will be important components in meeting this need.

The economic structures of livestock husbandry are unique in the developing world, where many livestock and poultry are raised in small household settings. Even when licensed vaccines are commercially available for livestock pathogens of concern in a region or country, many producers cannot afford to use them. Reliable statistics on the use of livestock vaccines across the developing world are very scarce. A survey performed in Tanzania in 2008–2009 provided useful socioeconomic data on household livestock keeping in a sub-Saharan African context. A majority of rural households in Tanzania reported livestock-related income. Approximately 60% of households reported the presence of livestock disease in their herd/flock during the year of the survey. Only about 29% of households reported any use of vaccination in their animals. It could be inferred that the small livestock holders in Tanzania have

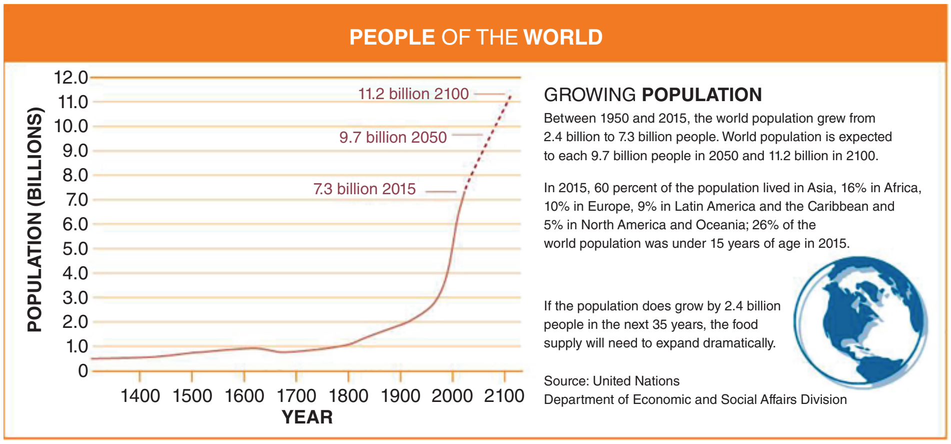

Figure 1.1 Global population growth in recent centuries, projected through 2100. Source: Reprinted with permission from Roth et al. (2016).

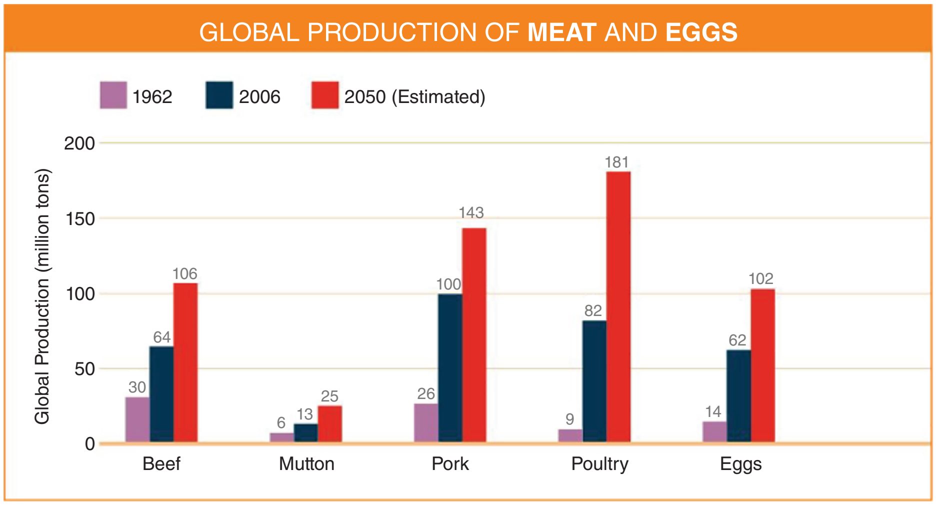

Figure 1.2 Global production of meat and eggs. Between 1962 and 2006 the production of major classes of animal-derived food increased by twofold or greater. Production of these food sources is projected to increase substantially again over the first half of the twenty-first century. Similar growth is reported for milk production, except on a larger scale: 344M tons in 1962, 664M tons in 2006, 1077M tons projected in 2050. Vaccines and other methods of controlling infectious diseases in livestock and poultry help to maximize food production. Source: Data from Table 4.18 of Alexandratos and Bruinsma (2012).

insufficient access to effective vaccines either due to cost or lack of availability, and the same is likely true in many other countries (Covarrubias et al. 2012).

Foot and mouth disease (FMD) virus is a tremendous burden to meat and dairy production in many parts of the world, especially developing countries. It is estimated that 2% of cattle in the world are infected with FMD virus in a year (Knight-Jones and Rushton 2013). The direct production losses from FMD – the majority of which are borne by China, India, and Africa – are estimated at roughly US$ 7.6 billion per year (Knight-Jones and Rushton 2013). Losses include not only diminished animal weight gain and milk production, but also loss of traction power when draft animals are infected. There are also indirect economic costs, such as restrictions to livestock export. In countries where FMD virus is endemic, vaccination has an important role in protecting cattle, pigs, and buffalo, thus reducing the economic impact of the disease. It is estimated that the world's livestock are immunized with 2.35 billion doses of FMD vaccine annually (Knight-Jones and Rushton 2013). The positive impact of FMD vaccination in endemic countries would be greater if vaccine doses were less expensive and induced longer-lasting immunity (Kitching et al. 2007). Even countries recognized as FMD free, which often cease vaccination, have an economic burden from the virus. They must maintain costly preventive measures and prepare resources to respond in the event of an outbreak emergency, such as vaccine banks (discussed in a section below).

Antibiotics are widely used to control bacterial pathogens of livestock and to promote efficient food production. However, there are increasing concerns related to antibiotic resistance associated with the extensive use of antibiotics in veterinary and human medicine (Dibner and Richards 2005). Producers may choose either vaccines or antibiotics to control some diseases based on cost, if both options are available. For example, swine ileitis caused by *Lawsonia intracellularis* can be controlled by either vaccination or antibiotics, along with good management practices. Swine producers will use the approved control method that is most cost effective. If regulatory requirements for a biologics company to obtain and maintain a license to produce the vaccine were to increase beyond what is essential, then the cost of the vaccine would increase and producers would opt to use less vaccine and more antibiotics. Affordable and available vaccines reduce reliance on antibiotics for animal health.

1.4 Vaccines for Control of Zoonotic Diseases

Vaccines to control zoonotic diseases in food animals, companion animals, and even wildlife have had a major impact on reducing the incidence of zoonotic diseases in people. Some examples of veterinary vaccines for zoonotic diseases that have been, or could be, used to control infections in animals, thereby reducing transmission of the infectious agent to people, include rabies, brucellosis, leptospirosis, influenza, Rift Valley fever, nipah, hendra, Japanese encephalitis, and Q fever. Without rabies vaccines, it is unlikely that families would be willing to keep cats and dogs as pets. Recombinant vaccinia-vectored rabies vaccines have also been used successfully in baits for oral vaccination campaigns to reduce the incidence of rabies in wild animals (Pastoret and Brochier 1996). Vaccines for brucellosis were instrumental in the *Brucella abortus* eradication program in the USA. Many countries continue to have severe problems with brucellosis in cattle, small ruminants, and people due to a lack of available *Brucella* vaccines for animals (FAO 2010). An additional concern related to *Brucella* vaccines is that they are live vaccines which can infect and cause symptoms in people (Ashford et al. 2004). New-generation safer vaccines for brucellosis are needed.

Similarly, vaccinating livestock against various *Leptospira* serovars can reduce the incidence of human leptospirosis, which in severe cases can cause miscarriage or death. The tapeworm parasite *Taenia solium*, which is transmitted between pigs and humans, is a major cause of adult-onset epilepsy in developing countries (Spickler 2005). In recent field trials, an experimental *T. solium* vaccine administered to scavenging pigs protected them against transmission of the parasite (Jayashi et al. 2012). These promising results suggest that pig vaccination could become an effective way to break the cycle of *T. solium* transmission to people in the developing world.

Emerging and exotic animal diseases are a growing threat to human and animal health and jeopardize food security (Figure 1.3). Increases in human and animal populations, with accompanying environmental degradation, global warming, spread of arthropod vectors, and globalized trade and travel, enhance opportunities for transfer of pathogens within and between species. The resulting diseases pose enormous challenges now and for the future.

In most of the world, increased demand for animal protein has resulted in intensified commercial food animal production and/or expanded "backyard" production.

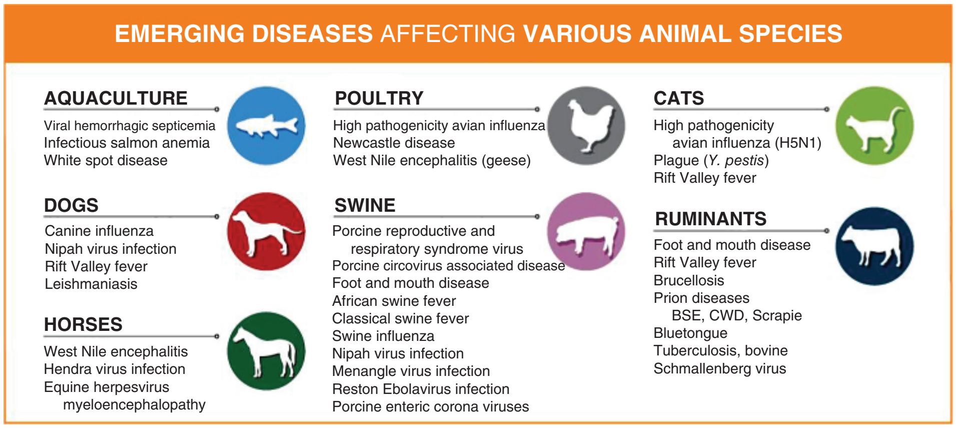

Figure 1.3 Emerging diseases affecting various animal species. Source: Reprinted with permission from Roth et al. (2016).

Both types of production present unique challenges for disease emergence and control. Large commercial operations with high concentrations of animals produce high-quality protein for human consumption at reduced costs. These operations typically have some degree of biosecurity, vaccination programs, and veterinary care. However, the high concentration of animals may facilitate the emergence of pathogens due to extensive replication in large numbers of animals, enhancing the potential for mutation and adaptation to the species. They also present concerns regarding animal welfare and environmental preservation. "Backyard" production of poultry, pigs, and small ruminants can efficiently use household waste for feed and can be an important supplement to dietary protein and income. However, the close interaction with humans, especially children, presents an increased risk of zoonotic disease transfer (e.g. avian influenza and *Brucella melitensis*). "Backyard" animal production rarely has biosecurity or adequate vaccination. Emerging zoonotic diseases of both food and companion animals are a major threat to public health. It is inevitable that the world will continue to experience emerging disease outbreaks in the coming decades. Rapid development of animal vaccines can play a key role in controlling emerging diseases.

There are several examples of vaccines successfully developed against emerging equine viruses, including Venezuelan equine encephalitis, West Nile, and hendra (Broder et al. 2013; Bowen et al. 2014). Vaccination against these agents lowers the risk of zoonotic infections. Several countries have used vaccines, together with other eradication measures, to control high pathogenicity avian influenza virus (H5N1) in poultry. From 2002 to 2010, it is reported that many billions of doses were administered to poultry, mostly in China (Chapter 18) (Swayne 2012). This practice is considered to have reduced disease and mortality in chicken flocks, while also reducing the number of human infections, which have very high fatality rates. Rift Valley fever virus, a devastating pathogen of ruminants and a virulent zoonotic agent, is seen as a prime target for animal vaccine development (Monath 2013). Continued development of more cost-efficient, safe, and effective vaccines against zoonotic agents will foster improvement of human health, animal health, and food security.

1.5 Vaccines to Improve Food Safety

Recently, vaccines have been developed to reduce the shedding of organisms that cause food-borne diseases in people. Vaccines are available for *E. coli* O157:H7 in cattle and *Salmonella enterica*, serovars *enteritidis* and *typhimurium*, in chickens. These vaccines typically do not improve the health of the vaccinated animal, but reduce the intestinal colonization and shedding of pathogens that may contaminate animal products for human consumption (Thomson et al. 2009; Desin et al. 2013). The severity of the *S. enteritidis* outbreak in people in the USA in 2010 due to consumption of contaminated eggs (Cima 2010) could have been reduced or prevented if the associated chickens had received an *S. enteritidis* vaccine. Numerous other microorganisms, common in livestock, cause food-borne disease outbreaks in people, so there may be future opportunities to broaden the use of livestock vaccines for food safety purposes.

1.6 Vaccine Banks

In countries where a particular animal infectious disease does not exist – either due to eradication or because it was never endemic to the region – vaccination against the agent will usually not be practiced. When there is no market for vaccines, the biologics companies do not have an incentive to develop, license, and manufacture them. However, there is often a continuing risk that the agent will be (re)introduced. This requires readiness to respond quickly to control an outbreak, especially because herd immunity to the agent no longer exists.

In the USA, the Department of Agriculture and the Department of Homeland Security have recognized the need to have approved vaccines for important animal diseases that are not currently present within the country's borders. US animal agriculture is highly vulnerable to the introduction of foreign diseases, most notably FMD. A Homeland Security Presidential Directive mandated the establishment of a National Veterinary Stockpile (NVS), a national repository that can deploy within 24 hours "sufficient amounts of animal vaccine, antiviral, or therapeutic products to appropriately respond to the most damaging animal diseases affecting human health and the economy" (Bush 2004). Although the USA is a partner in the North American FMD Vaccine Bank, the present supply is not sufficient to meet the needs of an FMD outbreak. European Union states, Japan, Australia, and New Zealand also maintain FMD vaccine banks (Hagerman et al. 2012). The World Organization for Animal Health has established vaccine banks for avian influenza, FMD, and peste des petits ruminants (PPR) and has shipped doses to many countries in the developing world.

Vaccine banks or stockpiles are expensive to establish and maintain, so robust funding is required. Also, establishing an emergency plan for vaccination against an emerging or foreign animal disease can be complicated from the regulatory standpoint. In some cases, a disease-free country does not issue a regular vaccine license, but issues a conditional license for use in the event of an outbreak. Safety and efficacy criteria for conditional licensure may be different from criteria for a vaccine used against endemic diseases. A functional program of foreign animal disease preparedness requires cooperation among veterinary and public health agencies, regulators, and vaccine manufacturers.

1.7 Successes and Challenges

As discussed above, one of the greatest successes in the use of vaccination to control an animal disease was the global eradication of rinderpest virus. This was achieved using the Plowright vaccine, a conventional live attenuated virus that was generated by serial passages of a virulent rinderpest strain in primary calf kidney cells (Plowright 1984). Other striking examples of vaccine successes and challenges can be seen in some important swine viruses. Aujeszky's disease virus (also called pseudorabies virus) has been successfully eradicated from swine herds in numerous countries, including the USA. An important innovation aiding that success was vaccines with glycoprotein gene deletions (Mengeling et al. 1997; Pensaert et al. 2004). These deletions allow diagnostic tests that differentiate between infected and vaccinated animals (the DIVA strategy). With these tools, it is possible to conduct screening and selective culling in the eradication campaigns, without forgoing the use of immunization to protect herds.

After its discovery in the late 1990s, the porcine circovirus 2 (PCV2) was found to be widespread in major swine-producing countries. It was etiologically linked to postweaning multisystemic wasting syndrome and other clinical syndromes with great economic impact. Subunit and inactivated virus vaccines for PCV2 were developed commercially, became widely adopted, and led to significant improvements in swine health and productivity (Beach and Meng 2012).

On the other hand, efforts to produce effective vaccines against porcine reproductive and respiratory syndrome virus (PRRSV) and influenza A viruses of swine (IAV-S) have been less successful. These economically important viruses have been identified for many years, but current vaccines do not provide reliable control of infection and disease. A major hurdle in both cases is the antigenic variability of the viruses. One concept for improved vaccines against antigenically variable viruses like PRRSV and IAV-S is to identify epitopes that are highly conserved across the various strains. Vaccines that target the conserved epitopes would have the potential to supply broad cross-protection (Khanna et al. 2014). Utilizing new adjuvants, vaccine vectors, delivery mechanisms, or rationally designed live attenuated viruses might also lead to more effective vaccines against these viruses.

Across the spectrum of livestock infectious diseases, there are many with no proven vaccines and others with inadequate vaccine options. Live and killed Newcastle disease virus vaccines are used extensively in some endemic countries, yet frequent outbreaks continue, possibly because genetic mutations in the pathogenic strains allow them to evade the immunity induced by the vaccines (Ashraf and Shah 2014). A live *Mycoplasma mycoides* subsp. *mycoides* vaccine against contagious bovine pleuropneumonia has existed in Africa for half a century, but problems with its efficacy and duration of immunity have been recognized (Jores et al. 2013). Improvements in vaccine technologies, such as adjuvants and recombinant vectors, can potentially aid the development of vaccines against many pathogens. However, one of the disadvantages faced in veterinary vaccine development is that the potential financial returns are much less than for human vaccines. Veterinary vaccines have lower sales prices and smaller potential market value. Consequently, there is a lower investment in research and development for animal vaccines compared to human vaccines, although the range of hosts and pathogens is greater.

1.8 Policies on Use of Vaccines in Disease Control Programs

In some situations, infectious disease agents pose a threat to animal health, human health, food security, or economic stability, but producers do not have the ability or strong incentive to pay for vaccination. Such situations may include endemic diseases in developing countries, zoonotic and food-borne diseases that do not cause serious sickness in livestock, and emerging or exotic diseases that have a small probability of spreading to the given region. For disease control and eradication programs, it is often necessary for governments or other entities to provide financial support. An example would be the current interest in eradication of PPR. Regardless of how the expense is met, a low cost per unit of vaccine is critical to achieving widespread vaccination of the susceptible livestock.

1.9 Summary

The consequences of livestock and poultry infectious diseases are felt throughout the world, regardless of wealth or veterinary medical infrastructure. When livestock diseases are not controlled effectively, global food production is diminished and public health is often put at risk. This explains the vital importance of vaccines for food-producing animals. The fact that so many people depend on livestock and poultry for their livelihoods and as a source of food limits policy options, complicates local and global trade decisions, and raises political sensitivities. It is inevitable that the world will continue to experience the emergence of new human and animal diseases in the coming decades. This challenge requires that veterinary, medical, and public health communities work together locally and internationally. Affordable, safe, and effective livestock vaccines will continue to be an important tool to protect human health, animal health, food safety, and food security.

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References

Alexandratos, N.B.J. and Bruinsma, J. (2012). World Agriculture Towards 2030/2050: The 2012 Revision. ESA Working Paper No. 12-03. Food and Agriculture Organization of the United Nations. www.fao.org/docrep/016/ap106e/ap106e.pdf

Ashford, D.A., di Pietra, J., Lingappa, J. et al. (2004). Adverse events in humans associated with accidental exposure to the livestock brucellosis vaccine RB51. *Vaccine* 22 (25–26): 3435–3439.

Ashraf, A. and Shah, M.S. (2014). Newcastle disease: present status and future challenges for developing countries. *Afr. J. Micriobiol. Res.* 8 (5): 411–416.

AVMA. (2010). Swine-use H1N1 vaccine approved under conditional license. JAVMANews. www.avma.org/javma-news/2010-01-15/swine-use-h1n1-vaccine-approved-under-conditional-license

Beach, N.M. and Meng, X.J. (2012). Efficacy and future prospects of commercially available and experimental vaccines against porcine circovirus type 2 (PCV2). *Virus Res.* 164 (1–2): 33–42.

Bowen, R.A., Bosco-Lauth, A., Syvrud, K. et al. (2014). Protection of horses from West Nile virus Lineage 2 challenge following immunization with a whole, inactivated WNV lineage 1 vaccine. *Vaccine* 32 (42): 5455–5459.

Broder, C.C., Xu, K., Nikolov, D.B. et al. (2013). A treatment for and vaccine against the deadly Hendra and Nipah viruses. *Antiviral Res.* 100 (1): 8–13.

Brown, G.B., Spickler, A.R., Galyon, J., and Roth, J.S. (2016). Descriptions of incursions of foreign, transboundary and emerging animal diseases. In: *Transboundary and Emerging Diseases of Animals* (eds. A.R. Spickler, J.A. Roth, J. Galyon and G.B. Brown), 96–100. Ames: Center for Food Security and Public Health, Iowa State University.

Bush, G.W. (2004). Homeland Security Presidential Directive 9: Defense of United States Agriculture and Food. United States Department of Homeland Security. www.gpo.gov/fdsys/pkg/PPP-2004-book1/pdf/PPP-2004-book1-doc-pg173.pdf

Chae, C. (2012). Commercial porcine circovirus type 2 vaccines: efficacy and clinical application. *Vet. J.* 194 (2): 151–157.

Chang, G.J., Davis, B.S., Stringfield, C., and Lutz, C. (2007). Prospective immunization of the endangered California condor (*Gymnogyps californianus*) protects this species from lethal West Nile virus infection. *Vaccine* 25 (12): 2325–2330.

Cima, G. (2010). Vaccine use up since Salmonella outbreak. *J. Am. Vet. Med. Assoc.* 237 (12): 1356–1357.

Covarrubias, K., Longin, N., and Zezza, A. (2012). Livestock and livelihoods in rural Tanzania: a descriptive analysis of the 2009 National Panel Survey. World Bank Open Knowledge Repository, Washington DC. https://openknowledge.worldbank.org/bitstream/handle/10986/17886/866280WP0Lives00Box385181B00PUBLIC0.pdf?sequence=1&isAllowed=y

Desin, T.S., Köster, W., and Potter, A.A. (2013). Salmonella vaccines in poultry: past, present and future. *Expert Rev. Vaccines* 12 (1): 87–96.

Dibner, J.J. and Richards, J.D. (2005). Antibiotic growth promoters in agriculture: history and mode of action. *Poult. Sci.* 84 (4): 634–643.

FAO. (2009). High Level Expert Forum – How to Feed the World in 2050. FAO, Rome. www.fao.org/fileadmin/templates/wsfs/docs/Issues_papers/HLEF2050_Global_Agriculture.pdf

FAO. (2010). *Brucella melitensis* in Eurasia and the Middle East. FAO Animal Production and Health Proceedings No. 10. FAO, Rome. www.fao.org/docrep/012/i1402e/i1402e00.pdf

FAO, IFAD, and WFP. (2014). The State of Food Insecurity in the World 2014. Strengthening the enabling environment for food security and nutrition. FAO, Rome. https://sustainabledevelopment.un.org/content/documents/1717The%20State%20of%20Food%20Insecurity%20in%20the%20World%202014.pdf

Hagerman, A.D.M., McCarl, B.A., Carpenter, T.E. et al. (2012). Emergency vaccination to control foot-and-mouth disease: implications of its inclusion as a U.S. policy option. *Appl. Econ. Perspect. Policy* 34 (1): 119–146.

Jayashi, C.M., Kyngdon, C.T., Gauci, C.G. et al. (2012). Successful immunization of naturally reared pigs against porcine cysticercosis with a recombinant oncosphere antigen vaccine. *Vet. Parasitol.* 188 (3–4): 261–267.

Jores, J., Mariner, J.C., and Naessen, J. (2013). Development of an improved vaccine for contagious bovine pleuropneumonia: an African perspective on challenges and proposed actions. *Vet. Res.* 44 (1): 122.

Khanna, M., Sharma, S., Kumar, B., and Rajput, R. (2014). Protective immunity based on the conserved hemagglutinin stalk domain and its prospects for universal influenza vaccine development. *BioMed. Res. Int.* 2014: 546274.

Kitching, P., Hammond, J., Jeggo, M. et al. (2007). Global FMD control – is it an option? *Vaccine* 25 (30): 5660–5664.

Knight-Jones, T.J. and Rushton, J. (2013). The economic impacts of foot and mouth disease – what are they, how big are they and where do they occur? *Prev. Vet. Med.* 112 (3–4): 161–173.

Mengeling, W.L., Brockmeier, S.L., Lager, K.M., and Vorwald, A.C. (1997). The role of biotechnologically engineered vaccines and diagnostics in pseudorabies (Aujeszky's disease) eradication strategies. *Vet Microbiol* 55 (1–4): 49–60.

Monath, T.P. (2013). Vaccines against diseases transmitted from animals to humans: a one health paradigm. *Vaccine* 31 (46): 5321–5338.

OIE. (2011). Final Report of the 79th General Session. OIE, Paris. www.oie.int/doc/ged/D11931.PDF

Pastoret, P.P. and Brochier, B. (1996). The development and use of a vaccinia-rabies recombinant oral vaccine for the control of wildlife rabies; a link between Jenner and Pasteur. *Epidemiol. Infect.* 116 (3): 235–240.

Pensaert, M., Labarque, G., Favoreel, H., and Nauwynck, H. (2004). Aujeszky's disease vaccination and differentiation of vaccinated from infected pigs. *Dev. Biol.* 119: 243–254.

Plowright, W. (1984). The duration of immunity in cattle following inoculation of rinderpest cell culture vaccine. *J. Hyg.* 92 (3): 285–296.

Roth, J.A. (2011). Veterinary vaccines and their importance to animal health and public health. *Procedia Vaccinol.* 5: 127–136.

Roth, J.A., Galyon, J., and Brown, G.B. (2016). Causes and consequences of transboundary and emerging diseases of animals: role of the veterinarian. In: *Transboundary and Emerging Diseases of Animals* (eds. A.R. Spickler, J.A. Roth, J. Galyon and G.B. Brown), 14–27. Ames: Center for Food Security and Public Health, Iowa State University.

Spickler, A.R. (2005). Taenia Infections. Ames: Center for Food Security and Public Health, Iowa State University. www.cfsph.iastate.edu/DiseaseInfo/factsheets.php

Swayne, D.E. (2012). The role of vaccines and vaccination in high pathogenicity avian influenza control and eradication. *Expert Rev. Vaccines* 11 (8): 877–880.

Thomson, D.U., Loneragan, G.H., Thornton, A.B. et al. (2009). Use of a siderophore receptor and porin proteins-based vaccine to control the burden of *Escherichia coli* O157:H7 in feedlot cattle. *Foodborne Pathog. Dis.* 6 (7): 871–877.

USDA-APHIS. (2014). Current Veterinary Biologics Product Catalogue. www.aphis.usda.gov/animal_health/vet_biologics/publications/currentprodcodebook.pdf