EMERGING AND RE-EMERGING ANIMAL DISEASES

Overcoming barriers to disease control

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Healthy Animals
Healthier World

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Contents

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A report produced for
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Introduction

Emerging and re-emerging animal diseases have in recent years been associated with outbreaks that have serious consequences for animal and human health. The World Organisation for Animal Health (OIE) defines an emerging disease as "a new infection or infestation resulting from the evolution or change of an existing pathogenic agent, a known infection or infestation spreading to a new geographic area or population, or a previously unrecognised pathogenic agent or disease diagnosed for the first time and which has a significant impact on animal or public health." A known or endemic disease is considered to be re-emerging if it shifts its geographical setting, expands its host range, or significantly increases its prevalence.

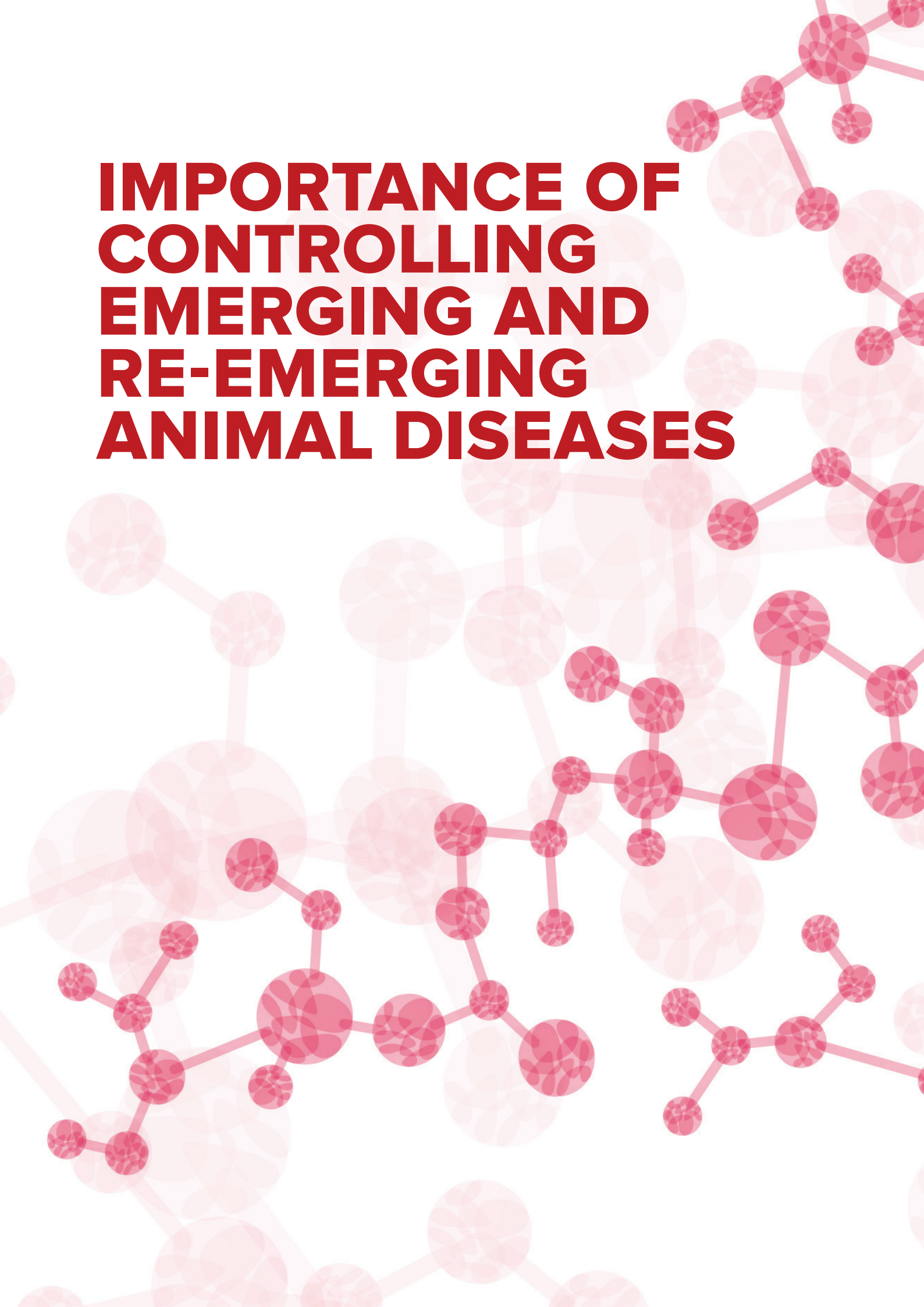
While animal disease outbreaks are not a new phenomenon, modern trends have dramatically increased the risks associated with them. In recent decades, rapid increases in human population and wealth have resulted in unprecedented demand for livestock products around the world. This in turn has led to the emergence of increasingly complex livestock systems and value chains in which the selection of animals is primarily based on production traits rather than disease resistance. The associated increase in enhanced biosecurity* measures on farms has also contributed to the increased vulnerability of livestock to disease threats, as regional or national eradication of infectious diseases means that animals in these areas are immunologically naïve and thus at increased risk from pathogen incursions. With growing demands on land use, intensified farming practices, increased transportation of livestock for trade purposes, and the evolution and mutation of pathogens themselves, the likelihood of further serious epidemics will grow.

* Please see the end of this report for a list of definitions and abbreviations.

In addition to their detrimental impact on animal health, animal diseases can directly impact human health. Approximately 75% of recently emerging animal diseases are zoonotic, meaning that they can be naturally transmitted between animals and humans, and approximately 60% of all human pathogens are of animal origin. Pathogens may be bacterial, viral, fungal or parasitic and the animal reservoirs of zoonotic pathogens include wild and domestic species. The routes of transmission to humans vary from indirect means through food, or via an insect vector, to direct contact with farm or pet animals or through exposure to environmental contamination.

In order to mitigate the risks associated with emerging animal disease, more robust surveillance and control measures need to be put in place, particularly in parts of the developing world where veterinary services and infrastructure remain limited and under-resourced. In the future, veterinary or animal medicines are likely to play an increasingly central role in effective disease control. While government, industry and regulators around the world have already taken important steps to ensure that veterinary medicines can be delivered quickly and effectively when needed, many challenges remain. This report assesses the current barriers to the efficient deployment of veterinary medicines. It provides recommendations for further actions that governments, regulators and industry can take, both to mitigate the risks of disease events, and to ensure the development, availability and deployment of new and innovative animal health products worldwide.

IMPORTANCE OF CONTROLLING EMERGING AND RE-EMERGING ANIMAL DISEASES



Importance of controlling emerging and re-emerging animal diseases

"Animal diseases... can have a devastating impact on animal production, trade in livestock and livestock products, food security, livelihoods, and, consequently, on the overall process of economic and social development."

Hiroyuki Konuma,
Assistant Director-General, FAO

Reducing the risk of emerging and re-emerging animal diseases is important in order to control their direct and indirect effects: from their obvious detrimental impacts on animal and human health to their broader economic implications in terms of the lost revenues and wider societal costs resulting from disease outbreaks. In the last decade, disease outbreaks have led to the culling of hundreds of millions of animals and have incurred costs running into the hundreds of billions of dollars. Avian influenza viruses, to take just one example, are estimated to have led to the culling of 200 million birds in Asia alone, with losses of more than 10 billion US dollars for the region's poultry sector. With current trends of human development, globalisation and climate change increasing the likelihood of emerging and re-emerging disease outbreaks, more robust surveillance, prevention and control measures will be needed in order to prevent future crises.

The primary impact of disease is the reduction in the size and health of animal populations. But outbreaks can also have wider and longer-lasting consequences on the overall health of animal production systems that can be difficult to measure, such as reduced fertility levels, which can result in lower productivity rates. Emerging and re-emerging animal diseases also have direct consequences for human health. Approximately 75% of emerging animal diseases are zoonotic, meaning that they can be passed between humans and animals and vice versa, and many have the potential to be disabling or even fatal if left untreated. The burden of disease on human health is quantifiable by estimating disability-adjusted life years (DALYs), the years lost due to ill-health, disability or early death as a result of disease. Zoonotic diseases, endemic and emerging, are estimated to account for 10% of all DALYs lost among human populations worldwide.

75%
Proportion of emerging animal diseases that are zoonotic

Animal diseases can also incur costs associated with human responses to outbreaks, such as the considerable costs associated with surveillance, prevention and control in susceptible human and animal populations; losses in revenue due to the closure of markets, trade restrictions and restructuring of industrial processes and management systems; and broader impacts on tourism and the wider rural economy. In many instances, the cost of diagnosing and treating diseases transmitted to humans from animals falls on governments or on patients themselves. Success in controlling the spread of animal diseases to humans will therefore help reduce the burden for private and public sector finances.

In addition to being a source of food, animals also serve as a store of wealth and a source of income, employment, foreign exchange, pleasure and companionship for people worldwide. The livestock sector alone accounts for almost half of the global agricultural economy. The potential impact of animal diseases on production and trade of animal products is therefore significant, especially given the expectation that livestock product demand in developing countries will double in the next 15 to 20 years. The trade of agricultural products can also provide an important route out of poverty in developing countries, where a large proportion of the population depends on animals for their income.

Livestock product demand in developing countries is estimated to double in the next 15 to 20 years

Research confirms that the ripple effects of emerging diseases on human health and community stability are most serious and long-lasting in developing countries, where poorer living conditions are associated with higher infection rates and a lower availability of proper treatment. The closer interactions between people, livestock and wildlife in these regions -- and the increasing incursion of humans into previously unsettled areas -- can facilitate the jumping of pathogens between species and make them hotspots for the emergence of novel zoonotic infections. As most developing countries have nascent export industries, they also require longer and more ambitious efforts to establish trust in the safety of their agricultural products after the outbreak of an animal disease. The financial impacts of trade restrictions imposed by importing countries following an outbreak of disease can often be higher than the direct losses due to the disease.

Emerging diseases can have serious and long-lasting implications for developing countries

Disease outbreaks can therefore be very costly in terms of their repercussions on both animal and human health and the economic burden their treatment imposes. The World Bank has estimated that the combined losses in trade, tourism and tax revenues due to animal disease outbreaks have amounted to approximately 200 billion dollars over the past decade. Additionally, uncertainty about the spread and consequences of zoonotic diseases can create widespread alarm among consumers and lead to dramatic shifts in buying behaviour, with serious implications for international trade in livestock products.

$200bn

The estimated cost of animal disease outbreaks over the past decade

Most animal health professionals and academic experts consider there to be a high risk of a major outbreak of an animal disease in the near future. Robust systems of surveillance, prevention and control of animal diseases, including the responsible use of veterinary medicines, can serve to minimise risks to animal and human health and encourage long-term economic growth. This requires increased investment in education, research and institutional reform at the local, national and international levels.

Responsible use of veterinary medicines can serve to minimise risks to animal and human health

EXISTING DISEASE CONTROL MEASURES AND THEIR IMPACT

A number of measures are available to producers and national governments to prevent disease events from occurring, to combat outbreaks when they do occur, and to reduce the likelihood of future outbreaks. In recent years, modern controls such as improved animal medicines have been increasingly used alongside surveillance and conventional control methods, which include stamping out (culling) and movement restrictions (including zoning, compartmentalisation, isolation and quarantine). These measures are reinforced by additional 'enablers of control' including international agreements, standards, guidelines and recommendations provided by organisations such as the OIE, the World Trade Organization's (WTO) reference organisation for international standards on animal health and zoonoses.

Control measures at the farm level

Animal medicines

The judicious use of veterinary medicines has an important role in reducing the risk of emerging and re-emerging animal diseases. In tandem with other disease control measures, they continue to play a key part in the prevention and eradication of dangerous diseases. In recent years, technological innovations have been instrumental in the design of better medicines, while genomics, high-throughput sequencing, and faster and wider data collection on outbreaks have improved our understanding of disease epidemiology and facilitated better control of animal diseases. A "One Health" approach has also been initiated to encourage the interaction between animal and human health services so as to address threats occurring at the interface between humans, animals and ecosystems and facilitate the adoption of new technologies for animal and human disease.

In tandem with other control measures, veterinary medicines continue to play a decisive role in combating animal diseases

Vaccines

Vaccines are biological preparations that are designed to produce immunity to a disease by stimulating (cellular and humoral) the production of antibodies. There are two main types of vaccine: inactivated vaccines which contain 'killed' disease-causing organisms; and live vaccines which contain live but attenuated pathogens that do not cause the disease when used. In both cases, one of the most important factors for the success of a new vaccine is its correct commercialisation and use in the field, which requires additional research post-development, correct incentives and enforceable guidelines for local stakeholders.

Correct commercialisation and use in the field is key to the success of new vaccines

Vaccines have proven effective in both preventing animal disease outbreaks and controlling the spread of highly infectious animal diseases. For example, they have contributed to the control efforts for avian influenza, a zoonosis of considerable international concern. According to the World Health Organization (WHO), UN Food and Agriculture Organization (FAO) and OIE, the best means of preventing the spread to humans of the highly pathogenic avian influenza (HPAI) strain, H5N1, is by controlling infection in poultry, in particular through vaccination when appropriate. Moreover, according to the FAO, "most endemic countries have shown a steady decline in the number of cases due, for the most part, to the HPAI control measures that have been applied." Vaccination accompanied by proper compliance and application, even though it does not preclude sub-clinical

Vaccines have proven effective in both preventing outbreaks and controlling the further spread of highly infectious animal diseases

infection or the circulation of the virus completely, has reduced viral shedding by poultry and consequently human exposure.

Antibiotics

Antibiotics are agents that inhibit bacterial growth. Unlike vaccines, they are most commonly used for the therapeutic treatment of clinically sick animals, not for disease prevention. Antibiotics have also been used for promotion of growth and feed efficiency, a controversial practice that has been prohibited in the EU and is questioned by the OIE and other international organisations. While antibiotics are sometimes used in a prophylactic mode in highly infected areas, over- and misuse is clearly a driver for the emergence of resistant strains. However, when correctly used, antibiotics and other antimicrobial agents do little to encourage the emergence of resistant strains and are not harmful to humans. The animal medicines industry's slogan, "as little as possible, as much as necessary", is indicative of the emphasis placed on responsible use. The OIE member countries have recently adopted standards on responsible and prudent use of antimicrobial agents in veterinary medicine for aquatic and terrestrial animals.

Farm management

Good farming practices are a crucial first step in ensuring that animals remain healthy and food is safe for human consumption

Good farming practices are a crucial first step in ensuring that animals remain healthy and food is safe for human consumption. More broadly, biosecurity measures seek to prevent the transmission of diseases by fostering better animal management and hygiene practices. Some of these measures include: control of health status, movement and entry of animals, personnel, feed and vehicles; disinfection of establishments, equipment and vehicles; maintaining an appropriate population density for the species in question; and proper waste management. When used in conjunction with close contact with veterinary services for disease diagnosis and herd health schemes, biosecurity offers an important means of protection from emerging diseases at the local level.

Control measures at the national level

Surveillance

Surveillance at all levels of the animal production chain is necessary to anticipate the emergence of new zoonoses

Surveillance is defined by the OIE as "The systematic ongoing collection, collation, and analysis of information related to animal health and the timely dissemination of information so that action can be taken." Surveillance of domestic and wild animal populations at all levels of the animal production chain is a necessary control measure that makes it possible to anticipate the emergence of new zoonoses and protect humans from possible infection. Surveillance should be complemented by reporting and compensation schemes once an infection or an outbreak is detected; offering compensation for animals destroyed gives farmers the incentive to report the occurrence of disease in their farm. Post-detection, continued surveillance and monitoring of infected or vaccinated populations is used to ensure the final eradication of the disease. Although many national and international systems are currently in place to monitor human and animal diseases, major gaps in surveillance remain, particularly the lack of adequate and consistent surveillance infrastructure in developing countries. Better integration of surveillance schemes for human and animal diseases is another key area for improvement.

Movement controls

Controlling the movement of livestock is often central to preventing disease and limiting its spread once an outbreak has occurred. In many cases, when a disease is first detected, infected animals are quickly isolated from the rest of the group so as to limit the further spread of disease. Quarantine procedures are another important means of preventing imported livestock, pets or competition animals from spreading diseases from abroad. Zoning and compartmentalisation are additional conventional practices, which entail the separation of an animal sub-population with a distinct health status, primarily on the basis of geographical criteria, for example defining a disease-free zone within an infected country.

Controlling the movement of livestock is often central to preventing disease and limiting its spread once an outbreak has occurred

Stamping out

Stamping out is the method of culling infected and suspect animals, and has been a common approach to controlling major disease outbreaks in most developed countries. Reliance on stamping out has increased as the proportion of immunologically naïve animals has grown. An important advantage of stamping out is the speed with which an area re-gains disease-free status after its implementation, allowing it to trade its products again. For example, in the case of foot-and-mouth disease, a highly infectious animal disease which carries considerable trade restrictions, a country can be declared free of disease within three months of an outbreak if stamping out is undertaken; the waiting time for a response based on vaccination is six months. During this additional time the country in question will likely incur considerable losses due to export restrictions. However, stamping out is only effective where the implications are fully understood and there needs to be a clear delineation of responsibilities and a timetable for implementing follow up measures to ensure that the pathogen has been removed. Stamping out has been increasingly criticised by consumers, producers and animal welfare activists for the unnecessary killing of healthy animals that it often entails. As a result, alternative, animal-sparing measures have been promoted in recent years.

Stamping out has been a common approach to controlling major disease outbreaks in most developed countries

Control measures at the regional and international levels

In addition to these measures at the local and national levels, intergovernmental organisations and supranational authorities have been taking additional steps to facilitate disease control. A number of new and existing initiatives have been designed to improve the capacity for surveillance, early detection and response to animal disease outbreaks at the regional and international levels. Examples of these initiatives include:

New initiatives have been launched to improve the capacity for surveillance, early detection and response to animal disease outbreaks

- **Codex Alimentarius.** Established by FAO and WHO in 1963, Codex Alimentarius develops harmonised international food standards, guidelines and codes of practice to protect the health of consumers and ensure fair practices in the food trade.

- **OIE codes.** The OIE publishes two codes (Terrestrial and Aquatic) and two manuals (Terrestrial and Aquatic) as the principle reference standards for its 178 member countries, and these cover animal health and zoonoses control measures.

- **VICH.** Launched in 1996, the trilateral VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) is an initiative for industry and regulators from the EU, the United States and Japan to implement a series of harmonised regulatory guidelines. Observer countries now participating in VICH include Canada, Australia, New Zealand and South Africa.

- **PVS Pathway.** OIE member countries have adopted its Performance of Veterinary Services (PVS) Pathway to create more sustainable and forward-looking animal health systems. Its main features include the systematic evaluation of members' national veterinary services based on international standards and assistance in the modernisation of national veterinary legislation.

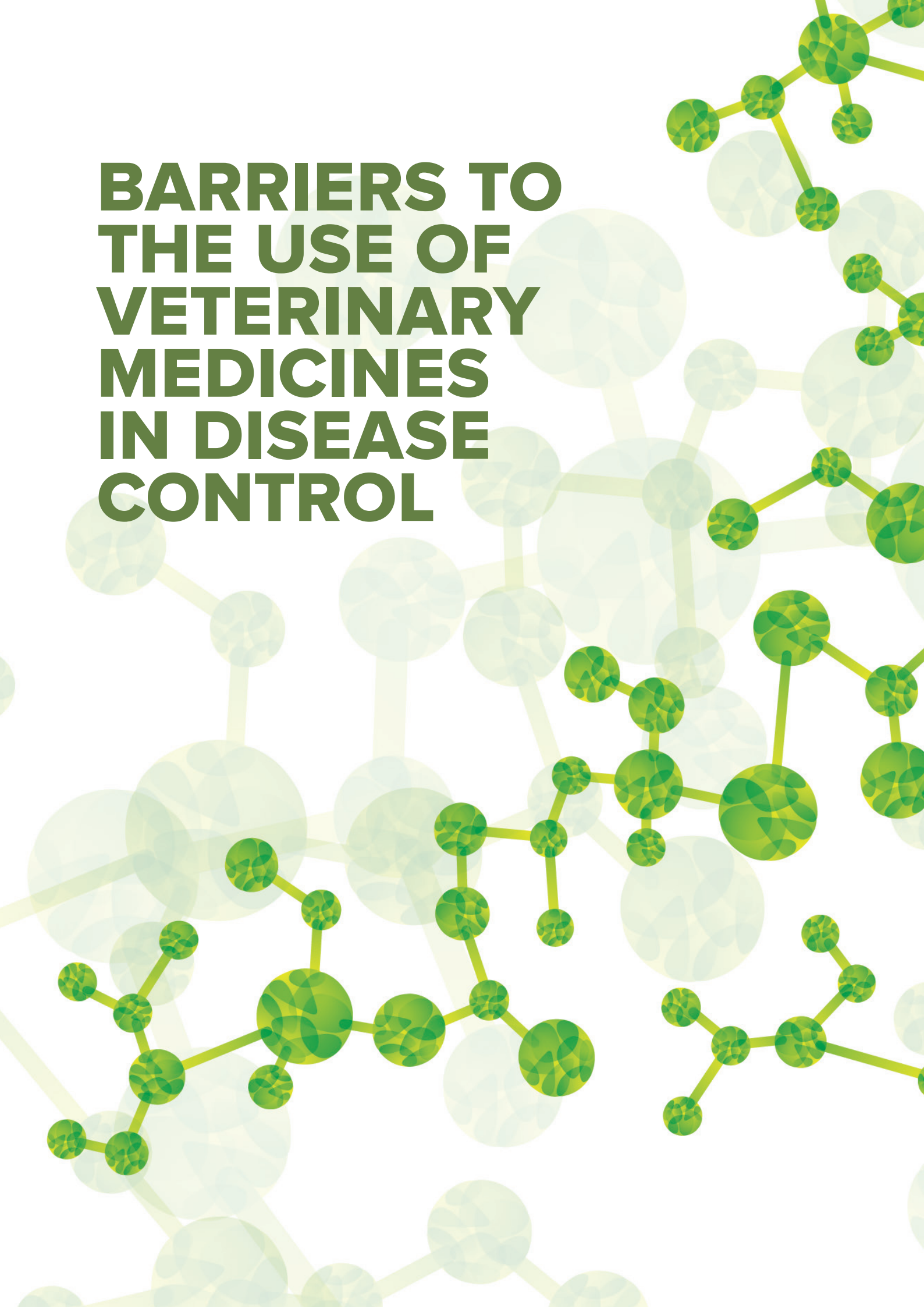
- **1-1-1.** The "1-1-1" licensing concept is based on a "1 dossier / 1 assessment / 1 decision" process for making the market authorisation of new animal health products easier throughout Europe. If implemented, the process will help to ensure the competitiveness of the animal health industry in Europe and overcome current regulatory obstacles by introducing a simplified marketing authorisation system.

- **GLEWS.** Set up in 2006, the GLEWS (Global Early Warning System for Major Animal Diseases) builds on the added value of combining and coordinating the alert and disease intelligence mechanisms of OIE, FAO and WHO in order to assist in prediction, prevention and control of animal disease threats, including zoonoses, through sharing of information, epidemiological analysis and joint risk assessment.

- **One Health.** The One Health concept was launched by the OIE, the WHO, FAO, UNICEF, United Nations System Influenza Coordination (UNSIC) and the World Bank to define a holistic approach for reducing the risks of infectious disease at the animal-human-ecosystems interface. It has served as a platform for greater collaboration between the OIE, the WHO, and the FAO in sharing responsibilities and coordinating global activities to address health risks. Active participants include dozens of scientific, medical and veterinary associations and institutions at international, regional and national level.

The actual impact of these regional and international measures has been difficult to estimate, and while it is widely accepted that these efforts can significantly reduce the risk of emerging diseases, a number of obstacles remain to their optimal application. These problems limit the capacity of national governments and international organisations to protect livestock and livelihoods, and to contribute adequately to the global public good.

BARRIERS TO THE USE OF VETERINARY MEDICINES IN DISEASE CONTROL



Despite their importance in controlling emerging and re-emerging animal diseases, veterinary medicines often face significant barriers to deployment. The long life cycle of animal medicines from initial development to end use is fraught with substantial obstacles at each stage. At the R&D stage, high costs and low profit margins often deter the development of new and innovative medicines. At the market authorisation stage, overly burdensome regulations, divergent legislative frameworks, and the lack of streamlined approval processes can result in further delays that limit the effectiveness of disease control strategies. Finally, once available on the market, the actual distribution and end use of veterinary medicines can face complications due to logistical problems, lack of government support, and limited veterinary experience and infrastructure on the ground.

Barriers to the research and development of veterinary medicines

Poor diagnostics

High costs and the limited availability of veterinarians who can carry out diagnostic controls creates lags and inefficiencies in responding to a disease outbreak

The availability of adequate diagnostic mechanisms is key to ensuring the rapid detection and efficient response to disease outbreaks. The collection of timely and accurate information regarding an outbreak is integral to understanding the disease's emergence and transmission cycles. Veterinary authorities must be able first to collect samples for laboratory analysis and then to officially identify the microbe and inform the national and international community about its emergence. However, the high cost and the limited availability of veterinarians who can carry out such diagnostic controls, especially in developing countries, creates lags and inefficiencies in responding to a disease outbreak early on. Furthermore, there are obvious difficulties in detecting novel emergent pathogens as diagnostic tools specific for those pathogens are as yet undeveloped. A good example for the use of new technologies is the Schmallenberg virus, the cause of a previously-unknown disease of ruminants which first occurred in Germany in 2011, and which was identified using 'deep sequencing' techniques in the blood of affected cattle. Only subsequent to this initial high-throughput screening -- a process which requires specialist sample preparation and instrumentation -- have Schmallenberg-specific diagnostic tests, and now a vaccine, been developed for use by veterinarians in the field.

Inadequate surveillance

Even where surveillance systems are well established, there is a tendency for them to be reactive or 'passive', which can result in costly delays

Barriers to surveillance include the reluctance of farmers and government officials to report outbreaks, due to the lack of established compensation schemes or to avoid trade restrictions when an outbreak is detected. In developing countries, surveillance is often inefficient because of the lack of adequate veterinary personnel and equipment. While there is a greater level of surveillance in developed countries, there is still a tendency for surveillance to be reactive or

'passive'. The development of medicines starts only once a problem is detected or reaches a certain threshold of perceived importance, which can result in costly delays. Good surveillance systems should be based on structures that facilitate communication between those individuals who interact with animals, usually farmers and pet owners, and those with animal health training and access to better resources and facilities, such as veterinarians.

Niche markets

Vaccines are most effective when they are designed to protect against specific local virus strains or serotypes. However, significant differences between local strains mean that there is oft en only limited demand for strain-specific vaccines. As it is not always financially viable for industry to develop vaccines for individual local strains, particularly in developing markets where monetary demand is limited, the regional specificity of strains can be a limiting factor for multinationals investing in new veterinary medicines. According to one animal health industry expert, "even if companies are engaged in developing new products, in many cases the research costs that the companies would have to mount would most probably be outweighed by the profit that they can make by selling these products to niche markets."

Regional specificity of virus strains means that it is not always financially viable for industry to develop new vaccines

Dealing with evolving strains

Another challenge is the need to regularly update vaccines as pathogens emerge and evolve. Epidemiologists recognise that, over time, many viruses naturally undergo antigenic drift, a gradual mutation in a virus' structure that requires new vaccines to combat its effects. As a result, many vaccines require continuous adaptation to confer the best protection against existing virus strains. The lags created at this stage are further exacerbated by the regulatory approval process that new and updated medicines must undergo.

The constantly evolving nature of viruses increases the commercial risk of investment in vaccines

Where pathogens are variable, robust surveillance is also critical to allow early detection and the rapid development of effective vaccines. In addition, mechanisms need to be put in place to allow the free sharing of pathogens in order to discern whether currently available vaccines are giving adequate coverage. The constantly evolving nature of microorganisms increases the commercial risk of investment in vaccines for pharmaceutical companies. In the past, pharmaceutical companies have sometimes been reluctant to invest in strain-specific vaccines because of the logistical issues and costs involved in keeping vaccines regularly updated.

High R&D costs

The research and development of new veterinary medicines is a drawn-out process that requires substantial investments over a long period. After a potentially useful compound has been identified and the medicine has been developed, it needs to go through a range of post-development controls, including toxicity studies, analyses of appropriate and efficient dosages for specific species, stability tests and field trials. According to the IFAH Benchmarking survey, this process typically

The development of a major new animal medicine typically takes 7-10 years and can cost up to $200 million

takes 7-10 years and can cost up to 200 million dollars. For a new vaccine, R&D alone can often take 3-5 years -- a considerable period of time given the need to combat infectious diseases as rapidly as possible in order to contain outbreaks and minimise the damage to human and animal health.

Limited markets and relatively low prices make pharmaceutical companies reluctant to invest in R&D for new animal medicines

Cost-effectiveness considerations are often one of the foremost constraints at the R&D stage. Compared to the potential returns from the production of human medicines, animal medicines attract smaller sales and lower prices, which make pharmaceutical companies reluctant to invest in R&D. In addition, there is evidence that the costs incurred and length of time required to develop new animal medicines are increasing rather than decreasing. In particular, companies are expending significant additional resources on mandatory defensive R&D required by regulatory authorities in order to maintain existing products in the market.

Concerns over intellectual property

In countries without effective regulatory frameworks, pharmaceutical companies face additional constraints on their investment decisions from the lack of effective patent protection for new animal medicines in many jurisdictions. For WTO members, animal medicines based on new compounds are protected by Article 39 of the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which precludes third parties from unfairly relying on proprietary data for commercial purposes. In countries with weak legal and regulatory frameworks, however, there are few efficient mechanisms for the protection of intellectual property, discouraging investments in new veterinary medicines.

Developing world challenges

Lack of technical expertise, financial resources and infrastructure makes R&D an even greater challenge for many developing countries

The above challenges are often compounded in the developing world. The process of developing vaccines for local or mutated strains requires additional funding and specialised personnel. Lack of technical expertise, financial resources and infrastructure to allow for the rapid development of animal medicines makes R&D an even greater challenge for animal medicine companies in many developing countries. Costs of production also tend to be higher, making production unviable.

Barriers to bringing veterinary medicines to market

Expensive and lengthy market authorisation procedures

The considerable cost of R&D can sometimes be comparable to the costs imposed by complex market authorisation procedures

Regulations are intended to ensure that medicines are rigorously tested, developed using standardised practices and used responsibly. They also establish a necessary legal basis for interventions in instances of disease outbreak, which can often mean depriving farmers of their livestock. However, current regulatory frameworks range from overly rigid in many developed markets to weak or non-existent across much of the developing world. In the former, the considerable cost

of R&D can sometimes be comparable to the costs imposed by complex market authorisation procedures, which result in delays that can limit the effectiveness of disease control strategies. According to IFAH's 2011 Global Benchmarking Survey of the animal health industry in Australia, Canada, the EU, Japan and the United States, between 2006 and 2011 the time required to register new products for major livestock species, companion animals and minor livestock species increased by an average of 16 months, 9 months and 11 months respectively. In addition, during this five-year period registration costs for new veterinary medicines increased by an average of 23% for major livestock species, 20% for companion animals and 7% for minor species.

Overly stringent standards

The high costs of market authorisation often discourage the development of new animal medicines

While it is important that regulations surrounding veterinary medicines remain rigorous to ensure that medicines are safely and responsibly administered, there is increasing concern within government and industry about over-stringency of manufacturing, quality and inspection requirements, with the result that the high costs of market authorisation often discourage the development of new medicines. In the United States and EU, animal medicine companies must submit the results of extensive post-development tests to national and sometimes supranational authorities before a product can be made available on the market. Companies also incur considerable costs in maintaining and defending their existing portfolio of animal health products. While quality control and post-development tests are essential, the rigidity of the approval process often delays the deployment of much-needed animal medicines.

Lack of streamlined approval processes

Due to the absence of legislation to quickly grant licences to vaccines of new strains, updated vaccines typically have to undergo the full regulatory approval process, resulting in significant delays and serious repercussions for animal health. While some progress has been made in simplifying procedures for minor production modifications, significant challenges remain. Barriers also exist in developing countries where many regulatory authorities only grant licences for vaccines and other veterinary medicines if they have been previously approved for use in the United States or the EU.

Divergent regulatory frameworks

Lack of uniform standards can cause delays that compromise the effectiveness of regional or global disease control strategies

Disparities in national legislative frameworks governing animal health can also pose problems. While the EU has made advances in terms of how medicines producers can apply for approvals -- for example, a centralised procedure now exists whereby approved products can obtain EU-wide market authorisation from the European Medicines Agency -- the process remains lengthy (18 to 36 months) and expensive. The lack of uniform standards across different regulatory bodies

is an important aspect of these delays. In the new EU centralised procedure for example, a single member state can object to the approval of a product and derail the entire process. The existence of divergent regulatory frameworks in different parts of the world adds further complexity to approval processes and compromises the effectiveness of regional or global disease control strategies.

Opposition to new technologies

There is increasing concern among scientists and within the industry that politics, rather than science, is driving some regulatory measures

New technologies are increasingly being developed to make animal medicines safer and more effective in combatting emerging and re-emerging diseases. However, public attitudes toward new technologies, such as genetically-modified (GM) vaccines, are often based on misguided information, undermining the development and introduction of novel vaccines and biopharmaceuticals. There is also increasing concern among scientists and within the industry that politics, rather than science, might drive some regulatory measures, in particular current attitudes toward the use of antibiotics in animals.

Weak regulatory regimes in developing countries

While overly stringent regulations can often hinder the registration of veterinary medicines in developed markets, stakeholders operating in developing countries must often contend with inadequate safeguards and a lack of transparency and consistency in national licensing processes. The concerns of politicians and businessmen that increased regulations and compliance procedures will render food exports less competitive has further hindered the development of modern regulatory regimes across much of the developing world. In countries with weak governance structures and high levels of corruption, the sponsorship of powerful elites has sometimes facilitated the distribution of poor quality vaccines rather than developing effective vaccines derived from data on local strains.

Barriers to the use of animal medicines

Lack of veterinary knowledge

Lack of understanding of how veterinary medicines work is a key barrier

Even after veterinary medicines are approved, their use is often complicated by a widespread lack of knowledge about how the medicines work, and a dearth of adequate surveillance mechanisms. In the absence of qualified veterinarians and supervision in many parts of the developing world, lack of understanding of how medicines work is a key barrier, often leading to incorrect, inconsistent and irresponsible use. According to an expert on emerging zoonoses working for the Australian government, “the lack of informed understanding on the part of the user is a major problem”. One of the arguments commonly used against the introduction of vaccines is that they can contribute to the persistence of a virus in a population if used inappropriately. Similarly, antibiotic resistance resulting from non-standard use of antibiotics as well as the circulation of counterfeit products undermines the effectiveness of existing medicines.

Weak veterinary infrastructure

Many developing countries still lack adequate disease monitoring and surveillance systems, have limited or weak regulations on animal welfare, hold livestock in small, fragmented farming units that render the administration of veterinary medicines impractical, and do not have the appropriate facilities to store and distribute vaccines. According to the FAO, “animal health veterinary and laboratory diagnostic services are not consistently well-resourced financially and they often lack sufficient personnel and adequate infrastructure.”

Administering veterinary medicines in small and disparate farming units can be difficult and highly resource intensive. Due to the lack of adequate surveillance in many countries, a blanket approach of universal vaccination is sometimes chosen in lieu of targeted vaccination programmes. Blanket approaches typically do not take into account age, production cycles and risk assessments of disease persistence or occurrence, and as a result they are often hugely expensive and may be ineffective.

Administering veterinary medicines in small and disparate farming units can be difficult and highly resource intensive

Practical issues such as poor transportation and storage methods in developing countries can also pose serious barriers to the use of veterinary medicines. Ensuring that vaccines are properly refrigerated may be particularly crucial to their effectiveness. Vaccines exposed to temperatures outside the recommended ranges can have reduced potency and protection. However, according to the WHO, nearly half of all vaccines in developing countries go to waste every year due to temperature spoilage. Storage and handling errors can be extremely costly and can also result in the loss of confidence among animal owners when repeated doses are required.

Poor transportation and storage methods in developing countries can pose serious barriers to the use of veterinary medicines

Ineffective and poor quality medicines

In recent years, small local companies have increasingly been involved in the production of veterinary medicines in emerging markets. While these companies have helped to fill important gaps in local medicine requirements, technical, financial and regulatory limitations can often mean that their products have sometimes been of inferior quality. In addition, in some instances, products offered in the market may not be well-adapted to local strains or have become outdated as microorganisms evolve. As a result, even if vaccines are available, their actual efficacy can sometimes be limited. Furthermore, once licensed, it can often be difficult to replace veterinary medicines that are no longer effective with new products.

The presence of poor quality vaccines can lead to a lack of trust among local stakeholders

Lack of government and private sector support

Finally, delivering animal medicines, and vaccination efforts in particular, have been hampered because they are not well supported or coordinated by the government. In many developing countries, central government veterinary institutions remain underfunded and deliver only basic animal health services. There is also often little commitment to the process of privatisation and many countries have no legal framework to establish successful collaboration between the public and private components of veterinary services and to ensure good governance. Where private veterinary practices exist, they often only benefit more profitable medium-to-large commercial farmers in urban or peri-urban areas. Similarly, in a number of countries, control programmes are undermined by policy uncertainty over small-scale commercial producers and the absence of public-private partnerships. In addition, in many jurisdictions, government administrators, farmers and other stakeholders continue to oppose vaccination for fear of incurring additional export restrictions that can have severe economic repercussions.

CASE STUDIES

Avian influenza

BASIC FACTS

Virus type:
Influenza type A, Orthomyxo-viridae family

Disease type:
Zoonotic

Geographic distribution:
Worldwide with Asian origins

Animals affected:
Primarily birds (food-producing, pets and wild birds)

Impact:
90-100% mortality in infected poultry (HPAI); 630 human infections, 375 deaths (H5N1, as of July 2013)

Veterinary medicines available:
Inactivated vaccines and recombinant vaccines

Avian influenza is a zoonotic, globally important disease of birds that can be categorised as either low pathogenic (LPAI) or highly pathogenic (HPAI) according to the virulence of the virus in animals. Outbreaks of LPAI are common around the world but LPAI typically causes no clinical signs or only minor illness in infected birds. LPAI strains are generally less of a threat to human health, although the LPAI strain H7N9 has caused more than 135 hospitalised human cases of severe influenza in China since February 2013, with a case fatality rate exceeding 30%. In addition, LPAI can have significant economic repercussions as a result of export restrictions and culling of birds, particularly in developing countries where the use of vaccines and other veterinary medicines is difficult due to weak veterinarian services and small farming units. Compared with LPAI, HPAI is more readily detected in poultry due to very high levels of mortality in infected birds, and can cause potentially catastrophic economic consequences, from significantly reduced livestock populations to lost export markets. Though relatively rare, sporadic human infections of HPAI have occurred in cases of close contact with infected birds and caused serious illness and even death.

Transmission and spread

Influenza viruses are shed in the oral, respiratory and faecal secretions of infected birds and spread via direct contact between healthy and infected birds, or indirectly via contact with contaminated equipment and people. Transmission to humans leading to clinical disease is a rare event but can take place in cases of close contact with infected birds or in heavily contaminated environments. The ability of the virus to infect a diversity of wild birds and other vertebrate hosts (including pigs), its prolonged environmental survival in favourable conditions, its zoonotic potential and its capacity for mutation via antigenic drift or antigenic shift, as well as the lack of completely effective vaccines for use in poultry, make avian influenza a particularly dangerous disease for both animal and human populations. Of greatest concern to human health would be for an avian influenza virus to adapt and become capable of sustained human-to-human transmission in the absence of pre-existing immunity in the population.

Over recent years there have been a number of major avian influenza epidemics and these have incurred substantial costs, including those related to the use of vaccination, stamping out policies and restrictions on international trade. This includes H5N1 outbreaks that, since 1996, have spread throughout Asia and into Europe and Africa, dominating veterinary and public health and featuring in the media. Globally, other subtypes with a lower profile, such as H9N2, continue to have a significant impact on poultry production and have the potential to cause global pandemics. A 2013 FAO report maintains that HPAI remains a “significant threat” to the poultry industry globally, having a destabilising effect on agriculture in countries where backyard farming of domestic ducks is common, degrading the food security and livelihood of millions of people and “maintaining a very real potential for emergence of a pandemic human influenza.” In 2013, the first probable case of person-to-person transmission of avian influenza (H7N9) occurred in China, although the ability of the virus to transmit itself between humans appears to be limited.

Control measures

Various controls are already in place for avian influenza across most of the world, including biosecurity and surveillance, stamping out, and regional vaccination programmes for poultry in high-risk areas. As there is no treatment for avian influenza once clinical signs appear, targeted stamping out without vaccination is the chosen control method in most developed countries, where early detection and compensation programmes are widespread. The use of such measures is not as common in developing countries because of the lack of logistical and financial resources, as well as relative institutional inexperience with complicated disease management methods. In addition, most developing countries have much greater variation of intensive and extensive poultry production systems and a far larger number of farmers involved which complicates the delivery of animal health measures.

H5N1 maintains a "very real potential for emergence of a pandemic human influenza"

Vaccination is typically only implemented in endemic areas as a preventative or during an outbreak as an adjunct control measure when all other measures are insufficient. Moreover, vaccination has to be accompanied by surveillance and movement controls to be effective because although vaccines may reduce the susceptibility, morbidity and mortality of birds subsequently exposed to infection, they do not prevent the shedding of potentially infectious levels of the virus.

Vaccination is typically only implemented when all other disease control measures have failed

Barriers to control

The effective deployment of veterinary medicines to combat avian influenza faces a number of challenges. Foremost among these is the difficulty of producing vaccines that are able to deal effectively with multiple and evolving strains of the virus. Public health systems already have institutionalised mechanisms for tracking virus strains that circulate in the human population and matching vaccines to those strains. However, the same level of coordination between the poultry industry, pharmaceutical companies and veterinarians has not yet been achieved. Variations also exist in the degree to which different countries that produce vaccines adhere to the OIE guidelines describing the development and quality assurance of avian influenza vaccines.

Producing vaccines that can combat multiple antigenic variants of the virus is a major barrier

The OIE also recognises that "the existence of a large number of virus subtypes, together with the known variation of different strains within a subtype, pose problems when selecting strains to produce influenza vaccines." In developing countries, limited financial and scientific resources make it especially difficult to update vaccines as new antigenic variants emerge, while lower profit margins create disincentives for industries to invest in the research and development of context-specific strains. Finally, overly burdensome rules for updated vaccines or the option for multi-strain vaccines in one registration make licensing expensive and lengthy, resulting in serious delays in the development and distribution of much-needed medicines.

Logistical barriers also hinder the use of avian influenza vaccines. In some cases, poultry vaccinations have to be administered bird-by-bird, implying an unsustainable cost, especially for smallholder producers. Another logistical challenge is that current vaccines cannot be effectively administered in poultry until they are fifteen days of age. As a result the re-emergence of the disease is possible through imported poultry that transmit the disease to non-vaccinated poultry, even in countries with strong integrated poultry industries where HPAI viruses have been eliminated.

Bluetongue

BASIC FACTS

Virus type:
Orbivirus, Reovirdae family

Disease type:
Non-zoonotic

Geographic distribution:
Africa, Asia, Australia, Europe, North America

Animals affected:
Domestic and wild ruminants (sheep, cattle, goats, buffalo, etc)

Impact:
Up to 30% mortality in infected sheep

Veterinary medicines available:
Live (modified and attenuated) and inactivated vaccines

Bluetongue is a non-zoonotic, non-contagious vector-borne disease, caused by a virus of the Reoviridae family with 25 known serotypes worldwide. It affects all domestic and wild ruminants, with sheep and cattle experiencing the highest rates of infection. The severity of the disease depends on the strain and morbidity can be very high in susceptible animals. Bluetongue outbreaks also cause direct economic losses through disease and mortality, loss of production, loss of milk yield, and declines in fertility. As bluetongue is not zoonotic, it poses no risks to human health and cannot be contracted or spread through food.

Transmission and spread

Bluetongue is transmitted by biting midges that are infected with the virus after ingesting blood from infected animals. The spread of the disease depends mainly on those ecological and climatic factors that favour biting midge populations; outbreaks are often seasonal, occurring at or shortly after the season of peak midge activity. Although bluetongue emerged in Africa and is endemic in many tropical areas, it has experienced dramatic geographical expansion in recent years, due to environmental factors and the growth of international trade links. A series of bluetongue outbreaks in Europe starting in 1998 illustrate the role played by a warming climate and the increased risks of spreading disease vectors (insects or other living carriers that transmit an infectious agent) through trading routes. As climate change becomes more of a concern in the future, the risks of bluetongue causing an epidemic will continue to increase. According to a leading expert on vector-borne diseases, “through changes to climate, one of the most competent vector species of midge has spread around southern Europe and further north than it had before” while at the same time midge vectors have become “better at being able to transmit the virus.”

Control measures

Vaccination is the most effective practical measure to minimise losses related to bluetongue in endemic regions

Bluetongue control measures include the surveillance of susceptible animals, quarantine, zoning, insect control and vaccination. Since controlling midge populations is not possible -- they are too numerous -- vaccination is the most effective practical measure to minimise losses related to the disease in endemic regions. A voluntary vaccination programme, combined with movement restrictions, successfully led to the control of the bluetongue virus-8 outbreak in the United Kingdom in 2008. Vaccines used against bluetongue are both live attenuated and inactivated. Live attenuated vaccines, until recently the only bluetongue vaccines commercially available, are relatively inexpensive and can provide long-lasting protection. However, they are not always sufficiently weakened and they can actually generate the disease they intend to prevent. Though more expensive, if properly produced and administered, inactivated vaccines can provide reliable and protective immunity from bluetongue. An efficient treatment method for infected animals is still lacking.

Barriers to control

As with the avian influenza viruses, bluetongue's various strains complicate disease control efforts. Each of the 25 different serotypes of bluetongue requires a different vaccine: use of vaccine strains other than the one(s) causing infection affords little or no protection. Over the last 15 years, there have been six different bluetongue serotypes in Europe alone. As a result, development of effective bluetongue vaccines requires publicly funded surveillance systems to identify and make available viruses that are circulating in the animal population so that pharmaceutical companies can develop the appropriate vaccines.

Administering vaccines, even after they are developed and licensed, continues to be logistically challenging because the number of strains present is unpredictable and varies among countries. For example, while only one serotype was detected in the United Kingdom during recent outbreaks, two or three different serotypes were present in parts of France and southern Europe. The presence of multiple serotypes makes it more difficult to know which response to mount in terms of vaccination. Another logistical challenge is that farmers in regions where multiple serotypes have been detected have to vaccinate multiple times if they want to protect against each strain. This is both costly and time-consuming to administer.

The unpredictability and variation of bluetongue strains makes vaccination logistically challenging

West Nile fever

BASIC FACTS

Virus type:
Flavivirus, Flaviviridae family

Disease type:
Zoonotic

Geographic distribution:
Worldwide

Animals affected:
Birds, reptiles, amphibians, mammals

Impact:
30-40% mortality in infected horses; 37,088 human infections, 1,549 fatalities (United States, 1999-2012)

Veterinary medicines available:
Live, inactivated and DNA vaccines available in North America (horses)

West Nile fever is the disease caused by West Nile virus (WNV), a mosquito-borne virus that primarily affects birds but also horses and humans. Originally confined to tropical areas, the disease has recently spread to temperate zones largely as a result of climate-related vector expansion and is now endemic in most regions of the world. Although this is a relatively rare occurrence, the virus can be transmitted to humans and becomes symptomatic in approximately 20% of cases. For 1% of humans symptoms can be severe or even fatal (usually among older or immunocompromised patients). Because of its potential for permanent neurological problems or death in humans, WNV remains a significant public health risk in endemic areas.

Transmission and spread

WNV is transmitted by mosquitoes, while birds are the most commonly infected animal and serve as the primary reservoir host. The disease is maintained between these two agents in endemic regions but it can spread to humans and horses under warm environmental conditions. The vast majority of human cases are caused by mosquito bites, and the virus cannot be transmitted directly from person to person. Recent climate change developments favour the emergence of WNV outbreaks by reducing the time that elapses between the mosquito bite and the transmission time, which is temperature dependent. Moreover, in recent years changes in the virus have resulted in higher mortality rates in birds. Less competent vector species are therefore becoming involved in the transmission process.

Prior to the 1990s, WNV occurred only sporadically and primarily in tropical regions, and was considered a minor risk for humans. However, in the past two decades it has spread globally, with the first case in the Western Hemisphere identified in New York in 1999. WNV is now endemic in Africa, Asia, Australia, the Middle East, Europe and North America. In 2012, the United States experienced an epidemic that resulted in the death of 286 people.

Control measures

Mosquito control remains the primary control measure for the prevention of WNV

Mosquito control and surveillance remain the primary control measures for the prevention of WNV. There are effective, licensed vaccines for use in horses, including inactivated WNV formulations and ‘chimeric’ recombinant vaccines, which express WNV proteins from a different virus backbone. Currently no human vaccines are available, although several vaccine candidates are under development. Though vaccination of horses means that they are protected from the disease, it does not break the transmission cycle as mosquitoes (and vaccinated animals) continue to be infected and capable of spreading the disease.

Barriers to control

Public concerns about GM-based vaccines have slowed the development of vaccines to combat WNV

Although vaccine development against WNV continues to progress, it faces a number of challenges. While modern vaccines have recently been developed to combat further spreading of WNV among horses (primarily in the United States), progress in developing human vaccines has been more limited, due in part to barriers to the acceptance of modern technologies such as genetic modification, which is used to construct recombinant vaccines currently available for horses. Public concerns about GM-based vaccines -- often based on misinformation rather than science -- have led to increasingly stringent safety requirements as well as heightened administrative burdens that have slowed WNV vaccine development. Although several clinical trials for humans are ongoing, including for inactivated, live attenuated, recombinant and DNA vaccines, it will likely take several years before any human vaccine is available. The expense of clinical trials for these vaccines is compounded by the difficulty of establishing their protective efficacy in the field, in view of the annual variation in the geographical location and incidence of WNV.

Another major challenge identified by WNV experts is the nature of the markets that these vaccines face: as outbreaks are unpredictable (with major disease events typically occurring every 4-5 years), the market for these vaccines is unreliable at best. Confronted with such a limited market, pharmaceutical companies do not have sufficient incentives to develop new and innovative medicines.

The impact of WNV has been limited in the horse industry through the effective deployment of vaccines and the linking of vaccination to the detection of the disease through improved surveillance. The recent outbreak in the human population in the United States indicates the need for a vaccine that allows at the very least the possibility of vaccinating people in the high risk categories. This requires a combination of vaccine development, high quality surveillance and improved epidemiology linked to public health systems that can respond proportionately to the threats.

Classical swine fever

BASIC FACTS

Virus type:
Pestivirus, Flaviviridae family

Disease type:
Non-zoonotic

Geographic distribution:
Central and South America, Europe, Asia, Africa

Animals affected:
Domestic pigs and wild boars

Impact:
Variable mortality, up to 100% in susceptible populations; hundreds of billions of dollars in trade losses

Veterinary medicines available:
Live vaccines (including oral vaccines for wild boars)

Classical swine fever (CSF) is a highly contagious disease caused by a species-specific virus that affects swine but is related to viruses affecting cattle and sheep. Highly virulent strains of the virus result in high levels of mortality among infected pigs. While the virus cannot be transmitted to humans and therefore poses no risk for human health, it can pose serious economic threats. In the developed world, the greatest costs result from trade restrictions imposed on both live pigs and pork products once an outbreak is reported. The 2006 outbreak in Germany, for example, led to the imposition of trade restrictions that amounted to a cost of 250-300 million US dollars. In developing countries, the cost is greatest for small farmers who depend on pigs for their income.

Transmission and spread

Transmission of CSF usually takes place through direct contact between infected animals. The virus can also be spread through the transportation of animals in contaminated vehicles and through feed since the virus can survive in pork products for months. The disease occurs in Central and South America, Europe, Asia and Africa, while North America and Australasia are disease-free. Following successful eradication programmes, Canada has been free of CSF since 1963, the United States since 1976 and Australia since 1961. In Europe in particular, CSF can be harboured in the wild boar population and transmission is facilitated by the movements of infected pigs. Notably, the virus can persist in contaminated pig pens for up to two weeks and can remain infective in frozen pig carcases and cured or salted pig products for long periods.

Control measures

In areas where outbreaks have not occurred, control measures include early detection and reporting, movement controls including strict import policies and quarantining of pigs, and effective hygiene measures, including protecting domestic pigs from contact with wild boars. Stamping out remains the main control measure used to prevent the further spread of disease during outbreaks. While effective vaccines are available, vaccination is used only rarely to limit the spread of the disease after an outbreak has already occurred. In countries which are free of disease, or where eradication is in progress, vaccination is normally prohibited. There are no effective treatments for CSF in infected animals.

Barriers to control

In the case of CSF, securing the financing for the research and the development of more effective vaccines is a key challenge. The market for CSF vaccines is considered too small given the cost of investment and the low level of perceived threat that the disease poses. Administering vaccines that are already available on the market can also be problematic. While programmes can now be carried out effectively in developed countries by task forces that vaccinate thousands of pigs in a few days, the problem lies in securing permissions to use the vaccine. In the absence of a reliable DIVA vaccine or diagnostic test, a number of disease-free countries refuse to import pigs or pork products that carry any form of CSF antibodies, even if the antibodies are present in pigs because they have been vaccinated. These countries are worried that pigs that have been infected and subsequently vaccinated can still transmit the virus.

Securing the financing for the research and the development of more effective CSF vaccines is a key challenge

Reluctance to vaccine uptake over the past 20 years has led to stagnation in efforts to develop a better vaccine. According to a leading expert on infectious diseases in pigs, the reluctance of politicians to allow vaccination remains one of the greatest barriers to the effective control of CSF in Europe. Given the expectation that an outbreak will re-occur in the next 3-5 years in continental Europe, resistance to the use of the vaccine among stakeholders remains one of the most important challenges in controlling the disease.

Political reluctance to allow vaccination remains one of the greatest barriers to the control of CSF

Equine influenza

BASIC FACTS

Virus type:
Influenza type A, Orthomyxoviridae family

Disease type:
Non-zoonotic

Geographic distribution:
Most of the world (except for New Zealand, Iceland)

Animals affected:
Horses, equids (donkeys, mules, zebras)

Impact:
Up to 10% mortality in infected horses; total cost of the 2007 Australian outbreak estimated at 1 billion Australian dollars

Veterinary medicines available:
Inactivated, live attenuated and recombinant vaccines

Equine influenza is a highly contagious respiratory disease of horses (and other members of the equidae family including donkeys and zebras) caused by two main subtypes of influenza type A viruses (H7N7 and H3N8). Equine influenza outbreaks are typically characterised by a rapid spread of the virus and very high infection rates in unvaccinated horses. However, clinical signs of illness usually resolve within a few days without complications and fatalities are rare. The virus does not cause disease in humans, and its economic impact is primarily due to the highly contagious nature of the virus and the disruption of equestrian activities. Nevertheless, the disease continues to pose a significant threat to the horse industry with large scale outbreaks, such as those in South Africa in 2003 and Australia in 2007, costing hundreds of millions of dollars.

Transmission and spread

The transmission of the disease occurs through direct contact with infected animals or through the transmission of the virus on clothing or equipment carried by humans that work with horses. Equine influenza can spread quickly in susceptible populations and cause outbreaks where conditions are most favourable, for example when horses are kept in close quarters, during transportation, and where mixing of horses from different locations occurs. The virus is often spread across borders by the movement of infected horses. With the exception of a small number of geographically isolated countries including New Zealand and Iceland, the disease has been found in all countries with significant equine industries and regular outbreaks are reported in European countries and the United States.

Control measures

Rapid diagnosis, movement restrictions and vaccination are the key control measures. Vaccines are widely available and routinely used for competition horses in Europe, the Americas, and Asia. In some countries vaccination is mandatory for horses that are competing in equestrian events and the International Federation for Equestrian Sports requires vaccination of horses every six months. Vaccines have been useful in limiting virus replication, reducing or eliminating clinical disease and reducing the risks of transmission. However, given strain variation, vaccines are not always successful in preventing infection. Moreover, vaccines are not always easy to obtain in developing countries. In tandem with vaccination, quarantine and the isolation of infected animals are also commonly undertaken during outbreaks.

During the 2007 Australian outbreak, vaccines were imported to slow the rate of transmission

The 2007 Australian outbreak provides a useful example of a successful disease control campaign. Although the outbreak was very costly -- with the total cost to industry an estimated 1 billion Australian dollars and government expenditures for quarantine measures and financial support totalling over 300 million dollars -- effective responses ensured that the disease was quickly controlled. During that incident, the imposition of extensive movement controls of all horses, a zoning system and vaccination of horses in buffer zones resulted in the eradication of the disease within four months of its detection. The collaboration between the equine industry, the veterinary authorities and registration authorities allowed the introduction and use of the vaccine and the eradication of the disease.

Barriers to control

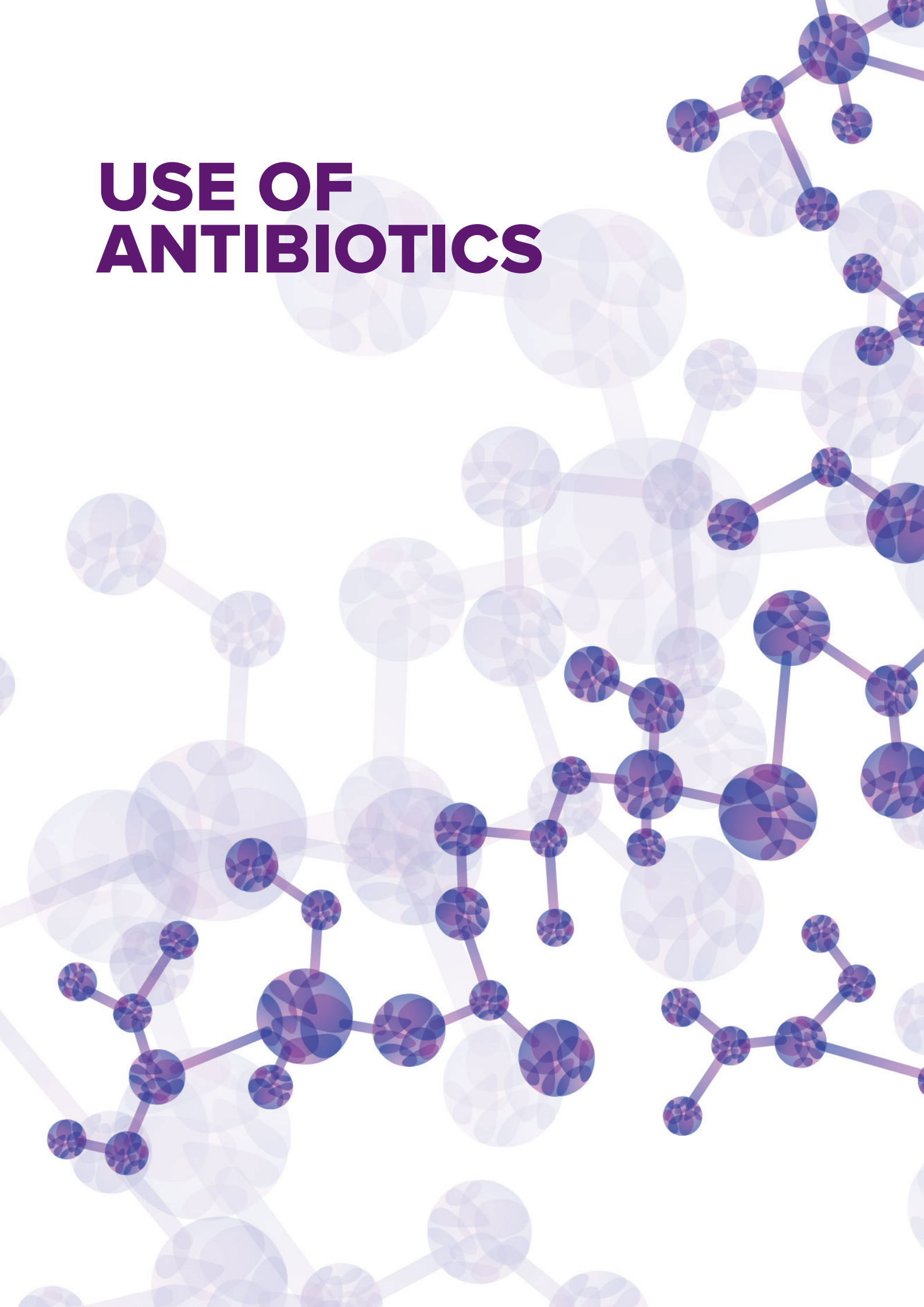
Important barriers exist to the development and use of equine influenza vaccines. Similarly to the avian influenza viruses, antigenic drift is an important issue and pharmaceutical companies often cannot update vaccines with the frequency that is recommended due to lengthy regulatory approval processes. Although the OIE Equine Influenza Surveillance Panel monitors the antigenic drift of equine influenza viruses and produces recommendations on appropriate antigens for vaccines, regulatory burdens often prevent manufacturers from updating the antigens with the frequency that experts recommend.

Regulatory burdens often prevent manufacturers from updating vaccines with the frequency that is recommended

Efforts also need to be made to harmonise regulations related to vaccination against equine influenza, particularly in competition horses. Though passport systems documenting an individual animal's medical and vaccination history are already a requirement for horses competing in some events (such as those organised by the International Federation for Equestrian Sports), they are not universally recognised. Improving passport systems and making them an international standard for all competition horses would help to prevent future outbreaks of equine influenza. In addition, greater use of DIVA vaccines that allow diagnostic tests to delineate between vaccinated animals and those naturally exposed to the disease would greatly improve control efforts.

Political opposition to vaccination against equine influenza has also impacted efforts to control the disease. Some governments have opposed the preventative use of equine influenza vaccines because of a perceived risk of creating a partially immune horse population, which would show no clinical signs of infection but would still have the capacity to infect other horses, complicating the ability to detect the presence of a new influenza outbreak. While the practice of preventative vaccination against equine influenza remains controversial, a large number of horse owners, industry stakeholders and veterinarians continue to support vaccination as the best means of protecting horses against future outbreaks of the virus.

USE OF ANTIBIOTICS



Alongside vaccines, antibiotics play a crucial role in ensuring control of emerging and re-emerging animal diseases. Like vaccines, antibiotics can be used both prophylactically to prevent infections developing in food animals and therapeutically in order to treat sick animals. In most cases, antibiotics are used for treatment after a disease outbreak has occurred. While antibiotics are sometimes used preventatively -- in intensively managed food-producing animals -- this practice remains controversial due to the potential development of resistance. Despite their clear benefits for animal and human health when used appropriately, antibiotics face multiple barriers in their development and use.

Regulatory barriers

The main barriers that exist with regard to the effective use of antibiotics are related to burdensome regulations and irresponsible implementation. Developed countries typically have slow and laborious processes of market authorisation for antibiotics. Extensive registration requirements, post-licensing surveillance requirements, legislated restrictions on use and bans on certain products can sometimes have a negative overall impact. While steps need to be taken to ensure that antibiotics are used responsibly, overly stringent legislation governing their development and use will inevitably have negative consequences on the development of new microorganisms, and in turn on animal welfare, disease management and food production.

Burdensome regulations and irresponsible implementation are two important challenges to the effective use of antibiotics

Developing new antibiotics

The time and cost involved in market authorisation has worked to deter many manufacturers from developing new antibiotics. New antibiotics are sorely needed as existing ones have diminished in effectiveness (in both human and veterinary fields) in recent decades, due mostly to the rise of resistant microbes. The relatively small size of the animal health market compared to the human medicine market also acts as a deterrent. According to an expert on animal medicines from the Royal Veterinary College, “industry is not particularly motivated to develop new substances because the market for new antibiotics, particularly on the animal health side, is limited. So the cost-benefit is questionable.” As a result of this, the European Commission (EC) and other governmental bodies have taken steps to fund the development of new antibiotics. In early 2013, the Innovative Medicines Initiative (IMI), the world’s largest public-private partnership in healthcare, launched a new programme to revitalise the development of novel antibiotics with significant funding from the EC. The new initiative is part of the EC’s Action Plan Against the Rising Threats from Antimicrobial Resistance, introduced in November 2011.

Distribution and end use

Ensuring correct use is perhaps even more challenging, especially in developing countries. Veterinarians are still required in the last stage of introduction to the market to make sure the medicine is used correctly and for the purposes for which it has been licensed. The inconsistency of regulatory frameworks among different countries adds to delays in the distribution of antibiotics. In many jurisdictions, unrestricted usage (without proper prescription), under-dosing and overdosing, sub-standard substances, use past the usage date, and lack of adequate diagnostic tools render control over use ineffective. The lack of scientific information on the appropriate levels of antibiotic for each species and their incorrect use at the farm level remain important challenges. Group treatment -- the treatment of an entire animal population rather than the targeting only of sick individuals -- is another common practice that is often necessary if the individual administering of antibiotics is impractical.

Competition with human medicine

Animal antibiotics face competition with human medicine

In addition, animal antibiotics also face competition with human medicine. Antibiotic use in food animal production can contribute to the emergence of antibiotic resistance (see below) in zoonotic pathogens, such as Salmonella. As a result, many international organisations have identified monitoring of antibiotic usage in animals as a key prerequisite for ensuring sound public health. In particular, the WHO has produced a list of Critically Important Antibiotics that it recommends should not be used in animals in order to preserve the benefits of antibiotics for human populations. The prioritisation of public health efforts makes the use of antibiotics to counter emerging and re-emerging diseases in animals more difficult. According to a 2011 report by the EC, the development of antibiotics for use in animals has been hampered by the uncertainty and difficulty of obtaining market authorisation for the veterinary sector.

Antibiotic resistance

Opposition to the use of antibiotics in livestock and other animal populations is often tied to the issue of antibiotic resistance (ABR). ABR is a form of resistance whereby some or all targeted bacteria are able to survive exposure to antibiotics. This resistance is a natural biological phenomenon but is amplified by the inappropriate use of antibiotics in both human and veterinary medicine. While ABR is a serious and growing problem in contemporary medicine, the risks of ABR are often misunderstood and sometimes used as a rationale for the introduction of unnecessarily strict legislation on the use of antibiotics in animals. Correct and responsible use of antibiotics considerably reduces the likelihood of ABR developing and can be vital in combating emerging diseases.

RECOMMENDATIONS FOR GOVERNMENTS, REGULATORS, INDUSTRY

There are many steps that governments, regulators and industry representatives can take to reduce obstacles to the control of disease, ensure the development and availability of veterinary medicines, and mitigate the risks of emerging and re-emerging animal diseases. Empowering veterinary services, strengthening governance, and improving local knowledge and infrastructure, particularly in developing countries, is a vital first step to ensuring that countries have the capacity to deal with disease events when they occur and the ability to introduce adequate safeguards against future outbreaks. Harmonising regulations and streamlining market authorisation processes is also crucial if medicines are to be made available in a timely and effective manner. Closer cooperation between governments, regulators and industry is needed in order to ensure the development and availability of new and innovative veterinary medicines. Finally, there is a need for increased integration and communication between animal and human health sectors to strengthen surveillance schemes and best utilise resources.

Empowering veterinary services and proactive risk management

Veterinary services should develop more epidemiological expertise at the local level in order to be better prepared to deal with endemic disease strains

Empowering veterinary services is one of the first steps that governments should take to improve the current situation. Veterinary services should develop more epidemiological expertise at the local level in order to be better prepared to deal with endemic disease strains. Understanding the local context of disease emergence and re-emergence will help explain their occurrence, give indications of their importance and lead to a proportionate response. Veterinary services should also develop better mechanisms for time-sensitive, risk-based surveillance and early detection. This will provide public health agencies with enough information to detect the emergence of these diseases and trigger early responses when necessary, rather than merely reacting to outbreaks.

More capable veterinary services at the national level will also support the development of locally applicable vaccines that will be more effective in each regional context. At present, multinational companies are the largest players in the development of strain-specific medicines and they have the best quality control measures in place. In the future, stronger national veterinary services will enable national companies to boost their own mechanisms for ensuring the delivery of safe and effective veterinary medicines.

Establishing proactive controls against outbreaks should be an important priority for national governments

Establishing proactive controls against the outbreak of emerging diseases, even though they might be difficult to predict and non-recurring, should also be an important priority for national governments. The outbreak of WNV in the United States in 2012, for example, could have been addressed faster had surveillance been more efficient and had the administrative authorities been prepared to coordinate their response. The relative lack of information and awareness on the impact of animal diseases – especially when compared to human diseases – illustrates the low priority assigned to these problems by many national governments.

Improved veterinary authorities with active surveillance mechanisms at their disposal allowing for early detection will reduce the lags currently seen in response to control programmes. A number of developing countries are already moving in this direction. In Thailand, for example, the public veterinary sector is growing rapidly and is projected to substantially increase the employment of vets over the next 10 years. The next step for national veterinary services in Thailand and other countries at a similar level of development will be to encourage greater public-private cooperation and build international networks, further improving their capacity for proactive risk management.

Enhancing national laboratory capabilities

National laboratories should be supported in order to facilitate the development of locally required vaccines and reduce foreign exchange transactions for the importation of veterinary medicines. In diseases caused by various strains of the same virus, scientific efforts should focus on developing multi-strain vaccines, in order to secure bigger potential markets and better incentives for pharmaceutical companies. In addition, efforts should be made to develop vaccines that can be more easily administered in order to improve the scope and efficiency of vaccination. For example, in preventing HPAI, improved vaccines can be developed that do not require injections of individual birds. Another important focus is vaccines that allow differentiation between infected and vaccinated animals (DIVA), which are available for some but not all pathogens.

The development of vaccines that can be more easily administered will improve the scope and efficiency of vaccination

These same laboratories need to be able to support surveillance by identification of pathogens and where appropriate isolation of the pathogen to support the development of diagnostics and therapeutics. After the initial R&D, it is also important to set minimum standards of quality at the national level in line with international standards in order to ensure efficiency. Increasingly, funding initiatives are supporting research partnerships between academics in developed and developing countries, such as the African Institutions Initiative of the Wellcome Trust. These collaborations aim to improve institutional capacity and empower researchers from developing countries.

Closer cooperation between animal and human health sectors

Considerable health and financial benefits can be reaped from enhanced understanding, communication and collaboration between the veterinary and human health sectors. Historically, these have operated in isolation, and although a ‘One Health’ agenda that seeks to improve collaboration, coordination and cooperation between the two sectors has been widely promoted, it has been less widely practised. Zoonotic diseases, having both animal and human hosts, clearly require integrated collation of surveillance data and communication between professionals in the medical, veterinary and wildlife health fields if disease trends are to be noted and acted upon appropriately. Other measures such as sharing of laboratory diagnostic facilities between the sectors or combined vaccination delivery programmes for livestock and humans would have cost-benefit advantages in resource-poor settings. Non-zoonotic animal diseases also profoundly influence

Considerable benefits can be reaped from enhanced understanding, communication and collaboration between animal and human health sectors

people's health via impacts on food safety, food security, nutrition, wealth and livelihoods. This interconnectivity should serve to underline the importance of combating animal diseases for both people and animals, and incentivise governments and industry to support R&D and infrastructure that deliver advances in animal health.

Closer cooperation with industry

Increased cooperation between industry, regulators and government is needed

Given the sizeable investment risks that producers of veterinary medicines face, governments and regulators should take greater steps to work alongside industry players. VICH is already a step in this direction since it brings industry and regulators -- two groups that have often viewed each other as mutual obstacles -- into close cooperation. As an OIE expert on the veterinary medicines industry argued, "the dialogue between industry and regulators is the only way forward -- those two groups must speak more with each other and collaborate on important issues".

Increased incentives are needed to encourage multinationals to invest in vaccine development

To increase the incentives for multinationals to invest in vaccine development, efforts such as the GALVmed programme should be promoted. GALVmed is a not-for-profit public-private partnership that seeks to make available and facilitate adoption of livestock health products by poor livestock keepers. GALVmed provides support in all stages of the development of livestock health products from product development and registration to distribution and the creation of value chains. Initiatives such as these ensure that industry is closely involved in efforts to develop new and innovative medicines in areas economically not viable for industry alone. Such examples need to be bolstered and replicated in more instances.

Public-private partnerships can serve as an important means of enhancing cooperation in the fight against disease

Government cooperation with industry can be institutionalised through the establishment of public-private partnerships. A notable example of such partnerships is the joint effort of FAO and IFAH to control African Trypanosomosis (sleeping sickness) following their signing of a Memorandum of Understanding to cooperate on the establishment of standards and protocols for quality control of trypanocidal drugs in 2008. In 2012, the two joined forces to submit to the OIE a set of pharmaceutical monographs to be published for the development and proper use of two medicines that can help control the disease. Once better surveillance mechanisms are in place and improved veterinary services and biosecurity are achieved, public-private partnerships can bring livestock owners and managers, veterinarians, officials and industry decision-makers together. These endeavours will encourage industry actors to be more closely involved in the overall effort to control emerging diseases and ensure that veterinary medicines are more effective and accessible.

Harmonising and streamlining regulation

One of the main themes to emerge from this report is the need for regulation to be simplified and streamlined so that medicines can be easily introduced across different markets. To ensure quality, international standards should be set transparently and complemented by national or regional legislation to enable an environment of good implementation and facilitate the availability and delivery of effective animal medicines.

Furthermore, the harmonisation of national regulatory frameworks should continue to be promoted in order to make the production of veterinary medicines more commercially viable. Significant efforts have already been made within the EU to harmonise the national regulations of member states. A further step in this direction is the work of the VICH, which brings together regulatory authorities from the EU, Japan, the United States, Canada, Australia, New Zealand and South Africa. However, greater efforts are needed elsewhere, particularly in the developing world where fragmented and disparate regulatory systems often stifle access to essential veterinary medicines.

Harmonisation of national regulatory frameworks should be promoted to make veterinary medicines more commercially viable

A second important area of focus should be streamlining the current regulatory processes so that updating a vaccine for new disease strains is possible without having to submit a full dossier of testing to secure approval. Such a change will significantly reduce delays in the introduction of veterinary medicines to the market. Removing the existing barriers during this stage in the life of animal medicines requires therefore the creation of global coordinated frameworks that will underpin streamlined, national and regional plans.

For developing countries, this underlines the importance of working towards a science-based licensing system that is based on internationally accepted guidelines but avoids aspects of the US or EU systems that can prove overly burdensome. At the same time, Mutual Recognition Agreements or similar free trade agreements and mechanisms could be a route to facilitate trade in high quality veterinary medicines and vaccines produced by large multinational pharmaceutical companies.

Improving application and post-vaccination measures

The effort to improve veterinary services should also target the better application of veterinary medicines in the field. This will need to entail an increased emphasis on the local understanding and application of medicines and it should be part of a comprehensive control programme. In this way, it will improve the understanding

Additional efforts are needed to ensure that medicines are understood and properly administered

of how the medicines work and of how to apply them, an area that some experts identified as the biggest deficiency of the current control programmes. It is particularly important to avoid blanket, universal vaccination practices in instances of limited outbreaks. An increased focus on biosecurity and broader responsible management of animal populations are also crucial at the local level.

Better management of antibiotic usage

Better management of antibiotic usage is needed for the control of emerging and re-emerging diseases

A number of steps can be taken to improve the benefits of antibiotics for the control of emerging and re-emerging diseases. The first obvious measure would be to better monitor their use, particularly targeting the big users in the farming industry in order to avoid the misuse problems frequently reported. Better management of antibiotic use through the implementation of international standards and an improved understanding of active dose rates will also limit wastage and contamination of the environment. Identifying the causative bacteria and its antibiotic sensitivity prior to treatment, completing the antibiotic course and considering administering supplementary preparations containing live bacteria and intended to restore beneficial bacteria, are all practices which should be used to reduce the likelihood of ABR development. In addition, there is scope for the industry to play an important role in this effort to improve the correct introduction of antibiotics by providing clear guidelines on their use. Finally, “good farming” and biosecurity practices can be further promoted to facilitate the safe and effective use of antibiotics.

Regional vaccine banks

Regional vaccine banks should be promoted in order to facilitate the use of vaccines in developing countries

Some of the barriers that hinder the delivery of animal medicines to developing countries can be overcome through regional vaccine banks. Vaccine banks can range from a virtual bank where there is a contract with a supplier, to physical storage centres for antigens or vaccines. Vaccine banks not only create incentives for national veterinary services to work together and harmonise their control measures, but they also provide a cost-effective way to distribute vaccines where there are outbreaks. In addition to enabling access to readily available vaccines, they also facilitate the production of new vaccines when they are required. The OIE has already established a number of vaccine banks, notably in Africa and Asia for avian influenza, foot-and-mouth disease and rabies.

ABBREVIATIONS AND DEFINITIONS

Abbreviations

ABR	Antibiotic resistance
CSF	Classical swine fever
DALY	Disability-Adjusted Life Years
DEFRA	Department for Environment, Food and Rural Affairs (United Kingdom)
DIVA	Differentiation of infected from vaccinated animals
EC	European Commission
FAO	UN Food and Agriculture Organization
GLEWS	Global Early Warning System for Major Animal Diseases
GMO	Genetically-modified organism
HPAI	Highly Pathogenic Avian Influenza
IMI	Innovative Medicines Initiative
LPAI	Low Pathogenic Avian Influenza
OIE	World Organisation for Animal Health
PVS	Performance of Veterinary Services
TRIPS	Trade Related Aspects of Intellectual Property Rights
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
WHO	World Health Organization
WTO	World Trade Organization
WNV	West Nile Virus

Definitions

Antigen	Any foreign, potentially harmful substance that causes the immune system to produce antibodies against it.
Antigenic drift	Variation of viruses through the mutation over time, resulting in a new strain of virus which cannot be inhibited as effectively by the antibodies that were originally targeted against it.
Antigenic shift	Process whereby two or more different strains of a virus (or different viruses), especially influenza, combine to form a new subtype having a mixture of the surface antigens of the original strains.
Antibiotics	Agents that inhibit bacterial growth. Unlike vaccines, they are most commonly used for the therapeutic treatment of clinically sick animals, not for disease prevention.
Antibiotic resistance	Form of medicine resistance whereby some or all targeted bacteria are able to survive exposure to antibiotics. This resistance is a natural biological phenomenon but is amplified by the inappropriate use of therapeutic antibiotics in both human and veterinary medicine, as well as the use of antibiotics for non-therapeutic purposes such as growth promotion.
Biological	A medicine, such as a vaccine, whose composition depends on proteins derived from living cells.
Biosecurity	A comprehensive set of measures intended to prevent and contain animal diseases in order to protect animal and human health from biological hazards.
Compartment	An animal subpopulation contained in one or more establishments under a common biosecurity management system with a distinct health status with respect to a specific disease or specific diseases.
Diagnostics	Practice of researching and identifying a possible disease and determining occurrence in animal populations.
Endemic	A term used to describe a disease that is constantly present in a particular population or geographical location.
Growth promotion	Controversial use of antibiotics to increase the rate of weight gain or efficiency of feed utilisation in animals.
Microbe	A microorganism, especially a bacterium causing disease or fermentation.
Market authorisation	Process of reviewing and assessing the dossier of a medicine before it is approved for use in a market.
Monitoring	The intermittent performance and analysis of routine measurements and observations, aimed at detecting changes in the environment or health status of a population.
Movement controls	Common animal disease control measure. Helps contain disease by limiting the movement of animals from infected area.

Pathogen	A bacterium, virus, or other microorganism that can cause disease.
Pharmaceutical	A medicine that typically consists of non-living chemical compounds.
Prophylaxis	Measure taken to maintain health and prevent the spread of disease.
Serotype	Distinct variation (or strain) within a specific virus or bacteria.
Surveillance	The systematic ongoing collection, collation, and analysis of information related to animal health, and the timely dissemination of information so that action can be taken.
Stamping out	The method of culling and destroying infected and suspect animals in and around a confirmed outbreak.
Vaccine	Biological preparations that are designed to produce immunity to a disease by stimulating the production of antibodies.
Vector	An insect of any living carrier that transmits an infectious agent.
Veterinary medicines	Medicines that deal with the diagnosis and treatment of diseases and injuries of animals, including vaccines and antiobiotics.
Viral shedding	The expelling of virus particles from an infected human or animal.
Zone/region	A clearly defined part of a territory containing an animal subpopulation with a distinct health status with respect to a specific disease for which required surveillance, control and biosecurity measures have been applied for the purpose of international trade.
Zoonoses	Diseases that can pass between animals and people and vice-versa.

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