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Rinderpest and peste des petits ruminants: state of play in disease eradication efforts

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Summary

Rinderpest virus and peste des petits ruminants (PPR) virus are highly pathogenic viruses causing disease primarily in cattle and small ruminants, respectively. Although the post-eradication process for rinderpest has been largely successful, gaps in preparedness for a future rinderpest reappearance remain, and the virus is still held in some facilities that have not been registered or inspected, posing a threat to the global community. The PPR Global Eradication Programme will need to overcome significant hurdles to reach a world free of the disease by 2030. Achieving this goal will be easier if plans are based on the best research and tools available, with proper involvement of communities. Focusing research and development efforts on the important remaining gaps should increase the efficiency of control and surveillance strategies, provided research outputs are effectively transferred to decision-makers. Researchers, stakeholders and implementing bodies should build on the experience of rinderpest to prepare for a post-PPR world. The animal health community should also be vigilant regarding other viruses, including those yet unknown, that could emerge as the niches of the rinderpest and PPR viruses become vacant.

Keywords

Cattle – Control – Eradication – *Morbillivirus* – Peste des petits ruminants – Rinderpest – Small ruminant – Surveillance – Transboundary disease.

Introduction

Rinderpest and peste des petits ruminants (PPR) are highly pathogenic infectious diseases primarily affecting cattle and small ruminants (sheep and goats), respectively. Both diseases are caused by viruses of the genus *Morbillivirus*. Although recent and multiple changes in the taxonomy of this genus have caused confusion in the animal health community, including the World Organisation for Animal Health (WOAH) [1], the names of the two viruses remain rinderpest virus (RPV) and peste des petits ruminants virus (PPRV) [2]. WOAH and the Food and Agriculture Organization of the United Nations (FAO) officially declared the eradication of rinderpest in 2011. This article reviews the ongoing efforts to avoid its reappearance. PPR, meanwhile, was identified as the target of a new global eradication campaign in 2015 [3], prompted by its similarities with rinderpest [4]. However, the two viruses are different in several ways, with many gaps in the understanding of PPRV molecular biology and epidemiology, and of the socio-economic context of PPR transmission and control. The PPR Global Research and Expertise Network was formed under the direction of WOAH and FAO to coordinate efforts in filling these gaps [5]. This article also reviews the recent progress in different fields of research and highlights important questions that must still be addressed to support the goal of global PPR eradication by 2030.

Rinderpest

Safety and preparedness

As the first, and thus far only, livestock disease ever globally eradicated, rinderpest has been a proving ground for how to manage the post-eradication world – not only how to minimise the risk of the virus reappearing in livestock, but also how to manage the response to a possible future reappearance. WOAH and FAO established the joint

Rinderpest Secretariat and the Rinderpest Joint Advisory Committee to coordinate the post-eradication strategy. The most important risk minimisation has been the effort to identify all countries still holding live RPV and persuade them to either destroy their stocks or register the holding laboratory with WOAH/FAO as a designated Rinderpest Holding Facility (RHF), with an alternative of transferring their RPV-containing material to an RHF in another country for safe storage. The current state of these efforts has been recently reviewed in detail [6]. Great progress was made in the early stages: a total of 44 laboratories in 35 countries in 2011 have since been reduced to 14 laboratories in 12 countries at the time of writing. However, at least seven WOAH Members continue to hold RPV-containing material in facilities that have not been registered or inspected, posing a threat to the global community [7].

Preparations for a possible reappearance of rinderpest were significantly aided by the publication of the joint WOAH/FAO Global Rinderpest Action Plan (GRAP) in 2018 [8]. However, the GRAP highlighted three important gaps between the situation at the time and full preparedness. These gaps arose from the decision to include established RPV vaccine strains in the definition of materials that are strictly controlled post-eradication. Firstly, this means that there has been no production of the most widely used 'Plowright' vaccine for more than 20 years, and the existing stocks are limited in quantity and out of date. To bridge this gap, new stocks will be made in 2024, notably for the African Union vaccine reserve at the African Union Pan African Veterinary Vaccine Centre (AU-PANVAC), using the WOAH/FAO-approved vaccine seed prepared and characterised at the RHF of the French Agricultural Research Centre for International Development, also known as CIRAD. In addition, there is a plan to increase stocks of the LA-AKO rinderpest vaccine developed in Japan [9], as this country has a national legal requirement to keep emergency stocks of vaccine, providing an additional resource in the event of a reappearance.

Secondly, the prohibition on keeping even vaccine strains means that national diagnostic laboratories had no suitable positive control to validate diagnostic tests for RPV (primarily reverse transcriptase polymerase chain reaction [RT-PCR]), removing the possibility of conducting their own tests on the occasional suspect cases, and thereby reducing the probability of rapid detection of a real case of rinderpest. A positive assay control, based on a modified RNA phage similar to that published for PPRV assays [10], has been developed but is not generally available.

The third gap was the requirement for any country that suffered a reappearance of rinderpest to conduct serosurveillance after eliminating the disease. However, the antibody enzyme-linked immunosorbent assay (ELISA) that was used during the eradication campaign, and that is known not to cross-react with anti-PPRV antibodies [11], was dependent on antigen produced by growing the RPV vaccine in cell culture. A project will begin in 2024 to develop an alternative antigen that does not require infectious virus but that can be recognised by the same highly specific monoclonal antibody. This will make the ELISA available should there ever be a reappearance of rinderpest.

Remaining research areas

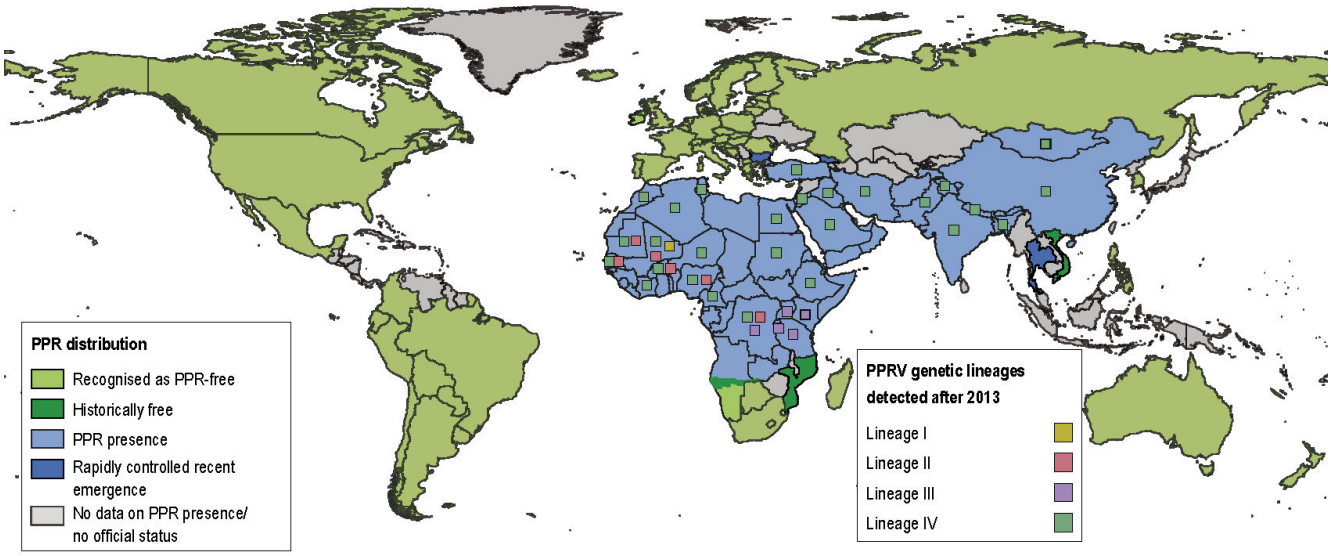
Since the formal announcement of rinderpest eradication, any activity involving RPV-containing materials has been strictly controlled, and there have been few such activities permitted. RHFs have been encouraged to sequence the genomes of their remaining stocks and then destroy the live RPV, a process that has been completed by one RHF so far, providing some interesting insights into RPV history and evolution [12]. It is hoped that other RHFs will also soon complete this process, simultaneously reducing the risk of the virus escaping from a laboratory and improving knowledge of the virus's evolution. The example provided by the sequencing of a measles virus from 1912 [13] has shown that important insights into the origins of viral diseases can be obtained from sequence data of historic isolates. The more that is known of the evolution and spread of measles virus, RPV and PPRV, the greater the capacity to judge the risks of new morbilliviruses emerging that can fill the niches left by the eradication of rinderpest and, soon, PPR.

Peste des petits ruminants

Distribution and host range

Since its launch, the PPR Global Eradication Programme has had a substantial effect on the control of the disease, with 68 of 78 countries having developed a PPR national strategic plan [14], and a reduction in outbreak reports between 2015 and 2019 [15]. Some countries that never reported PPR have successfully applied for official freedom recognition. Despite these encouraging results, the geographic distribution of the disease has not been effectively reduced, with none of the countries affected by PPR having been able to free themselves of the disease (Fig. 1). The recent outbreaks of PPR in countries that had not previously reported the disease, e.g. Georgia [16], Mongolia [17], Bulgaria [18], Burundi [19], Thailand [20] and Rwanda [21], illustrate the extent of the problem and the constant vigilance required to avoid further PPR spread, notably through commercial animal trade. In some cases of emergence in new areas, the disease was rapidly contained (e.g. Georgia, Bulgaria, Thailand); however, PPR has become more established in other areas, notably in Mongolia [22] and China (see Fig. 1).

The outbreak in Mongolia was particularly notable due to its unprecedented impact on wildlife, with mass mortality reported in Mongolian saiga-antelope and deaths in several other wildlife species [23]. Previous reports had already



PPR: peste des petits ruminants

PPRV: peste des petits ruminants virus

Figure 1

Global distribution of peste des petits ruminants

Countries are coloured in blue if PPR has been officially reported at least once within their borders. Information on presence of different PPRV genetic lineages within a country is provided only for data collected after 2013 (i.e. less than ten years before this publication). World administrative boundaries used in the map are based on shapefile data accessible at: https://public.opendatasoft.com (accessed in July 2023). This representation does not imply expression of any opinion on the part of the authors concerning the legal status of any country, territory, city or area, or concerning the delimitation of frontiers and boundaries.

Note: this figure was produced based on data available in January 2024

highlighted that many wild artiodactyls, camels and suids are susceptible to PPR infection [24-26], but this was the first report of heavy mortality in such species in the field, along with a realisation of the potential impact of PPR on biodiversity. It prompted the proposal of guidelines for the control of PPR in wildlife populations [27]. However, the full range of species susceptible to PPR is not yet defined and probably depends on many factors, including the health status of the animals, environmental factors and the virulence of the PPRV strains (e.g. Eloiflin *et al.* [28]). In-depth studies of host immune responses to PPRV may help in identifying which species and breeds are most impacted by the disease, as well as which play a role in its transmission (e.g. Eloiflin *et al.* [29], Baron *et al.* [30]). Good field data will also be required to characterise PPRV circulation in complex environments such as at the wildlife–livestock interface [31]. Careful risk assessments are needed to prioritise resources for PPR research and control to avoid the most devastating effects on both livestock and endangered wildlife populations [24].

Epidemiology of the disease

Important progress in understanding the epidemiology of PPR has been made in recent years through a wide range of approaches. Field data is key for designing vaccination strategies and evaluating their efficacy [32]. In addition, carefully planned field studies remain of primary importance to characterise the distribution and prevalence of the virus in host populations. However, diagnostic tools need to be further developed and validated to study the role of wildlife in PPRV transmission [33,34]. Although the survival of PPRV in the environment is being explored [35,36], little is known about its stability in different media such as fomites, water, bedding and carcasses under different environmental conditions, thus restricting the accuracy of transmission models.

Affordable sequencing technologies have increased the capacity to study PPRV molecular epidemiology. The distribution of the four PPRV genetic lineages is now better understood, although there is still a lack of recent genetic data from many countries affected by PPR (see Fig. 1 for a review of data from the last ten years). Importantly, lineage IV has been spreading in West Africa (reviewed in Dundon *et al.* [37]; Fig. 1), where it appears to be supplanting other West African lineages. This suggests an increased capacity for replication and/or transmission that should be investigated as a priority to evaluate the impact of these changes on control and surveillance strategies. Full genome sequencing can provide important information on the origin of outbreaks and PPRV evolution, including, notably, possible adaptations to nonstandard hosts (e.g. Benfield *et al.* [38]). However, PPRV sequencing efforts and bioinformatic

analyses must follow strict quality control guidelines to be useful [39].

The importance of animal movement – notably from trade and pastoralism – in PPRV circulation is well documented, including evidence from sequencing data (e.g. Spiegel and Havas [40], Bataille *et al.* [41]). Field studies aiming at characterising livestock mobility can provide valuable information for disease surveillance and control [42,43]. In general, better identification of risk factors for PPRV transmission has improved the power of risk analyses to predict PPR occurrence (e.g. Ruget *et al.* [44]). Participatory epidemiology methods are increasingly used to collect information directly from communities and other field actors on disease occurrence, host populations and other key factors in PPR transmission (e.g. Lysholm *et al.* [45]). Integration of communities' knowledge of the disease can improve understanding of patterns of virus circulation and help identify possible transmission hotspots [46].

Developments in diagnostic and control tools

Many pathogens can cause symptoms in small ruminants similar to PPR, and laboratory tests are critical to discriminate these. All the basic diagnostic tools and vaccines are already in place for global PPR eradication (reviewed in Kinimi *et al.* [47]). Well-characterised ELISA kits to detect anti-PPRV antibodies are available [48,49] and the ability of these assays to deal with sera from wildlife and other nonstandard hosts is currently being characterised [34]. A number of novel assays for PPRV-specific antibodies have been developed (e.g. Berguido *et al.* [50], Logan *et al.* [51]), but none so far that match ELISA for simplicity and capability of high throughput. The original gel-based RT-PCR assays for PPRV are being replaced with the more sensitive real-time PCR assays (RT-qPCR), of which a number have been published and are in use in different laboratories. Ring trials have shown that some RT-qPCR assays are less sensitive than others, highlighting the need to follow recommendations from the WOAH Reference Laboratory Network for PPR on best practice [52,53].

Several laboratories have developed assays based on loop-mediated isothermal amplification (LAMP) technology, which is faster and cheaper than gel-based RT-PCR [54] and may have advantages over RT-qPCR for laboratories with low throughput requirements. An interesting feature of LAMP assays is that they can be carried out without prior purification of RNA [55]. They may therefore be carried out in the field using a suitable heating block run from a vehicle battery. Lateral flow tests with sensitivity similar to antigen ELISA assays are available [56,57] for rapid confirmation of outbreaks in the field (e.g. Jones *et al.* [58]). However, field testing is unlikely to be used in normal practice, since few affected countries have the funds to equip and incentivise their field veterinarians to carry out specific assays. Moreover, most countries rely on clinical observations for immediate diagnosis, with occasional transfer of samples to a testing laboratory for confirmation.

Extensive experience over more than 20 years has shown that the live attenuated PPRV vaccine based on PPRV/Nigeria/'75/1 [59,60] is safe and effective. This vaccine has been used in most affected countries, with the major exception being India, which has developed its own vaccines (reviewed in Saravanan *et al.* [61]). It has been shown that the most widely used Indian vaccine strain (based on PPRV/Sungri/96) and the Nigeria/'75 vaccine are equally effective against all genetic lineages of PPRV [62]. However, the concern remains that some countries are still using poorly characterised and validated vaccines (e.g. Kwiatek *et al.* [63]).

One of the few practical issues with the PPRV vaccines has been their general thermolability even when lyophilised, requiring a cold chain for delivery to the field. This problem has received significant attention in the last five to ten years, bringing together scientists and vaccine manufacturers to improve methods of preparation of the vaccine, with significant progress [64,65]. In addition, new stabilised liquid formulations of the vaccine are appearing [66] and may provide another way of simplifying delivery of vaccines to the point of use. AU-PANVAC has set up quality control for thermostable PPR vaccine preparations, and it is expected that this will improve the quality of these vaccines and their availability to those countries that need them.

With these vaccines, it is not possible to serologically distinguish vaccinated from infected-recovered animals; i.e. a so-called DIVA (distinguishing infected and vaccinated animals) test is not currently available. Although such a test is not essential for the eradication of PPR (rinderpest was eradicated without one), it would greatly simplify the closing stages of the eradication process in individual countries, and especially in the post-eradication stage. A number of potential DIVA vaccines have been developed, though more extensive testing on safety and duration of protection will be required before commercial production. One alternative is the genetic modification of the vaccine virus to alter its antibody profile [67], with a new test to identify the novel, non-PPRV antibodies. Most of the research, however, has focused on the use of viral vectors to express the PPRV H glycoprotein (reviewed in detail in Rojas *et al.* [68]). Vaccinated animals have anti-H antibodies but not anti-N antibodies; thus, existing ELISA kits could provide a DIVA test.

Strategies for surveillance and control

Experience from the last decade shows that vaccination organised purely at the national level may have limited success in many regional contexts. The re-emergence of PPR in Morocco and China despite successful control campaigns illustrates the problem that countries may face as

they apply mass vaccination while still having difficulties in controlling transboundary animal movements [69,70]. Socio-economic instability in many regions is also likely to make control of human and animal movements even more difficult, thereby increasing PPR risk [40]. Faced with this situation, the second phase of the PPR Global Eradication Programme proposes defining areas (which often cross country borders) that are part of the same network of PPRV circulation, and encourages countries to focus coordinated control efforts on such 'episystems' [14]. Identification of these episystems should be based on robust epidemiological and PPRV genetic data. This point needs to be considered when designing governance of, and allocating resources to, PPR control strategies.

When resources are limited, risk analyses are vital to predict PPR occurrence, develop vaccination strategies, and prioritise surveillance and vaccination efforts (e.g. Ruget *et al.* [44], Nkamwesiga *et al.* [71]). The surveillance system used should be regularly evaluated to ensure that appropriate resources are allocated to passive and active surveillance [72]. Different tools and methods are available for the economic assessment of vaccination campaigns [73,74]. Transmission models have also been shown to be efficient in evaluating different vaccination strategies [75,76]. However, research outputs seem to be only rarely translated into strategies applied in the field, possibly because of poor communication between researchers and decision-makers.

Involvement of local communities and other animal health actors is key to the success of PPR eradication [14]. An increasing amount of research shows the importance of considering knowledge, culture and perception of communities to improve understanding of the local context of PPR circulation (e.g. Lhermie *et al.* [77], Jones *et al.* [78]) and to adapt control strategies to these contexts [46,79]. Improving communication and access to vaccines in communities, especially for women, drastically increases trust and vaccine uptake (e.g. Bikaako *et al.* [80], Nuvey *et al.* [81]), even in systems where livestock owners must pay for the vaccines [82,83]. In areas that are difficult to reach for Veterinary Services, involvement of communities, notably as state-approved animal health actors, can play an important role for last-mile vaccine delivery and for disease surveillance, if those communities are provided with good incentives and integrated into an efficient surveillance system.

Conclusions

The PPR Global Eradication Programme has entered its second phase, with significant hurdles to be overcome to reach a world free of the disease by 2030. Achieving this goal will be facilitated if efforts are based on the most advanced research and tools available. Focusing research and development efforts on important remaining gaps (summarised in Table I) should also increase the efficiency of control and surveillance strategies. Experience with the eradication of rinderpest

Table I

Research priorities on rinderpest and peste des petits ruminants

Disease/main theme	Research priorities
Rinderpest	
Surveillance and preparedness	• Completion of 'Sequence and Destroy' projects to remove RPV-containing material • Registration and inspection of unregistered facilities holding RPV-containing material
Diagnostic tools	• Availability of positive controls for PCR assays • Development of a highly specific ELISA assay for RPV antibody detection
Peste des petits ruminants	
PPR host range	• Identification of markers of PPRV virulence and of host susceptibility
PPR epidemiology	• Evaluation of the role of atypical hosts in PPR transmission • Assessment of the risk of PPR transmission from different materials (meat, waterholes, fomites, etc.) • Systematic gathering of information on key transmission factors (animal movement, density, etc.), notably through participatory approaches, to produce risk maps of PPR occurrence and transmission • Investigation of rapid spread of African lineage IV
Diagnostic tools and vaccines	• Development and validation of serological and non-invasive methods adapted to atypical hosts (e.g. wildlife) • Integration of field diagnostic tests in surveillance activities • Confirmation of efficacy and safety of DIVA vaccines with validated differential diagnostic tests
Surveillance and control strategies	• Definition of episystems and development of coordinated strategies at the level of episystems • Development of control strategies based on epidemiological and socio-economic research outputs • Improvement of communities' engagement in surveillance and control efforts
All morbilliviruses	
Evolution and risk of emergence	• Evaluation of the risk of new morbillivirus emergence

DIVA: distinguishing infected and vaccinated animals
ELISA: enzyme-linked immunosorbent assay
PCR: polymerase chain reaction
PPR: peste des petits ruminants
PPRV: peste des petits ruminants virus
RPV: rinderpest virus

shows that the effort will not stop with the successful eradication of PPR from animal populations. It is important to start building on the experience of rinderpest to prepare for a post-PPR world and ensure everything is in place to limit the risk of PPR reappearance. The animal health community should also be vigilant regarding other viruses currently circulating at low frequency that could emerge as the niches of RPV and PPRV become vacant. Such commitment is needed to ensure sustainable contribution to food and economic security, community resilience and biodiversity conservation.

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Peste bovine et peste des petits ruminants : le point sur les efforts d'éradication

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Résumé

Le virus de la peste bovine et celui de la peste des petits ruminants (PPR) sont des virus à pathogénicité élevée qui occasionnent des maladies affectant principalement les bovins pour le premier et les petits ruminants pour le second. Si le processus post-éradication de la peste bovine a été globalement couronné de succès, des failles ont néanmoins été détectées concernant l'état de préparation en cas de résurgence future de la peste bovine ; en outre, il reste encore quelques établissements dans le monde qui détiennent du virus bovipestique sans avoir été inspectés ni habilités à cette fin, ce qui fait peser une menace sur la communauté mondiale. Le Programme mondial d'éradication de la PPR devra surmonter d'importants obstacles pour atteindre son objectif d'un monde indemne de PPR en 2030. Il sera plus facile d'y parvenir si les plans qui le composent sont conçus en se basant sur la recherche la plus avancée et sur les meilleurs outils disponibles, avec une participation effective des communautés. Le recentrage des efforts de recherche et de développement sur les lacunes importantes relevées à ce jour devrait améliorer l'efficience des stratégies de lutte et de surveillance, à condition que les résultats de la recherche soient effectivement communiqués aux décideurs. Les chercheurs, les parties prenantes et les organismes chargés de la mise en œuvre devraient s'inspirer de l'expérience acquise avec la peste bovine pour préparer le monde post-PPR. La communauté de la santé animale devrait également exercer une grande vigilance à l'égard d'autres virus – y compris ceux que nous ne connaissons pas encore – susceptibles d'émerger à mesure que se libèrent les niches précédemment occupées par les virus de la peste bovine et de la PPR.

Mots-clés

Bovins – Contrôle – Éradication – Maladie transfrontalière – *Morbillivirus* – Peste bovine – Peste des petits ruminants – Petits ruminants – Surveillance.

La peste bovina y la peste de los pequeños rumiantes: estado actual de los esfuerzos encaminados a erradicar la enfermedad

A. Bataille & M.D. Baron

Resumen

El virus de la peste bovina y el virus de la peste de los pequeños rumiantes (PPR) son virus altamente patógenos que causan enfermedades principalmente en bovinos y pequeños rumiantes, respectivamente. Aunque el proceso de poserradicación de la peste bovina ha sido en gran medida exitoso, persisten deficiencias en materia de preparación

ante una futura reaparición de esta enfermedad, dado que el virus aún está presente en algunas instalaciones que no han sido registradas o inspeccionadas, lo que supone una amenaza para la comunidad mundial. El Programa mundial de erradicación de la PPR deberá superar importantes obstáculos para que el mundo esté libre de la enfermedad para 2030. Alcanzar este objetivo será más fácil en la medida en que los planes se basen en las mejores investigaciones y herramientas disponibles y se cuente con la debida participación de las comunidades. Centrar los esfuerzos de investigación y desarrollo en las importantes deficiencias que aún persisten debería aumentar la eficacia de las estrategias de control y vigilancia, siempre que los resultados de la investigación se comuniquen eficazmente a los responsables de la toma de decisiones. Los investigadores, las partes interesadas y los organismos de ejecución deberían basarse en la experiencia adquirida con la peste bovina para prepararse para un mundo pos-PPR. La comunidad dedicada a la sanidad animal también debe mantenerse alerta ante otros virus, incluidos aquellos aún desconocidos, que podrían surgir a medida que queden vacantes los nichos ocupados por los virus de la peste bovina y la PPR.

Palabras clave

Control – Enfermedad transfronteriza – Erradicación – Ganado bovino – *Morbillivirus* – Pequeño rumiante – Peste bovina – Peste de los pequeños rumiantes – Vigilancia.

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