

# Rinderpest eradication: challenges for remaining disease free and implications for future eradication efforts

K. Hamilton <sup>(1)\*</sup>, M.D. Baron <sup>(2)</sup>, K. Matsuo <sup>(1)</sup> & D. Visser <sup>(3)</sup>

(1) World Organisation for Animal Health (OIE), 12 rue de Prony, 75017 Paris, France

(2) The Pirbright Institute, Ash Road, Pirbright, Surrey, GU24 0NF, United Kingdom

(3) Department of Agriculture, Western Cape, Muldersvlei Road, Elsenburg, 7607, South Africa

\*Corresponding author: keithhamilton@ksu.edu

## Summary

In 2011, the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) declared global freedom from rinderpest, formally announcing that rinderpest virus infections had been eliminated from susceptible livestock populations. At the same time, it was recognised that rinderpest virus, and material containing rinderpest virus, remained stored in an unspecified number of facilities across the world. Although natural infections had been eliminated, there remained a risk that rinderpest could reoccur if such infectious material accidentally leaked or was intentionally released from one of these facilities into a susceptible animal population. To minimise this risk, the OIE and FAO, with the support of international partners, set in place a framework to: reduce the quantity of remaining rinderpest-virus-containing material; ensure that such material was only stored in high-security facilities; regulate any handling or manipulation of the virus; maintain vigilance amongst livestock keepers and Veterinary Services in the post-eradication era; and develop contingency plans to deal with any suspected or actual reoccurrence of rinderpest disease. In 2016, five years after the declaration of global freedom from rinderpest, official reports to the OIE show that virus and virus-containing material remain stored in 21 countries worldwide in 22 separate facilities, of which only five have been inspected and approved for holding rinderpest virus or vaccine. There is still much work to be done to further reduce the risk of a reoccurrence.

## Keywords

Bioterrorism – Eradication – International cooperation – Livestock disease – Rinderpest – Risk – Sequestration – Stockpile.

## Introduction

Rinderpest, otherwise known as cattle plague, was one of the most feared diseases of livestock. It mainly affected buffalo and cattle, with occasional overspill into wildlife species. The disease is caused by infection with rinderpest virus, which is a member of the genus *Morbillivirus* in the family *Paramyxoviridae*. It is in the same group of viruses as canine distemper virus, peste des petits ruminants (PPR) virus, and the human pathogen, measles virus (1). With mortality rates approaching 100% in some susceptible herds, rinderpest decimated cattle populations on many occasions throughout history, as waves of epizootics spread from Asia into Europe and the Middle East in the last two

millennia (2). Latterly, in the late 19th century, it was introduced to Africa and swept across the continent, killing millions of animals in what became known as ‘the great African rinderpest pandemic’ (2).

From the early 18th century, efforts at control focused on what are now considered the classical zoosanitary measures, i.e. separating and killing infected animals and their contacts. Such measures were used with success in the 19th and early 20th centuries in Europe (3). In the 20th century, the advent of pathogen detection and characterisation technologies, together with vaccines that were safe and provided long-lasting immunity against all strains of the virus, enabled effective control strategies to be employed much more widely. It was thanks to these

technologies and the characteristics of the virus (which has a single serotype and relatively high genetic stability), coupled with decades of coordinated action, that it was possible to eradicate the disease. The collective political will which was needed to sustain investments in time, resources, and human capital ensured the campaign's success.

The last case of rinderpest was reported in a buffalo in Kenya in 2001 (4). It took a further ten years of reviewing data on ongoing surveillance before the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) could declare with confidence that the world was free from rinderpest. After smallpox (which had been eradicated by 1980), rinderpest is only the second infectious disease to have been eradicated through human efforts. However, as was the case with smallpox, the eradication of rinderpest leaves the worldwide scientific and veterinary community with the problem of how to ensure that the disease does not re-emerge when stocks of infective material are still held in a number of countries.

Finding ways to store this material securely is essential, particularly as there are concerns that rinderpest could be used by terrorist groups or criminal gangs as a bio-weapon. Some authors refer to the introduction of rinderpest into Europe in the 12th century by invading Mongol armies, who brought their cattle with them, as one of the early examples of bio-warfare (5). It is difficult to know whether the invading Mongols intended to use rinderpest as a weapon, but 800 years later, in the 20th century, scientists working on agro-warfare programmes in several states, including Canada, Germany, the United States of America (USA) and the Union of Soviet Socialist Republics (USSR), did include rinderpest in their bio-weapons research and development programmes (6). Today, rinderpest is still considered to be a potential bio-weapon agent and, as such, it is feared that terrorists may be tempted to use it. Although natural infections have been eliminated, potentially infective material accumulated over the past century (including virus that had been grown in laboratories, stocks of vaccine virus, and diagnostic samples collected during outbreaks) remains stored in freezers in a number of laboratories around the world (7). The potential for accidental or intentional release of this material into a susceptible animal population now poses a risk for reoccurrence of disease. The impact of such an occurrence is potentially very high, since a complete ban on vaccination against rinderpest has been in force for some years, meaning all livestock populations in all countries are now fully susceptible to rinderpest virus infection.

On declaration of global freedom from rinderpest, the international community agreed that there was an urgent need to put in place a global framework to maintain freedom and minimise this risk of an accidental or intentional release of virus. This paper describes some of the actions taken to

establish this framework and discusses the challenges that lie ahead.

## Legal framework

In late 2009, the OIE and FAO tasked a group of experts (known as the FAO/OIE Joint Committee on Global Rinderpest Eradication) to advise the Director Generals of both organisations on whether there was enough evidence to make the declaration of global freedom. These experts, all of whom were highly involved in the eradication campaign, were also charged with developing guidance on ways to mitigate the risk of a reoccurrence of rinderpest (8). The Committee's recommendations were the basis for OIE and FAO Resolutions adopted at the OIE and FAO annual general meetings in 2011, which declared global freedom and set in place a framework for maintaining this status. This framework was strongly influenced by the World Health Organization (WHO) guidance on smallpox sequestration and the advice of WHO experts who had gained considerable experience of handling smallpox after its eradication.

By passing the OIE and FAO Resolutions in 2011, Member Countries of the two organisations agreed to:

- i) maintain vigilance and report suspected cases of rinderpest to the OIE
- ii) destroy material containing rinderpest virus or ensure it is stored safely and securely in high-containment facilities
- iii) prohibit any and all manipulation of rinderpest-virus-containing material (RVCM) (including vaccine manufacture) unless approved by the national Veterinary Services, the OIE and FAO.

The global vaccination ban was also maintained and countries were required to ensure rinderpest disease remained a part of veterinary training and continuing professional development curricula. In addition, to keep the number of RVCM repositories to a minimum, the OIE and FAO were required to jointly designate officially approved rinderpest holding facilities to which countries should be encouraged to transfer their stock (there are currently five such facilities worldwide) (9, 10). Several other resolutions were also passed in the subsequent years to reinforce these activities.

In the post-eradication era, the OIE and FAO established a new expert committee (the FAO–OIE Joint Advisory Committee on Rinderpest), whose role has been to provide technical advice to both organisations on rinderpest post-eradication activities. Specifically, their role includes providing advice on the approval of facilities for holding

rinderpest material and on the approval of any proposed activities involving the use or manipulation of RVCМ, for example research or vaccine manufacture. Implementation of the framework and management of the expert committee has been coordinated by a joint FAO–OIE Secretariat.

In the wake of rinderpest eradication, the OIE's international trade standards needed to be updated. Revised standards (in Chapter 8.15. of the OIE *Terrestrial Animal Health Code*, 'Infection with rinderpest virus') require countries to continue surveillance for the disease and to report annually to the OIE on the status of RVCМ held in their countries. The latter requirement provides a legal basis for a mechanism to monitor global stocks and evaluate progress with destruction and sequestration. The chapter also describes what countries should do in the event of a suspected or confirmed case of rinderpest, how this would affect global freedom, and how country and global freedom could be restored (11).

## Remaining stocks of RVCМ

The requirement for annual reporting on remaining stocks of RVCМ has a dual purpose. Firstly, it allows the OIE and FAO to monitor progress with destruction and sequestration. Secondly, it is hoped that the process of transparently reporting these data will encourage countries to comply with their commitment. The report presented at each year's OIE General Session clearly shows to all Member Countries which countries have (or have not) submitted reports, which have destroyed or sequestered rinderpest material, and which have taken no action.

The willingness of countries to report has been promising, with all 180 OIE Member Countries (OIE Member Countries include all those with significant livestock populations) responding to the official OIE annual survey in the first two years that the survey was active (2014 and 2015) (7). However, thus far, only a few countries have taken action to destroy or transfer their remaining RVCМ. In 2015, the OIE reported that 24 countries held RVCМ in a total of 27 facilities (7). The following year, in 2016, those numbers had dropped only slightly, with the organisation reporting that RVCМ was held in 21 countries in 22 facilities. After the publication of the official report for 2016, an additional three countries informed the FAO–OIE Joint Rinderpest Secretariat that they had destroyed or sequestered RVCМ, but this still leaves 18 countries that have stocks of infectious material. In addition, it is worth noting that the 2016 survey also contained reports from two countries that had discovered previously undeclared RVCМ (12, 13), which suggests that more undocumented stocks are likely to surface in years to come.

## Consolidating stocks of RVCМ in approved holding facilities

The OIE and FAO are responsible for approving and overseeing the high-containment facilities which store remaining rinderpest virus stocks on behalf of the international community. The process for approval was adopted in an OIE Resolution specifying the requirements and mandate for two types of facilities. The first type would act as a highly secure repository for material containing wild-type rinderpest virus that countries were unwilling to destroy. Although there is no valid reason to retain stores of rinderpest virus, some countries may want to take a 'just in case there is a future need' approach and retain ownership of these stocks, in which case it is better for these stocks to be secured safely. The second type would maintain, and test the quality of, stocks of manufactured rinderpest vaccine (the vaccine being itself an attenuated form of rinderpest virus). Each approved facility has to agree to maintain the specified requirements and is bound by a mandate. Regular inspections and reporting ensure compliance with the mandate. In addition to acting as guardians of RVCМ, the facilities are required to provide technical services to the international community to support global freedom from rinderpest (14).

The OIE and FAO jointly decide which laboratories they consider to be suitable and then the final decision on which facilities are to be approved is made by the passing of a Resolution by the OIE World Assembly of Delegates. This ensures that the international community is in agreement with the selection. At the OIE General Session in May 2015, five facilities in four countries (one each in the USA, the United Kingdom [UK] and Ethiopia, and two facilities in Japan) were approved to store RVCМ (14). Since then, an additional facility in France has applied and has been inspected; the facility will now be considered by the FAO–OIE Rinderpest Joint Advisory Committee and their recommendation passed to the OIE and FAO.

There is currently no restriction on the total number of facilities which can be approved globally and several additional countries have put their laboratories forward for approval as rinderpest holding facilities, or are considering doing so. There has been little progress in getting countries to agree on shared regional storage, with the notable exception of countries in Africa. In 2010 the African Union –Interafrican Bureau on Animal Resources (AU–IBAR) adopted a regional strategy for sequestering remaining stocks of rinderpest virus on the African continent (15). AU countries agreed that they would nominate the AU Pan African Veterinary Vaccine Centre (AU–PANVAC) in Ethiopia to be the single rinderpest holding facility for the African continent and all AU countries agreed to destroy material or transfer it to this centre, which is situated in Debre Zeit (16). The AU–PANVAC facility is one of the

five centres already approved as a holding facility for RVCM (14). In accordance with the AU regional strategy to sequester remaining stocks of rinderpest virus, five AU Member States have already transferred the RVCM that they wish to archive to the AU-PANVAC facility, destroying what is not stored.

### **Encouragement through communication and advocacy**

Resolutions adopted by intergovernmental and regional organisations are 'soft' legal instruments. They are generally implemented through trust and solidarity. Attempts to enforce or police such agreements by other means may be time-consuming, fruitless and counterproductive.

Shortly after the declaration of global freedom, the OIE and FAO launched an advocacy and communications campaign to encourage countries to take action on remaining stocks quickly and decisively whilst there was still momentum. The core messages of the campaign were that, since rinderpest had been eradicated, there was no benefit in a country storing virus and that it would only be a burden of responsibility for a country to do so. An outbreak of rinderpest in the post-eradication era could have devastating consequences and would undermine the decades of work that had gone into eradicating the disease. If there was an accidental release of rinderpest virus from a facility, or if it was acquired and released by criminals, not only would the country (and possibly its trading partners and neighbours) incur significant production and economic losses, but the country would also suffer international embarrassment and lose credibility (17).

These messages were disseminated through a media campaign which included a short film (first aired to the OIE World Assembly of Delegates in 2012) (18), a pamphlet entitled 'Ten reasons not to store rinderpest virus' (17), press releases, and scientific publications (7, 19). The FAO–OIE Secretariat and other key figures linked to rinderpest were proactive, speaking at conferences, meetings, and conventions. This process of advocacy is ongoing, with several regional meetings being held in the last two years. During these meetings, leaders of national Veterinary Services and/or laboratories have been encouraged to move forward in the destruction or sequestration of their RVCM and reminded of the impact of the disease and the need for continuing surveillance and appropriate testing of suspected cases. FAO is producing material for use in advocacy campaigns at livestock-keeper level as well as at the level of national Veterinary Services (20). A specific challenge over the next 10–20 years is going to be ensuring that expertise is maintained to deal with any re-emergence of the virus that may occur, and ensuring that sensitivity to the clinical appearance of the disease is sufficiently high that any outbreak that may occur is detected in a timely manner.

## **International partnerships**

The OIE–FAO post-rinderpest-eradication campaign was supported by a number of intergovernmental organisations, including WHO, the Biological and Toxin Weapons Convention (BWC), and the G7 Global Partnership Against Weapons of Mass Destruction. These organisations shared their technical expertise and experience and through their networks and annual meetings they provided a platform on which to reach high-level officials and press for destruction and sequestration of the virus. The WHO had much to share from its experiences with smallpox, and was also keen to learn more about rinderpest eradication in order to inform its own polio-eradication policies, in what is hoped will soon be a polio-free world.

Financial support and secondment of experts from a number of countries allowed the OIE and FAO to maintain a core secretariat and implement activities aimed at advocacy, oversight and capacity-building.

## **Research aimed at maintaining freedom from rinderpest**

To reduce the risk of accidental laboratory escape immediately after the declaration of global freedom from rinderpest, and before a mechanism for research approval and oversight was in place, there was a moratorium on research involving the manipulation or handling of RVCM (19). Once the OIE–FAO mechanism for approval and oversight had been established, several research projects were proposed. To be approved, such proposals had to demonstrate that the work could be carried out safely (without risk of laboratory escape of rinderpest virus) and that the research aimed to sustain freedom from rinderpest or improve food security, or had significant benefits for public health or animal health (21).

One of the first projects approved by FAO and the OIE was research into finding an alternative to attenuated rinderpest virus vaccines. Vaccines were a centrepiece of many rinderpest control programmes and, in the post-eradication era, it was deemed important to have stocks of vaccines ready for use in case there was a reoccurrence of disease. However, there is little commercial incentive to manufacture rinderpest vaccines in a rinderpest-free world and public funds are very limited, as they are needed to support a long list of other animal health priorities. Given also that it is not possible to distinguish animals that have been given the rinderpest vaccine from animals that have been previously infected [there is no Differentiating Infected from Vaccinated Animals (DIVA) vaccine or test], trying to find an alternative to attenuated rinderpest virus

vaccines was considered a priority. This work was based on the old observation that rinderpest virus vaccine can protect sheep and goats against the closely related PPR virus (22). It was therefore reasonable to see if attenuated PPR virus vaccines could protect cattle against rinderpest. PPR virus vaccines are produced in large amounts in many countries due to the high prevalence of this disease in large parts of the developing world. Unfortunately, when the study was carried out, neither of the PPR vaccines tested was able to fully protect the cattle from rinderpest infection (23), meaning that, for the foreseeable future, it will be necessary to keep emergency stocks of rinderpest virus vaccine. An important question will be the location of these stockpiles; one has already been established at AU-PANVAC in Ethiopia, but at least one stockpile needs to be established in Asia, and agreements put in place to govern its use on a regional basis.

To address concerns that destruction of rinderpest virus isolates would lead to the loss of important historical data and biological material which might one day be needed for research (concerns that may discourage destruction of isolates of wild-type rinderpest virus), the OIE has offered to support genetic sequencing of remaining isolates, on condition that the virus stocks are destroyed after they have been sequenced. If for any unforeseen reason it becomes necessary to use rinderpest virus isolates for research in the future, the viruses could be reconstructed using these genetic sequence data (24). The sequence data could also be used for phylogenetic studies and forensic epidemiology investigations, should there be a reoccurrence of disease. Several approved rinderpest virus holding facilities have expressed an interest in engaging with this process, and the work has already commenced at one (the Pirbright Institute in the UK). It was decided that the sequence data from these projects should be put into the public domain, joining the already existing virus genome sequence data that had been generated through previous research studies.

## Discussion

### The risks of reintroduction

Since rinderpest virus infection has been eliminated from susceptible livestock populations, the only plausible route for a reintroduction to cattle would be through an accidental laboratory escape or an intentional introduction. Whilst acts of agroterrorism have been relatively rare (25), concerns have been expressed about the possibility for rogue groups (terrorists or criminals) to use rinderpest as a bio-weapons agent. An outbreak of rinderpest would gain global media attention because of the disease's eradicated status, and it would undermine the decades of investment and effort that went into achieving this. The economic consequences would be significant owing to the cost of control and loss

of access to international markets for affected countries. These highly visible impacts, combined with the relatively low cost and ease of dissemination, might make rinderpest an attractive option for such groups. There is evidence that terrorists have been exploring the possibility of using high-impact animal pathogens as bio-weapons (26).

The risk of an accidental release from a facility is also real – the last confirmed case of smallpox in humans was the result of the leakage of variola virus from a laboratory in the UK in 1978 (27) – and this risk has been highlighted by the escape of foot and mouth disease virus from a facility in the UK in 2007 (28). Whilst it is beyond the scope of this paper to quantify such risks, the probability of a laboratory accident or of rinderpest virus falling into the wrong hands is higher when potentially infective material is stored in a greater number of locations around the world (29), including in low-biosecurity settings or where government regulation is weak.

### Preparedness against a reintroduction

The initial post-eradication effort took advantage of the momentum gained from the declaration of global freedom and it is now important that momentum is maintained even though rinderpest is not getting so much attention in the media. Work is continuing on adding a global contingency plan to the framework, which includes identifying and consolidating remaining stocks of vaccine to contribute to an emergency vaccination plan. Only limited stockpiles of vaccine and seed virus were still stored globally at the time of declaration of rinderpest freedom and, as mentioned above, there is no commercial incentive to maintain capacity for vaccine manufacture for an eradicated animal disease. An ongoing challenge for those preparing the international response plan for any future rinderpest outbreak is to ensure the maintenance and continuous quality checking of rinderpest vaccine reserves since, apart from Japan, no country is now manufacturing fresh stocks of rinderpest vaccine.

### Challenges to virus destruction/containment

Although progress is being made, at the time of writing (mid-2016) it has become clear that not all countries are going to destroy and/or sequester their remaining stocks of virus in the immediate future, and that destruction and sequestration has become a mid- to long-term objective. A clear challenge, therefore, is how to encourage as many countries as possible to destroy their remaining material or transfer it to a high-security facility. Destruction of RVCM is relatively simple. It is low cost and does not require specialist equipment. The process for shipping material to a high-containment laboratory should also be relatively straightforward, and assistance, if needed, can be requested from the OIE or FAO. There are, therefore, no technical or financial barriers to destruction or sequestration of RVCM.

Without an in-depth analysis, which is beyond the scope of this paper, it is not possible to say exactly what the main barriers are which prevent countries from fulfilling their obligations. However, it is likely that several factors contribute and that the size of the role they play will vary depending on the setting. In some instances there may be perceived research or commercial value in retaining stocks of rinderpest virus. However, in a world where rinderpest has been eradicated and research is forbidden, the research potential and commercial value should be negligible. Moreover, it is possible for countries to retain their ownership of the material, through a Material Transfer Agreement, whilst transferring it for safekeeping to an approved rinderpest holding facility. Some countries might wish to maintain stocks of vaccine virus for manufacture of vaccines should there be a reoccurrence of disease within their own borders or in neighbouring countries, a position which is understandable given the absence of internationally available stocks of vaccine outside Africa. Other countries may take pride in keeping their own national stocks. In some countries which are poorly resourced, have weak governance or lack strong leadership, the veterinary authorities may not even know why they are holding onto stocks of rinderpest, or else may not be sure who is responsible for taking action. These factors should be considered when developing strategies to encourage countries to comply with the obligations they committed to in 2011.

In the case of the stocks of virus that remained following the eradication of smallpox, efforts to encourage countries to transfer their stored virus to official holding facilities were relatively successful, and infectious material is now officially held in just two facilities: the Centers for Disease Control in the USA and the State Center for Virology and Biotechnology (Vector) in Russia, with WHO being responsible for oversight. Two factors may have facilitated the consolidation of smallpox material into just these two laboratories during the 1980s. Firstly, the leakage of variola virus and subsequent death of a woman in the UK in 1978 highlighted the risks of storing and handling the virus and may have encouraged countries to transfer their remaining material. Secondly, at the height of the Cold War, when smallpox sequestration was under way, the geopolitical situation divided the world into two groups of countries, the Eastern Bloc and the Western Bloc, creating stronger alliances within these blocs. Countries aligned with the Western Bloc were more likely to send their smallpox viruses to the Centers for Disease Control and Prevention (CDC) and those aligned with the Eastern Bloc would be likely to send them to Vector. By 2011, the USSR had broken up, the Cold War was over, and many countries had developed a greater sense of independence. The destruction and sequestration of rinderpest virus is, therefore, taking place against a very different geopolitical backdrop. So far, the only group of countries to agree to sequester their

RVCM in a single selected facility have been the African Union countries, who chose the AU-PANVAC facility in Ethiopia. As noted earlier, these countries have already taken action to transfer such material – in 2015–2016, five of them were known to have destroyed rinderpest material or have transferred it to an approved facility – and the African Union should be applauded for taking this initiative in 2010 before eradication had formally been announced.

## **Synthetic biology**

While the focus on destroying or securely sequestering all remaining rinderpest virus is an important one, it has to be recognised that the release of existing stock is not the only possible source of a re-emergence of virus. Even if all stocks of RVCM were destroyed, synthetic biology would allow the same viruses to be reconstructed from genetic sequence data which are already in the public domain. Synthetic biology offers opportunities and risks: the opportunity to recreate virus if there were some unforeseen research need in the future and the risk that ‘tech-savvy’ criminals or terrorists could synthesise rinderpest virus for their own ends. Currently, the synthesis of rinderpest virus is forbidden (unless approved by the OIE and FAO). However, the rapidly expanding number of private companies offering to synthesise genetic material and proteins from sequence data and the absence of a comprehensive regulatory framework for synthetic biology makes risk mitigation a challenge. An assessment of the risks posed by synthetic biology in terms of maintaining global freedom from eradicated diseases needs further study.

## **Hopes for eradicating other diseases**

After the success with smallpox and rinderpest, and as the polio eradication campaign enters what is hoped is its final stage, thoughts turn to the possibility of eradicating other diseases. The OIE and FAO have launched a Global Strategy for the Control and Eradication of PPR, and some experts in the human health sector have talked about the possibility of eradicating measles. It is important that lessons from the rinderpest post-eradication experience are shared with those charged with developing policies to maintain freedom from other diseases which have been eradicated. In future, consideration could be given to initiating some key post-eradication activities at an earlier stage, before global freedom has been declared, for example late in the eradication campaign. In particular, a system for monitoring remaining laboratory stocks of pathogen could be put in place; a limited number of holding facilities could be approved; vaccine stocks could be consolidated; and destruction and sequestration of remaining stocks of virus could be initiated before freedom has been declared. Research could also be reviewed and, if needed, conducted to provide information important for maintaining freedom, for example on the potential survivability of the disease

agent in different tissues and substrates. The post-rinderpest activities also led to some unintended consequences, which should be avoided for future cases of pathogen eradication, for example the comprehensive restrictions on holding any kind of rinderpest virus-associated material, which were put in place to prevent rinderpest re-emergence and ensure the strongest imaginable safeguards, left diagnostic laboratories without materials to maintain their diagnostic tests for rinderpest.

## Conclusion

Ultimately, the maintenance of global freedom from rinderpest relies on countries themselves taking action. Weaknesses in national Veterinary Services in many parts of the world mean that some countries would be better prepared to tackle a reoccurrence of rinderpest than others. As there is still a risk from rinderpest, it will be important that training and veterinary curricula (particularly for government veterinarians) continue to sensitise veterinarians to the clinical and pathological presentations of rinderpest and that OIE Reference Laboratories maintain diagnostic capabilities to investigate suspected cases. It is also important that countries and international donors continue to invest in strengthening the ability of national Veterinary Services to control all animal disease threats.

Sustained investment will be needed to support the implementation of the framework for maintaining global freedom. Because rinderpest post-eradication activities are not within the core missions of either the OIE or FAO, they

are supported with extra-mural funds provided by donors, and it will therefore be important to convince donors of a mid- to long-term need for such investment.

In 2016, with official reports to the OIE stating that RVCM is stored in 22 facilities in 21 countries worldwide, and with five facilities in four countries approved as rinderpest holding facilities (and several other countries also considering putting their institutes forward for approval) it is difficult to visualise an end point. Will the international community agree to destroy all remaining stocks of rinderpest virus and material? Will virus be stored in a specified minimum number of approved facilities? And what will that number be? Even if total destruction is achieved, how will the risks from synthetic biology be mitigated?

These are questions that the international community will need to seriously consider in the coming years.

## Acknowledgements

The authors thank the USA Defense Threat Reduction Agency, the UK Foreign and Commonwealth Office, and Canada Department of Foreign Affairs, Trade and Development for their support to the work of the FAO–OIE Joint Rinderpest Secretariat. They also wish to acknowledge the contributions to the post-eradication process of their colleagues in the FAO–OIE Joint Rinderpest Secretariat, particularly Dr Samia Metwally, Dr Aldo Dekker and Ms Tianna Brand.

## L'éradication de la peste bovine : difficultés du maintien du statut indemne et conséquences pour les prochaines tentatives d'éradication

K. Hamilton, M.D. Baron, K. Matsuo & D. Visser

### Résumé

En 2011, l'Organisation mondiale de la santé animale (OIE) et l'Organisation des Nations Unies pour l'alimentation et l'agriculture (FAO) ont annoncé officiellement l'élimination de l'infection due au virus de la peste bovine dans les populations d'animaux d'élevage sensibles, déclarant ainsi la planète indemne de cette maladie. Parallèlement, les deux organisations faisaient état de l'existence d'un nombre indéterminé d'établissements dans le monde détenant des stocks du virus bovine ainsi que des produits contenant ce virus. Malgré l'élimination de l'infection chez ses hôtes naturels, un risque de réapparition de la peste bovine subsiste en cas de fuite accidentelle ou d'émission délibérée de ces produits infectieux dans les populations animales sensibles à partir de l'un de ces

établissements. Afin de minimiser ce risque, l'OIE et la FAO soutenus par leurs partenaires internationaux ont mis en place un cadre visant plusieurs objectifs : réduire les quantités restantes de produits contenant le virus de la peste bovine dans le monde ; veiller à ce que ces produits ne soient stockés que dans des établissements de haute sécurité ; réglementer les conditions de détention et de manipulation du virus ; poursuivre la surveillance exercée par les éleveurs et les Services vétérinaires au cours de la phase post-éradication ; concevoir des plans d'urgence visant à faire face à toute réapparition suspectée ou confirmée de la peste bovine. En 2016, soit cinq ans après la déclaration de l'éradication mondiale de la peste bovine, il ressort des rapports officiels adressés à l'OIE que 21 pays détiennent encore des stocks du virus de la peste bovine ou des produits contenant ce virus, répartis en 22 établissements distincts dont seulement cinq ont fait l'objet d'une inspection et ont été dûment habilités à détenir des stocks de virus de la peste bovine ou de vaccins contre cette maladie. Il reste donc encore beaucoup à faire pour continuer à réduire le risque de réapparition de la peste bovine.

#### **Mots-clés**

Bioterrorisme – Coopération internationale – Éradication – Maladie du bétail – Peste bovine – Risque – Séquestration – Stocks de réserve.



## **Erradicación de la peste bovina: dificultades para mantener la ausencia de enfermedad y repercusiones en las futuras actividades de erradicación**

K. Hamilton, M.D. Baron, K. Matsuo & D. Visser

#### **Resumen**

En 2011, la Organización Mundial de Sanidad Animal (OIE) y la Organización de las Naciones Unidas para la Alimentación y la Agricultura (FAO) anunciaron oficialmente que las infecciones causadas por el virus de la peste bovine habían sido eliminadas de las poblaciones sensibles de ganado, declarando así que el mundo quedaba libre de la enfermedad. Al mismo tiempo, significaron que un número no especificado de instalaciones dispersas por el mundo albergaban muestras del virus y otros productos que lo contenían. Aunque las infecciones naturales habían quedado eliminadas, subsistía el riesgo de reaparición de la peste bovine si en una de esas instalaciones se producía una fuga accidental o una liberación intencionada de material infeccioso y este entraba en contacto con una población animal sensible. Para reducir al mínimo tal riesgo, la OIE y la FAO, con apoyo de colaboradores internacionales, definieron un dispositivo encaminado a: reducir el volumen de material restante con contenido viral de la peste bovine; garantizar que ese material fuera conservado únicamente en instalaciones de alta seguridad; reglamentar toda manipulación del virus; mantener la vigilancia entre cuidadores de ganado y Servicios Veterinarios en el periodo posterior a la erradicación; y elaborar planes de emergencia para responder a toda reaparición, presunta o confirmada, de la peste bovine. En 2016, cinco años después de la declaración de ausencia mundial de peste bovine, los informes oficiales remitidos a la OIE daban fe de que había virus y productos que

lo contenían en 22 instalaciones situadas en 21 países del mundo, de las que solo cinco habían sido inspeccionadas y homologadas para albergar virus de la peste bovina o vacunas contra la enfermedad. Queda pues mucho trabajo por delante para reducir en mayor medida el riesgo de reaparición.

#### Palabras clave

Cooperación internacional – Enfermedad del ganado – Erradicación – Peste bovina – Reserva – Riesgo – Secuestro – Terrorismo biológico.



## References

- King A.M.Q., Adams M.J., Carstens E.B. & Lefkowitz E.J. (eds) (2012). – Virus taxonomy. Ninth report of the International Committee on Taxonomy of Viruses. Elsevier Academic Press, Cambridge, Massachusetts.
- Barrett T. & Rossiter P.B. (1999). – Rinderpest: the disease and its impact on humans and animals. *Adv. Virus Res.*, **53**, 89–110. doi:10.1016/S0065-3527(08)60344-9.
- Spinage C.A. (2003). – Cattle plague: a history. Kluwer Academic/Plenum, New York, Boston, Dordrecht. doi:10.1007/978-1-4419-8901-7.
- World Organisation for Animal Health (OIE) (2016). – Animal health status 2001. Available at: [http://web.oie.int/hs2/sit\\_mald\\_cont.asp?c\\_mald=5&c\\_cont=1&annee=2001](http://web.oie.int/hs2/sit_mald_cont.asp?c_mald=5&c_cont=1&annee=2001) (accessed on 15 September 2016).
- Scott G.R. (2000). – The murrain now known as rinderpest. *Newsl. Trop. Agric. Assoc., UK*, **20** (4), 14–16.
- Middlebury Institute of International Studies at Monterey, James Martin Center for Nonproliferation Studies (CNS) (2008). – Chemical and biological weapons: possession and programs past and present. Available at: [www.nonproliferation.org/wp-content/uploads/2016/03/2008-Chemical-and-Biological-Weapons\\_-\\_Possession-and-Programs-Past-and-Present.pdf](http://www.nonproliferation.org/wp-content/uploads/2016/03/2008-Chemical-and-Biological-Weapons_-_Possession-and-Programs-Past-and-Present.pdf) (accessed on 21 September 2016).
- Hamilton K., Visser D., Evans B. & Vallat B. (2015). – Identifying and reducing remaining stocks of rinderpest virus. *Emerg. Infect. Dis.*, **21** (12), 2117–2121. doi:10.3201/eid2112.150227.
- Food and Agriculture Organization of the United Nations (FAO) & World Organisation for Animal Health (OIE) (2011). – Joint FAO/OIE Committee on Global Rinderpest Eradication. Final report. FAO, Rome.
- World Organisation for Animal Health (OIE) (2011). – Resolution No. 18. Declaration of global eradication of rinderpest and implementation of follow-up measures to maintain world freedom from rinderpest. In Final Report of the 79th OIE General Session, 22–27 May, Paris, 337–342. Available at: [www.oie.int/fileadmin/Home/eng/Media\\_Center/docs/pdf/RESO\\_18\\_EN.pdf](http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/RESO_18_EN.pdf) (accessed on 14 September 2016).
- Food and Agriculture Organization of the United Nations (FAO) (2011). – Resolution 4/2011. Declaration on rinderpest eradication. In Report of the Conference of FAO, 37th Session, 25 June to 2 July. Available at: [www.fao.org/docrep/meeting/017/MB767E/MB767E00.htm](http://www.fao.org/docrep/meeting/017/MB767E/MB767E00.htm) (accessed on 15 September 2016).
- World Organisation for Animal Health (OIE) (2016). – Chapter 8.15. Infection with rinderpest virus. In Terrestrial Animal Health Code. Available at: [www.oie.int/index.php?id=169&L=0&htmfile=chapitre\\_rinderpest.htm](http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_rinderpest.htm) (accessed on 25 September 2016).
- World Organisation for Animal Health (OIE) (2016). – Final Report of the 84th OIE General Session, 22–27 May, Paris. Available at: [www.oie.int/fileadmin/Home/eng/About\\_us/docs/pdf/Session/2016/A\\_FR\\_2016\\_public.pdf](http://www.oie.int/fileadmin/Home/eng/About_us/docs/pdf/Session/2016/A_FR_2016_public.pdf) (accessed on 14 September 2016).
- Food and Agriculture Organization of the United Nations (FAO) (2016). – FAO advocacy brings more countries and resources together to destroy and sequester rinderpest virus stocks in designated holding facilities. Available at: [www.fao.org/ag/againfo/home/en/news\\_archive/2016\\_destroy\\_sequester\\_rinderpest\\_virus\\_stocks.html](http://www.fao.org/ag/againfo/home/en/news_archive/2016_destroy_sequester_rinderpest_virus_stocks.html) (accessed on 25 September 2016).
- World Organisation for Animal Health (OIE) (2015). – Resolution No. 25. Designation of facilities as approved for holding rinderpest virus containing material. In Final Report of the 83rd OIE General Session, 22–27 May, Paris. OIE, Paris, 168. Available at: [www.oie.int/fileadmin/Home/eng/About\\_us/docs/pdf/Session/A\\_FR\\_2015\\_public.pdf](http://www.oie.int/fileadmin/Home/eng/About_us/docs/pdf/Session/A_FR_2015_public.pdf) (accessed on 15 September 2016).
- African Union–Interafrican Bureau for Animal Resources (AU–IBAR) (2012). – The post rinderpest eradication strategy. Available at: [www.au-ibar.org/component/jdownloads/finish/77-sd/1551-the-post-rinderpest-eradication-strategy](http://www.au-ibar.org/component/jdownloads/finish/77-sd/1551-the-post-rinderpest-eradication-strategy) (accessed on 25 September 2016).
- African Union–InterAfrican Bureau for Animal Resources (AU–IBAR) (2010). – Eighth Conference of Ministers Responsible for Animal Resources in Africa, 13–14 May, Entebbe, Uganda. Available at: [www.rr-africa.oie.int/docspdf/en/2010/AU-Ministers-Conference-Entebbe.pdf](http://www.rr-africa.oie.int/docspdf/en/2010/AU-Ministers-Conference-Entebbe.pdf) (accessed on 15 September 2016).

17. World Organisation for Animal Health (OIE) & Food and Agriculture Organization of the United Nations (FAO) (2016). – Ten reasons for not maintaining or storing rinderpest virus. Available at: [www.oie.int/fileadmin/Home/eng/Media\\_Center/docs/pdf/Ten\\_reasons\\_leaflet\\_bandejaune.pdf](http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Ten_reasons_leaflet_bandejaune.pdf) (accessed on 13 September 2016).
  18. World Organisation for Animal Health (OIE) (2013). – OIE urges countries to destroy rinderpest stocks. Available at: [www.youtube.com/watch?v=XLIpwsIPY2Y](http://www.youtube.com/watch?v=XLIpwsIPY2Y) (accessed on 25 September 2016).
  19. World Organisation for Animal Health (OIE) (2012). – Call for countries to comply with moratorium on research using live rinderpest virus. Press release, 23 July 2012. Available at: [www.oie.int/for-the-media/press-releases/detail/article/call-for-countries-to-comply-with-moratorium-on-research-using-live-rinderpest-virus/](http://www.oie.int/for-the-media/press-releases/detail/article/call-for-countries-to-comply-with-moratorium-on-research-using-live-rinderpest-virus/) (accessed on 19 September 2016).
  20. Food and Agriculture Organization of the United Nations (FAO) (2016). – Advocacy and communication. Available at: [www.fao.org/ag/againfo/programmes/en/rinderpest/what\\_fao\\_Advocacy.html](http://www.fao.org/ag/againfo/programmes/en/rinderpest/what_fao_Advocacy.html) (accessed on 25 September 2016).
  21. World Organisation for Animal Health (OIE) & Food and Agriculture Organization of the United Nations (FAO) (2013). – FAO–OIE Rinderpest Joint Advisory Committee, Meeting Report, 26–27 February, Rome. Available at: [www.oie.int/fileadmin/Home/eng/Media\\_Center/docs/pdf/JAC3\\_Report\\_docx\\_V4\\_June29\\_with\\_annexes.pdf](http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/JAC3_Report_docx_V4_June29_with_annexes.pdf) (accessed on 21 September 2016).
  22. Taylor W.P. (1979). – Protection of goats against peste des petits ruminants with attenuated rinderpest virus. *Res. Vet. Sci.*, **27**, 321–324.
  23. Holzer B., Hodgson S., Logan N., Willett B. & Baron M.D. (2016). – Protection of cattle against rinderpest by vaccination with wild-type but not attenuated strains of peste des petits ruminants virus. *J. Virol.*, **90** (10), 5152–5162. doi:10.1128/JVI.00040-16.
  24. Baron M.D. & Barrett T. (1997). – Rescue of rinderpest virus from cloned cDNA. *J. Virol.*, **71**, 1265–1271.
  25. Elbers A. & Knutsson R. (2013). – Agroterrorism targeting livestock: a review with a focus on early detection systems. *Biosecur. Bioterror.*, **11** (Suppl. 1), S25–S35. doi:10.1089/bsp.2012.0068.
  26. Olson D. (2012). – Agroterrorism threats to America's economy and food supply. FBI Law Enforcement Bulletin, February 2012. Available at: <https://leb.fbi.gov/2012/february/agroterrorism-threats-to-americas-economy-and-food-supply> (accessed on 19 September 2016).
  27. Shooter R.A. (1980). – Report of the investigation into the cause of the 1978 Birmingham smallpox occurrence. Her Majesty's Stationery Office, London.
  28. Logan P. (2007). – Final report on potential breaches of biosecurity at the Pirbright site 2007. Health and Safety Executive, Bootle, United Kingdom.
  29. Fournié G., Jones B.A., Beauvais W., Lubroth J., Njeumi F., Cameron A. & Pfeiffer D.U. (2014). – The risk of rinderpest re-introduction in post-eradication era. *Prev. Vet. Med.*, **113** (2), 175–184. doi:10.1016/j.prevetmed.2013.11.001.
-