

AFRICAN UNION INTERAFRICAN BUREAU FOR ANIMAL RESOURCES





A Rinderpest Exit Strategy for Africa

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1. Introduction

Ruminant livestock support the food security and livelihoods of almost a billion people. In many developing countries, livestock keeping is a multifunctional activity. Beyond their direct role in generating food and income, livestock are valuable assets, serving as a store of wealth, collateral for credit and an essential safety net during times of crisis. Livestock are central to mixed farming systems. Ruminants in particular consume vast quantities of plant materials that are not digestible by humans. Thus, ruminant livestock convert unusable plants into 15 percent of total food calories and 25 percent of dietary protein consumed annually. And, not least, they produce valuable manure for fertilizing and conditioning crops and soils and provide draught power for ploughing and transport.

Almost 80 percent of the world's undernourished people live in rural areas and most depend on agriculture, including mixed livestock husbandry, for their livelihoods. The livestock sector contributes 40 percent of the value of world agricultural output, and it is one of the fastest growing sub-sectors of the agricultural economy.

Animal diseases reduce production and productivity, disrupt local and national economies, threaten human health and exacerbate poverty. Additionally, presence of major transboundary animal diseases in national herds and flocks restricts the ability to export livestock and their products from many African countries. The potential to add value to the ruminants owned by both pastoralists and commercial producers can be increased if they have access to export markets for their livestock and their products.

Until recently, rinderpest was the most dreaded of all African cattle diseases. Just over 100 years ago, it was introduced to the continent through the Eritrean port of Massawa from where it spread, firstly to Ethiopia (and became a contributing factor to the Great Ethiopian Famine) and from there to east, south and west Africa within a near continent-wide pandemic associated with massive losses to both domestic cattle and wildlife populations as well as severe human hardship.

Only the final stages of its southwards spread in 1896 –1897 (a decade after its beginning) are extensively chronicled. Little was known of (contemporary) disease events further north, and that the first indication of rinderpest's approach was the news of its presence on the north bank of the Zambesi River around 1893, where it was held up for three years. Eventually, infected cattle crossed the river into Zimbabwe and rinderpest reached Bulawayo in March 1896. Describing its subsequent spread the historian Edmonds writes of it "leaving a never-to-be-forgotten stinking desolation. The country was full of cattle and big game both of which the disease decimated; it destroyed about 97% of the cattle". Policies to limit the spread of the infection by the compulsory slaughter of trek oxen on the completion of journeys southwards can only have added to the mayhem. In an attempt to prevent its southern spread an east-west fence was constructed but this failed to halt transmission and the virus reached the extreme south of the country in the same year (1896).

The epidemic swept across Botswana in 1896, spreading along the transport routes towards Mafikeng, reaching South Africa within two months of crossing the Zambezi. In 1897 the Transvaal lost 980,000 head of cattle while in 1897/98 Cape Colony lost 1.3 million head. The infection reached Lesotho in 1897 and spread to Namibia in 1898. The depth of the disaster led to the birth of international efforts to find prophylactic methods of control.

Through a combination of stringent zoosanitary controls and the extensive use of a new prophylactic method based on the simultaneous administration of rinderpest immune serum and live rinderpest virus (the serum-simultaneous vaccination method), it was possible to eradicate the virus from southern Africa in a relatively short period, By 1902, Zimbabwe, Lesotho, and Orange River Colony were free of rinderpest and by 1903 Swaziland, Mozambique and Transvaal were also free and by 1905 it could not be found south of Tanzania, where it continued to circulate. In the ensuing years, the position of Tanzania with regard to control of Africa's rinderpest situation became unique with the national veterinary service assuming responsibility for preventing any repetition of the disastrous spread of rinderpest to her southern neighbours where cattle populations were again totally susceptible. Tanzania thus became "keeper of the gate" – a position she maintained for almost a century.

Having crossed Sudan within the great pandemic wave, rinderpest reached the French and British colonies of West Africa in 1890 by travelling the Sahel route from Darfur via Wadai (Chad) into the Fulani cattle of West Africa. The disease ultimately spread further west to reach Dakar in June 1892. During this initial spread, cattle losses in French West Africa and German Cameroon were said to have approached 98%. After 1891-1892, the plague seemed to disappear from the French Colonies but in 1915 a fresh wave of infection returned, again from the east. Various sanitary cordons were put in place as a means of preventing westward spread and, though these delayed the spread, they could not prevent it. Benin was infected in 1916, as was Burkina Faso and Mali. Ghana was infected in 1916. The Ivory Coast, Mauretania, and Senegal were infected in 1917 along with the Gambia and Guinea. Togo became infected in 1918. Liberia and Sierra Leone appear to have been spared involvement, however the outcome of the situation was that after 1914-18 the virus was endemic in all West African countries, and indeed throughout Central and Eastern Africa.

In North Africa, apart from Egypt which became endemically infected after 1903, Libya experienced a single outbreak in 1966 but an endemic situation never materialized.

In the aftermath of the great pandemic, for many years the cattle populations of sub-Saharan Africa remained endemically infected providing a background from which further local epidemics could arise. In contrast to the earlier successes in southern Africa, neither colonial nor newly independent veterinary services were able to do more than control the incidence of the disease across this enormous tract, mainly due to difficulties in controlling the sanitary movement of (at times infected) nomadic livestock. This situation did not change until it became apparent that an ethos of transnational co-operation was required.

In 1948 an African Conference on Rinderpest was held in Nairobi, Kenya which recommended the creation of an African Rinderpest Bureau, although this had to await the establishment of the empowering Commission for Technical Cooperation in Africa South of the Sahara (CCTA) and the Foundation for Mutual Assistance in Africa South of the Sahara (FAMA) in 1950. The Bureau was launched in 1952 as the Inter-African Bureau of Animal Health (IBAH). In 1970 this body broadened its responsibilities to include Animal Production and was renamed the InterAfrican Bureau for Animal Resources (IBAR). In 1964 Heads of State of the emergent Organisation of African Unity (OAU) determined that the CCTA would become the Scientific and Technical Committee (STRC) of the OAU with IBAR as one of its specialised units.

Given the growing understanding among Directors of Veterinary Services of the need for concerted action against rinderpest the OAU/STRC and IBAR moved to start a joint, inter-African campaign supported by Member States and International Development Partners aiming to eradicate

rinderpest through mass vaccination. This first attempt, Joint Project 15 (JP15), developed a strategy based on three consecutive rounds of annual mass vaccination in a series of phases involving different national veterinary services at different times between 1962 and 1973. JP15 demonstrated that the only way rinderpest could be eradicated from sub-Saharan Africa was through interstate cooperation and although the strategy of phases may have been fundamentally flawed, it was not until 1980 that rinderpest resumed its spread across sub-Saharan Africa, caused by the re-emergence from endemic foci in Mauretania (lineage 2) and Western Ethiopia (lineage 1). By spreading eastwards and westwards into 34 sub-Saharan countries the virus reprised much of a distribution that had occurred nearly 100 years earlier within the first African pandemic while undoing the gains of the JP15 endeavour.

In 1981 a joint AU/IBAR/FAO/OIE meeting proposed another continental campaign and a new funding initiative to tackle rinderpest. This led to the development of the Pan African Rinderpest Campaign (PARC). The PARC Project was officially launched through the signing of a Financing Agreement between the EU and the AU (represented by the Secretary General) on the occasion of the First Conference of Ministers of Livestock Affairs in Addis Ababa, on July 3rd, 1986. Additional support was provided by the Japanese Government through an FAO Trust Fund, by the British Overseas Development Agency, and by the Governments of Belgium, Italy and Nigeria. In West Africa, FAO, through its Technical Cooperation Programme, had already assisted national veterinary services to implement emergency vaccination projects in order to "put out the fires" but had enjoyed less success elsewhere.

Between 1986 and 1999 the PARC programme was active in 35 countries and involved components designed to provide emergency vaccine relief to several badly affected countries followed by protective vaccination in the remaining participating countries. At all times the programme was in concurrent operation across the rinderpest affected region of the continent. Mindful of the fact that the lack of an exit strategy under the JP15 scheme had undermined the ability to obtain international recognition of a rinderpest-free status (which a number of countries had actually achieved), while allowing the virus to persist in others without a shared understanding of the lurking threat, in 1989 the OIE moved to rectify this situation. The so called OIE Pathway provided a set of guidelines which allowed a previously rinderpest-infected country to be recognised as rinderpest-free with that status being internationally recorded. PARC fostered and promoted this protocol although it could only be activated once a country was sufficiently confident that vaccination under PARC had controlled rinderpest to the point that it was willing to stop vaccination and engage in surveillance measures that would prove that the virus was no longer circulating by declaring provisional freedom from the disease.

As shown below (Table 1), PARC member countries were somewhat hesitant to stop vaccination and move to surveillance even though, in West Africa at least, rinderpest was last seen more than 20 years ago. Effectively then, the number of years of possible surveillance was limited by the continuation of vaccination.

Country	Last rinderpest	Year stopped	Declared Provisional
	reported	vaccination	Freedom under PARC
Benin	1987	1999	no
Burkina Faso	1987	1988	Yes, 1989
Cameroon	1983	1999	no
CAR	1983	1997	Yes, 1999 zonal

Table 1. The	position of PARC countrie	es with respect to the OII	E Pathway at the end of 1999

Djibouti	1975	NA	No, historical?
Egypt	1986	1996	Yes, 1996
Eritrea	1995	1997	Yes, 1999
Ethiopia	1995	1997 but only partial	Yes, 1999 zonal
Gambia	1965	1990	Yes, 1990 but no
			progress
Ghana	1988	1996	Yes, 1997
Guinea Bissau	1986	never vaccinated	no
Guinea Conakry	1968	1996	1996
Kenya	1996 – later 2001	1998 but only partial	Yes, 1999 but zonal
Mali	1988	1997	1997
Mauretania	1988	1998	no
Niger	1986	1997	1997
Nigeria	1987	1996	no
Rwanda	1933	1997	no
Senegal	1968	1996	1997
Sierra Leone		1989	no
Somalia	1999	1998	no
Sudan	1999	1997 but zonal	Yes, 1997 but zonal
Tanzania	1997	1997	Yes, 1998 but zonal
Chad	1983	1999 but vaccinating in	Yes, 1989 but zonal
		sanitary cordon	
Тодо	1986	1998	1996
Uganda	1994	1999 but still	no
		vaccinating in some	
		parts	

Although it took two rounds of international cooperation in the costly mass application of vaccine to reach a point where rinderpest was no longer visible as a disease, the JP15 experience taught that there was a very real need to verify apparent success by the development of a substantial volume of technical surveillance data. The whole of the PARC programme was rocked by the detection in Kenya in 1994 of a Lineage 2 rinderpest virus killing wildlife, marking the apparent re-emergence of a rinderpest virus strain which had not been detected for some 30 years.

rinderpest region – the Pan-African Programme for the control of Epizootics (PACE). This programme ran from 2000 to 2006 and provided serological data and disease surveillance data allowing a number (but not all) of PARC/PACE countries to progress their interactions with the OIE to the point of obtaining recognition as rinderpest free (Table 1). In support of these activities it also developed disease data management skills and disease diagnostic skills across the region.

In the period since the end of PACE, progress in individual countries has been maintained through bilateral funding with FAO and through an EU assisted AU-IBAR programme for the so-called Somali ecosystem (SERECU). As these programmes draw to a close, AU-IBAR is concerned about the need to maintain continuing rinderpest surveillance, although a number of issues mitigate against the continued presence of rinderpest, namely:

• The presence of national serological and surveillance data from all previously rinderpest infected African countries failing to detect evidence in the years after ending vaccination and this evidence being accepted by the OIE as sound evidence of freedom from rinderpest when matched by an absence of disease reports (Dickens – it should be borne in mind that

this evidence is not shared between member states as the dossiers are not published and not in the public domain, so OIE members have to take what they are told in good faith - and it is not politically correct to questions the probity of the OIE process).

- A livestock population reverting to full susceptibility which should readily indicate the disease and likely to select for virulent rather than mild clinical syndromes.
- The absence of rinderpest in wildlife populations which were shown by PARC to be important indicator hosts.

Not withstanding the forthcoming OIE-FAO international declaration of global freedom from rinderpest in 2011, AU-IBAR is mindful of the historical failures of the past regarding the consequences of failing to detect small foci of infection in Africa. It is also aware of the enormity of the investments made by donors and national veterinary services to reach a point where the continent has probably been restored to the rinderpest-free state it enjoyed more than a century ago. Nevertheless, the livestock disease surveillance systems in Africa remain the frailest of any continent and, mindful that the high surveillance standards attained under PACE have not been maintained during the last five years, AU-IBAR now wishes to indemnify the continent against any disaster by attempting to restore them. At the same time, many African countries wish to add value to their livestock and livestock products through the development of export markets. However, international movement of livestock, meat and other livestock products is now subject to standards of disease control developed by OIE and regulated by WTO which require that these animals and products emanate from countries and zones internationally recognized as free from certain diseases not only through lack of diagnosis of these diseases but also through the negative results of auditable surveillance data. Furthermore, countries and the development partners are looking to support livestock disease control programmes that do not tackle only one disease, as was the case with rinderpest, but have the objective of controlling diseases more generally, and in this respect, of particular importance are those which are interfering with the export trade of livestock and their products. Another concern of the development partners is surveillance for, and timely control of, emerging infectious diseases (EIDs) that affect animal and human populations. Changes of the ecosystem due to population growth, economic development, increased farming as well as demand for and production of animal food, intensification of trade, of movement of people and goods and climate change pose new threats and require the world to adapt in preventing, detecting and responding to these changes and threats. EID events are dominated by zoonoses (60.3% of EIDs): the majority of these (71.8%) originate in wildlife. They are increasing significantly over time (Jones et. al, 2008). The past decades' increase in emergence or re-emergence of infectious disease, mostly coming from animals and due to the ecosystem changes mentioned above (Garrett 1994, De Salle 1999, Gibbs 2005, Glenn et.al. 2008), call for a more integrated approach to these components.

2. Descriptive Risk Analysis of the Residual Threat of Rinderpest following official declaration of World Eradication

2.1 Preamble

The OIE pathway culminating in each country's declaration of freedom from infection already specifies criteria that, if met, render the risk of continued existence of rinderpest virus negligible. This descriptive analysis is therefore a discussion of 'what's the worst that could happen? - and how might we protect against it?'

We identify two broad risk issues:

- 1. risks that might remain *despite* the OIE pathway being complied with, and;
- 2. risks that might remain because for whatever reason some countries did not follow the pathway correctly or the pathway has not delivered the confidence it was designed to do.

This analysis deals with issue (1).

Responsibility for risk issue (2) has effectively been taken by OIE/FAO within their decision-making process culminating in the decision to make the announcement of World eradication. (it appears to me that there is a finite possibility that FAO will not be in a position to join OIE in this announcement as they do not seem interested in obtaining and presenting the data on which a report could be based) Furthermore, it is the case on the ground that after some considerable time nowhere in the world have we seen rinderpest come back after being declared gone. This is taken as clear demonstration that the programme of clinical followed by serological surveillance prescribed in the OIE pathway has performed as it was designed to do, and therefore the likelihood of risk issue (2) being significant is negligible.

It also follows from this that when considering risk mitigation measures against risks under issue (1) there is little value in continuation of formal serological surveillance. It can be argued that the serology has already done its job and arrived at its conclusion at the end of the OIE pathway and declaration of freedom. Thus, in the analysis below we focus on strengthening syndromic surveillance as a risk mitigation measure. Continued sero-surveillance for rinderpest has little ongoing value for the livestock keepers, whereas syndromic surveillance linked to differential diagnosis and possible remedial action against other diseases as found, does.

2.2 Perceived hazards/threats of continued rinderpest activity

1. Wild rinderpest virus persists:

a. As subclinical/mild disease in areas where serological surveillance has been incomplete for reasons such as insecurity and uncontrolled transboundary movements of livestock.

b. Deep frozen in Veterinary Laboratories in pathological specimens or as tissue culture isolates.

- 2. Vaccine virus persists:
 - a. Deep frozen in national, regional or field veterinary laboratories.
- 3. Threats to cattle from other morbilliviruses (other viruses emerge/adapt to fill niche left vacant by rinderpest eradication).
 - a. PPR jumps species to cattle;
 - b. novel morbilliviruses.

These threats are described in the tables below...

2.3 Descriptive analysis of threats associated with risk issue (2)

1a	
Hazard characterization	Rinderpest persists as subclinical/mild disease / most likely lineage 2 in this scenario
<u>Evidence</u>	All lineages can 'go mild' under conditions of long-term endemicity. It is well discussed by Roeder, Taylor,& Rweyemamu (2006).
	This may apply to the Somali ecosystem, the last place rinderpest virus was isolated (and it was lineage 2).
	Taylor (1986) describes evidence that in certain conditions both lineage 1 and 2 viruses can loose virulence in cattle and cause only mild or sub-clinical disease.
	"The famous pandemic that started in Ethiopia in 1887 had passed through Sudan, Northern Nigeria and had reached Senegal in 1902 and died out. A second wave moved over much the same ground in 1915 but was well observed. This virus was probably lineage 2 because we have a lineage 2 from Nigeria in 1958. What is interesting is that during the course of the epizootic, the virus at the leading edge so to speak was highly virulent but the virus residues remaining behind were noticed to be losing virulence.
	Egypt could go several years without cases and then be caught up in an epizootic. In Egypt in 1984 I isolated a virus from a feed lot, which turned out to be lineage 1. In cattle that I inoculated the clinical signs were described as mild.
	Peter Roeder found accounts in the far east suggesting that the Asian virus can also decrease in virulence - in other words they all can." Taylor W. P. (pers. comm.)
	Barrett <i>et al.</i> (1998) reports that lineage 2 was detected in East Africa after apparently circulating in cattle undiscovered for ~30years. Species of wildlife acted as sentinels after clinical disease remained unreported in cattle until PDS was carried out (Mariner and Roeder, 2003).
	Representative rinderpest virus isolates have been shown in experimental inoculations to cause mild but detectable disease in cattle and fatal disease in several wildlife species (Wamwayi <i>et al.</i> , 2002). Outbreak investigations (Kock <i>et al.</i> , 1999), laboratory studies with local isolates as well as participatory epidemiological (Mariner and Roeder, 2003) and serological investigations have indicated that buffaloes, lesser kudu and warthogs are the main wildlife species involved with cattle in a multi-host system of transmission. Conventional wisdom has been that cattle are the principal maintenance host in the multi-host system. Wildlife populations, although severely affected when outbreaks occur, are believed to be tangential in terms of virus maintenance within the ecosystem.

1a	
risk factors what are the factors that	Areas that experienced long term endemicity are more at risk. Mild strains were first recorded in Tanzania in the 1950s after the virus had been endemic for 50 or more years. Similarly in Somalia. In Egypt mildness was also associated with long term residency. Similar circumstances existed in Vietnam and Cambodia.
increase or	Two of the three African stories are associated with pastoralists.
decrease the likelihood of this happening?	Pastoral herds need to be of sufficient size to maintain cycle of virus transmission for long term. In mathematical modelling studies (Mariner <i>et al.</i> , 2010) cattle systems of four communities of 2,500 head each were able to support long term transmission that extends beyond the duration of most blanket vaccination programs.
	Places where vaccination campaigns historically had patchy coverage, due to remoteness and/or conflict are therefore most at risk of persistence of virus circulation.
	A pocket of cryptic virus would always show up serologically – therefore ongoing (after 2009/2010) persistent foci are only likely to exist in areas where sero-surveillance has been incomplete.
	The selection pressure for a change in virulence would be entry to large susceptible populations which exist now. Arguably this happened in Tanzania in the early 1980s with Somali virus that had drifted south. It happened in Egypt.
where?	Areas of Africa where there exists the necessary mix of risk factors i.e.:
Given the risk	 large enough populations of cattle – probably large pastoral herds;
factors described, are there places	 history of sub-optimal vaccination campaigns;
(geographic areas)	history of incomplete serosurveillance.
or situations (e.g. cattle systems) where the risk is greater?	East Africa (Barrett <i>et al.</i> , 1998) more specifically the Somali ecosystem? / In affected and recovered cattle / in areas where serological surveillance has been incomplete NOTE: where there has been adequate sero-surveillance this would have detected serological evidence of circulating disease no matter how mild or sub-clinical " <i>The Somali ecosystem in East Africa is the only area of concern as a possible focus of infection remaining in the world</i> ." (Mariner <i>et al.</i> , 2010). The affected portions of the Somali ecosystem consist of southern Somalia and the semi-arid regions of northeastern Kenya (Mariner and Roeder, 2003; Tempia <i>et al.</i> , 2003). The more northerly portion of the ecosystem, the Ogaden in Ethiopia, northern Somalia and Somaliland have been free of evidence of infection based on results of repeated serologic surveys (Mariner <i>et al.</i> , 2010).
	Mariner and Roeder (2003) report the results of participatory disease searching (PDS) that were successful in describing occurrence of mild rinderpest (rinderpest-compatible events) in cattle of Somali herders that would explain how the virus was maintained in cattle during the years when no clinical cases were reported or discovered by sero-surveillance.
<u>risk assessment</u>	We consider this threat to be largely hypothetical. The OIE pathway followed before declaration of freedom precludes continued persistence of active foci. In areas such as Southern Sudan and the Somali Ecosystem serological surveillance has been supplemented by participatory disease searching before declaration of freedom has been made.
	A bigger risk is from stored virus being used in unauthorized and unsupervised animal experimentation in poorly secured facilities (see below).

1a	
risk mitigation options	Continued serosurveillance is too expensive and not sustainable the very reason this risk may exist is that serosurveillance has not been effective in the past therefore an alternative strategy is needed.
recommendations	Experience from the circulation of mild virus in the past shows that pastoralists knew what was going on. The Masai used to come into Arusha and report mild rinderpest in case anyone was bothered but by the way they were not. At least they reported. In Somalia-Ethiopia Jeff Mariner found that the herders knew all about what was going on but didn't bother to report – or had no way to do so.
	Participatory Disease Searching (PDS) has been proven to be effective (Mariner et al., 2003)
	However, for a sustainable strategy the focus will need to be wider than rinderpest alone. Therefore a syndromic surveillance system is recommended with focus on more than one syndrome, such that other diseases of importance to livestock owners are dealt with.
	Some wildlife species are more acutely affected by strains that are mild in cattle and therefore act as sentinels – buffalo were sentinels in 1994 – also lesser kudu and eland (Barrett, 1998) therefore wildlife surveillance may be useful
	In mathematical modelling studies (Mariner et al., 2010), it was a common finding that the prevalence of infection was well below 1% of the population. This suggests that it is very unlikely that randomized clinical surveillance, at any achievable, or affordable, level will detect rinderpest. Further, the low annual mortality (<1%) is unlikely to provoke alarm on the part of farmers or veterinarians. This indicates that passive reporting systems may be less effective in detecting mild rinderpest in the Somali ecosystem. Only surveillance programs that reach deeply into the communities, such as participatory disease surveillance programs (Mariner <i>et al.</i> , 2003), or so-called 'zero reporting' (Cameron, 2009) have any real chance of finding active outbreaks.
	Cameron (2009) believes that passive surveillance outweighs all other surveillance techniques and provided there is a connection between the owners and the vet services and the vet services transmit information then you have a very sensitive system with the proviso that the population is unvaccinated.
	On balance, what is needed is a syndromic surveillance system where the onus is on livestock owners to report to veterinarians, but where veterinarians play a very active role in informing livestock owners of the syndrome case definitions and also actively interact with livestock owners in order to maximise reporting.

1b	
Hazard characterization	Virus persists Deep frozen in Veterinary Laboratories in pathological specimens or as isolations in tissue culture
evidence	It is known that these materials exist.
risk factors what are the factors that increase or decrease the likelihood of this happening?	The key issue here is how cattle might be exposed and infected from this source Factors would include poorly controlled laboratories Accidental release of material from the laboratory

1b	
where? Given the risk factors described, are there places (geographic areas) or situations (e.g. cattle systems) where the risk is greater?	Wherever cattle populations exist close to veterinary laboratories that handle RP pathological samples.
risk assessment	This is an unquantifiable, but present, risk that requires mitigation.
risk mitigation options	The obvious thing is to destroy all the samples where virus may exist.
recommendations	

2a	
Hazard characterization	Vaccine virus remains that <i>could</i> return to virulence
<u>evidence</u>	Vaccine stocks may remain deep frozen in national, regional or field veterinary laboratories. While vaccine strains of virus pose less of a risk of re-emergence of rinderpest disease, there has been some evidence that, very rarely, vaccine strains of rinderpest virus may return to virulence.
	Russian vaccine caused disease on three occasions (Peter Roeder pers. comm.). There is no concrete evidence that Plowright's vaccine ever did this but it cannot be ruled out. There has been no resolution of the various reports of Kabete O sequences from samples taken from sick animals in East Africa. One of the reports relates to an outbreak in Tanzania in the course of which 13 animals died so there was something unusual going on, best thought of as vaccine reversion.
	This might be explained by the fact that vaccine strains have not been cloned. Therefore, a vaccine could be composed of viruses of varying pathogenicity in which viruses with very low pathogenicity, selected by the attenuation process, predominate. It has been proposed that if the vaccine has been subjected to improper storage, or mishandled in some way, the opportunity might arise for selection of virulent virus at the expense of the mild strains in the vaccine.

2a	
risk factors what are the factors that increase or decrease the likelihood of this happening?	The key issue here is how cattle might be exposed and infected from this source Factors would include poorly controlled laboratories Accidental or malicious release of material from the laboratory
where? Given the risk factors described, are there places (geographic areas) or situations (e.g. cattle systems) where the risk is greater?	Wherever cattle populations exist close to veterinary laboratories that handle RP virus or that keep vaccine
risk assessment	While vaccine strains of virus pose less of a risk of re-emergence of rinderpest disease, there has been some evidence that, very rarely, vaccine strains of rinderpest virus may return to virulence.

2a	
<u>risk mitigation</u> options	The obvious strategy is to destroy all the virus except any that is need which should be kept in one place along with any vaccine stocks / seeds.
recommendations	If there is to be 'extra' PDS surveillance around the Somali ecosystem (for the threat of cryptic foci) then it makes sense to have any laboratory virus / vaccine stock also in this area, where the extra surveillance acts as a safeguard against accidental release.
	Virus destruction
	It is anticipated that there will be an international announcement regarding the eradication of field rinderpest virus some time during 2011. Whereas FAO and the OIE may press for the subsequent destruction of rinderpest stocks not being held for research purposes, once stocks are registered on the FAO database their actual fate will be determined by national governments. Nevertheless it is anticipated that the AU will work together with FAO and the OIE in seeking the voluntary destruction of stocks of virulent and attenuated viruses. The Joint Division is in favour of surrendering African rinderpest virus stocks to a central holding unit within Africa. However, any viruses that are retained in a national research laboratory must be sequenced so that any subsequent virus escape can be fully back-traced.
	Where a country wishes to make a voluntary but certified destruction, the Joint Division is prepared to assist in this activity, in collaboration with the AU, the FAO EMPRES GREP and possibly the OIE in so doing.
	It will be for the AU to determine if it wishes to limit the number of research establishments holding rinderpest viruses.
	Rinderpest antigen in ELISA kits
	The positive controls for the current rinderpest/PPR immunocapture ELISA kit contain live attenuated rinderpest and PPR viruses. In their present configuration these kits would not be acceptable in Africa once a declaration of eradication has been made. Therefore, these antigens need to be replaced with materials made with recombinant protein technology which presents no technical problems. The only issue relates to the inclusion of new kit definitions in the OIE Manual of Diagnostic Tests and Vaccines which requires that a validation exercise is undertaken. The Joint Division is prepared to undertake this exercise together with the FAO and OIE Reference Laboratories for Rinderpest and PPR.

3a and b Hazard characterization	Threats to cattle from other morbilliviruses (other viruses emerge/adapt to fill niche left vacant by rinderpest eradication): a. PPR jumps species to cattle b. novel morbilliviruses
evidence	In this respect, the southward spread of ppr virus currently occurring in Africa and the risk of it establishing in other species than sheep and goats, e.g. large ruminants and wildlife. The risk of other morbilliviruses establishing in cattle as canine distemper virus has established in lions for example. It is proposed that when animal and human populations reached a critical size some sort of proto-rinderpest virus evolved to become rinderpest and possibly spread to humans to become measles. It is not known if any such proto-morbillivirus still exists and could re-evolve into a pathogen for cattle, or whether an existing fully evolved morbillivirus virus such as PPR could assume the same role. At the present time there is no understanding of any incidence of non-rinderpest, non-PPR morbillivirus infections in cattle in Africa but what is almost certain is that for the first time ever the world large ruminant population is totally susceptible to rinderpest.

3a and b	
risk factors	Poorly understood.
what are the	
factors that	
increase or	
decrease the	
likelihood of this	
happening?	
where? Given the risk factors described, are there places (geographic areas) or situations (e.g. cattle systems) where the risk is greater?	Particularly areas where PPR is known to be a problem and where small ruminants, cattle and/or wildlife are mixed
risk assessment	In the post rinderpest era there is an unquantifiable risk that an existing morbillivirus such as PPR may gain access to cattle (which are susceptible) or one of several wildlife species which are also susceptible. In addition there may be as yet unrecognised morbilliviruses circulating in African livestock populations, the dissemination of which had been blocked by previous rinderpest vaccination, and which could exploit the growing number of rinderpest susceptible cattle.
risk mitigation options	Within the proposed strengthening of a laboratory network in west and east Africa, a collaborative monitoring project will be established with the FAO-IAEA Joint Division to ensure the existence of reference facilities and back-stopping within each network.
recommendations	

2.4 Other threats considered and disregarded

During early discussions in this analysis we identified a 'hypothetical' threat that **Rinderpest** virus may persist in affected and recovered cattle. This is contrary to the accepted view that immune responses of recovered animals totally eliminate the virus (as shown by many pathological studies in the 1960s), but viral RNA has been said to persist in recovered animals providing periodic expression of an antigen which gives continued stimulation to the immune system which may explain why one successful vaccination of an animal provides lifelong immunity.

We regard this threat as purely theoretical and it has never been seen in real life. If it exists it can only threaten where there are cattle still alive in areas that had outbreaks in the past. This narrows down the areas of possible concern to those that have had active rinderpest disease outbreaks within the lifetime of current cattle populations – e.g. within the last 10 years... since 2000. According to data in Table 1, only Kenya reported disease since 2000, though reasonable doubt perhaps remains over other countries in the Somali ecosystem. This threat would at any rate be effectively mitigated against by the same measures targeted against threat (1a).

2.5 Conclusions

The descriptive QRA shown above concludes that:

- The threat that rinderpest persists as subclinical/mild disease is largely hypothetical. The OIE pathway followed before declaration of freedom precludes continued persistence of active foci.
- The threat that virus persists deep frozen in veterinary laboratories in pathological specimens or as isolations in tissue culture is an unquantifiable, but present, risk that requires mitigation.
- The threat that vaccine virus remains that *could* return to virulence is a theoretical possibility only.
- In the post rinderpest era there is an unquantifiable risk that an existing morbillivirus such as PPR may gain access to cattle (which are susceptible) or one of several wildlife species which are also susceptible. In addition, there may be as yet unrecognised morbilliviruses circulating in African livestock populations, the dissemination of which had been blocked by previous rinderpest vaccination, and which could exploit the growing number of rinderpest susceptible cattle.

The key recommended responses to these threats are, broadly:

- 1. A surveillance strategy that would be sustainable in the post-rinderpest world, yet would be effective at detecting any re-emergence of rinderpest or rinderpest-like syndromes, and;
- 2. A programme to remove existing rinderpest viruses from all but essential and carefully controlled locations.

A rinderpest exit strategy combining these two elements is described in more detail below.

3. Relevance of proposed actions

3.1 Need for a rinderpest exit strategy

With regard to rinderpest, while it is believed that rinderpest virus no longer circulates in African livestock and wildlife populations, virulent and attenuated virus strains remain sequestered in laboratories in frozen pathological material, as isolates, and as stocks of vaccine. AU-IBAR will propose a risk reduction strategy aimed at removing the threat of the virus escaping from research laboratories through the destruction of all such stocks. However, should a member state consider further research absolutely necessary, AU-IBAR will insist that it is undertaken within an approved BSL3 security level laboratory and under international oversight. Such a unit would be required to report its holdings of virulent virus and protocols of proposed experimentation. It would not be allowed to retain vaccine virus seed stocks.

These considerations would equate to Africa's rinderpest exit strategy and are more fully discussed below.

3.2 Disease surveillance

3.2.1. Introduction

African countries are realizing the potential extra value of their livestock populations if a disease free status is obtained which allows them to export. Indeed, Botswana and Namibia, through establishment of disease free zones, have exploited this export potential for many years.

In Africa, rinderpest re-emergence has occurred under a variety of circumstances. In the 1980s there was a failure to appreciate the dangers of known foci of infection which remained after the JP15 campaign ended and which eventually re-entered the nomadic cattle criss-crossing the Sahelain region of the continent. In the 1990s the virus that re-emerged appeared to have remained in a cryptic state for some 30 years but had more likely evaded surveillance in a remote part of East Africa where it had undergone a series of virulent to avirulent cycles well recognised by the animals' pastoral owners.

The small number of African countries that have still to be recognized by the OIE as being rinderpest-free in accordance with the conditions for surveillance laid out in the Terrestrial Animal Health Code are unlikely to impinge on the epidemiology of virus survival (e.g. Liberia) and it is increasingly clear that these conditions will be met in time for there to be an international global announcement in 2011 that rinderpest is no longer a circulating virus, although some strains will remain in research facilities and/or vaccine storage facilities.

In India, the post-eradication era has now included 15 years of routine disease surveillance and reporting and with no reoccurrence of the disease the continent is considered secure from rinderpest. Vaccine is no longer manufactured and the only virulent strain remaining is held in a high security facility. However, due to the long time scale to produce results in parts of Africa, the post-eradication era is only now beginning and prudence requires an exit strategy built around sound continued high quality disease surveillance based on the accumulation of data on the incidence, epidemiology and differential diagnosis of diseases causing the stomatitis-enteritis but failing to confirm rinderpest the level of confidence in its inability to reappear will grow.

 A proposed syndromic surveillance programme will not only support control of diseases affecting export trade and control of two important zoonoses, but also ensure vigilance regarding rinderpest disease so, in the unlikely event of an outbreak, early warning, coupled with contingency plans and emergency preparedness (which includes immediate access to the vaccine in the vaccine bank proposed above), will enable rapid stamping out and return to a disease free status.

3.2.2. Syndromic surveillance

The first steps towards controlling and preventing the diseases of livestock affecting trade, and also to control zoonotic EIDs, is a surveillance system that is networked for exchange of disease information and a diagnostic network that ensures investigation of field surveillance results and confirms and shares the diagnoses with quality control and assurance.

It is proposed that this can be accomplished through the institution of a syndromic surveillance programme designed to find and differentiate the diseases restricting the export trade of ruminant livestock and their products, restore surveillance standards, restore disease informatics, develop databases on transboundary animal diseases across the region, develop laboratory networks and promote further wildlife surveillance.

The following three syndromes are proposed:

- 1. Stomatitis-enteritis syndrome or rinderpest-like conditions which include, besides rinderpest, the trade restricting diseases PPR and FMD, and also MCF, IBR and BVD/mucosal disease included for differential diagnosis purposes.
- 2. A pneumonia syndrome to capture the trade restricting pleuropneumonias (CBPP and CCPP) and for differential diagnosis, pasteurella pneumonia, maedi visna and Jaagziekte.
- 3. An abortion syndrome to capture the trade restricting diseases brucellosis and RVF. With respect to these diseases, as well as having a major constraint on export trade, they are also important zoonoses and surveillance for these diseases will be important to human health as well as livestock health and trade.

The technical content of a syndromic surveillance programme will be developed by international consultants and AU-IBAR and its introduction to national veterinary services will be through AU-IBAR who will assume responsibility for back-stopping the standards of surveillance over the next five years. Data management will be standardised and the regional results will be used by AU-IBAR to determine regional disease trends and formulate control policies. In this context AU-IBAR will attempt to retrieve the epidemiosurveillance routines conducted under the PACE programme¹. National surveillance budgets will be provided, routed through AU-IBAR.

There is a need to sustain and refine disease surveillance systems which should include the introduction of the syndromic surveillance concept to aid in capturing the especially dangerous pathogens which contribute to the syndromes. The syndromic surveillance programme will be concentrated in the region of Africa most recently infected with rinderpest, i.e. the sub-Saharan

¹ One of the criticisms of the PACE programme was that, while it introduced good surveillance, there was little follow up of surveillance results through control activities which targeted the constraints to animal health that were revealed.

region, and should include those countries with large ruminant populations that are interested in the development of export markets for them. The countries in sub-Saharan Africa where cryptic rinderpest was most recently discovered are those in Eastern Africa within the EGAD and EAC Regional Economic Communities. They have large cattle populations and are very interested in the export of ruminant livestock and their products.

Syndromic surveillance must be carried out in cattle, sheep and goats. However, wildlife are regarded as highly sensitive indicators for the continued presence of rinderpest in cattle because of the severity of their reactions even to strains that only produce mild clinical signs in cattle (and which are therefore difficult to diagnose). Among a group of ultra sensitive wildlife species (buffaloes, giraffe, warthog, eland and kudu) buffaloes play a particularly important role by virtue of their relatively close contact with cattle and the fact that die-offs in buffaloes are relatively easily observed. This species is also regularly surveyed numerically so population crashes are also relatively easily observed. In addition, as mentioned above, more than 70% of EIDs are emanating from wildlife and they can also harbour other trade-related TBDs, for example FMD.

Components to monitor sensitive wildlife population numbers will be included and hunting activities will be used to collect and test serum from any target species becoming opportunistically available. Novel methods of sampling wildlife populations will be explored.

Features to be included across the region designed to discover, monitor and analyse the trade related syndromes and minimise the risk of failing to find rinderpest are:

- Strengthening the use of disease information databases and analysis within a GIS environment
- Introduction of veterinary investigation protocols with defined sampling protocols
- Use of participatory techniques in disease investigation to enhance and verify sensitivity of veterinary investigations and passive reporting
- Define and introduce appropriate diagnostic algorithms with emphasis on cost effectiveness (including morbillivirus diagnostics)
- Institutionalise risk-based active surveillance in wildlife by mapping of wildlife populations and density, and identifying strategic surveillance and sampling sites
- Conduct risk analysis on results of passive surveillance and on epidemiological and ecological information
- Map livestock movements (pastoral and value chains) and, after the risk analysis, follow up with targeted surveillance, including use of participatory disease search techniques: there is need for a training programme to set up these procedures
- Through IBAR, raise awareness of CVOs to the issues relating to discovered distribution of the trade related diseases and the finalisation of GREP and the need to maintain vigilance for rinderpest
- Promote commodity based accreditation of livestock products by evaluating risk factors associated with particular livestock commodities destined for domestic and international markets and possible measures to ameliorate identified risks; provide scientifically sound product quality documentation in respect of animal and human pathogens.

Within the syndromes to be investigated, individual case definitions will be used to define the nature of the aetiological agent. Case definitions will include the following:

- Species affected
- Duration of illness
- Epidemiological criteria
- Numbers and condition of animals affected
- Clinical observations
- Use of rapid field (penside tests)
- Laboratory diagnostic confirmation.

Case definitions will allow for a graded interpretation by the investigating team:

Suspect cases meet the clinical and epidemiological criteria. All cases reported that meet the suspect case definition must be investigated through the national surveillance programme resources. A typical information flow is that the farmer informs the field veterinarian who then informs the district veterinary department, which will then inform the relevant Government authorities and/or the relevant institution. The aim should be to mobilise an investigation team within 24 hours.

Probable cases are suspect cases which had been clinically and epidemiologically investigated. They meet the clinical case definition and some additional criteria such as positive rapid field (pen side) test and epidemiological criteria but have not yet fulfilled the criteria for a confirmed case. Clinical samples will be collected for laboratory confirmation from all probable cases.

Confirmed cases meet the clinical and epidemiological criteria and have been confirmed by laboratory tests. The definition includes the criteria rendering a probable case into a confirmed case.

All suspect, probable and confirmed cases and the results of the case/outbreak investigations and laboratory investigations should be recorded in the disease information database.

As an example, rinderpest, case definitions are shown in Appendix 1.

3.2.3. Training and training modules

AU-IBAR will work closely with FAO and OIE to develop appropriate standard training modules for application by member states through national training courses financed within the scope of the present project. On-going surveillance/disease investigation will be financed at national level.

3.3. Back-stopping emerging morbillivirus threats

In the post rinderpest era there is an unquantifiable risk that an existing morbillivirus such as PPR may gain access to cattle (which are susceptible) or one of several wildlife species which are also susceptible. While rinderpest vaccination was widespread, exposure to PPR was unlikely to result in infection but with the withdrawal of rinderpest vaccine this situation has changed and PPR infection of cattle will be an increasingly common event. In general, they do not exhibit clinical signs and are unlikely to be virus transmitters, however this situation does not always apply to young stock and the chance of PPR being transmitted between cattle and thereby gaining in virulence for cattle could be a possibility. The same scenario is more likely to occur through transmission of PPR among the many highly susceptible game animal species followed by transmission back to cattle.

In addition, there may be as yet unrecognised morbilliviruses circulating in African livestock populations [or indeed in any livestock population], the dissemination of which had been blocked by previous rinderpest vaccination, and which could exploit the growing number of rinderpest susceptible cattle.

Any changes in PPR pathogenicity would be noted within the passive surveillance system but within the proposed strengthening of a laboratory network in East Africa, a collaborative monitoring project will be established with the FAO-IAEA Joint Division to ensure the existence of reference facilities and back-stopping to minimise the threat of failing to recognise the emergence of a new morbillivirus threat.

3.4. Complementary actions

3.4.1. Retention of virulent rinderpest stocks

During the course of the proposed project AU-IBAR will independently act in pursuit of several associated risk reduction issues. At this time it is expected that these actions will be jointly promoted by AU-IBAR in collaboration with FAO and OIE.

Within the likely global post-eradication situation, rinderpest virus may continue to exist within national high security research laboratories where the existing stocks will be regarded as national property and come under the responsibility of the appropriate national authority. However, in the event of a security breakdown, an accidental escape or malicious release of the virus and its re-introduction to a totally susceptible cattle population could lead to catastrophic results. By mid 2010 OIE-FAO questionnaires will have been circulated, seeking to establish a database of retained rinderpest virus strains including vaccines and possible infectious material. The responses will be deposited with the FAO-IAEA Joint Division (Vienna) in the form of an international holdings and sequences rinderpest database. In the event of a virus escape the database will help to pinpoint the source of the problem. In 2011 a series of OIE and FAO resolutions will bind members of both Organisations to retain all rinderpest strains and other infectious material in high security facilities (BSL3 level laboratories or equivalent). Any rinderpest vaccine manufacture, including safety testing, would also be undertaken in a high security laboratory (BSL3 or equivalent) but subsequent vaccine storage could be at a lower security level.

The AU-IBAR considers that as far as Africa is concerned, the risk of an escape from a high security facility should be reduced to nil by the pursuit of a continent-wide non virus retention policy. Accordingly, once the response to questionnaires has been completed, the AU-IBAR will press Ministers to order the destruction of any remaining virus stocks. In addition and on behalf of the international community, FAO and OIE will be asked to establish the principle of international oversight and regulation of facilities holding rinderpest viruses [including vaccine stocks] in the post-declaration period.

It is expected that, in support of the international community, FAO and OIE will ensure the maintenance of an international rinderpest reference laboratory capable of providing confirmation of any suspect samples submitted to it and by virtue of sequence analysis, of pinpointing the most likely source of infection.

3.5 Vaccine Bank Contingency Planning

Under a global contingency plan to be developed by FAO, AU-IBAR will propose the maintenance of a rinderpest vaccine bank for the five years following an announcement of global eradication from the field. During that time disease surveillance for rinderpest will be continued within the syndromic surveillance strategy proposed above. After that time, and depending on the outcome of the AU-IBAR risk reduction strategy aimed at the destruction of all virulent rinderpest stocks in Africa, the vaccine bank might be destroyed or renewed. Beyond that point a vaccine virus seed stock would be retained by PANVAC (in anticipation that it will have a BSL3 laboratory and the approval of the Government of Ethiopia).

Under the contingency plan a rinderpest vaccine bank will be produced by PANVAC within its BSL3 facility and held in readiness for any emergency situation, again subject to the approval of the Government of Ethiopia.

In this context PANVAC proposes to assume ownership of a stock of rinderpest vaccine seed consisting of live attenuated Kabete O virus at around the 100th passage level in calf kidney cells (classic Plowright vaccine). It also proposes to manufacture five million doses of this vaccine and retain it within PANVAC in Debre Zeit, All seed storage and manufacturing will be undertaken within a BSL3 level facility. In the event that these security arrangements cannot be forthcoming, PANVAC will outsource storage and manufacturing to alternative, approved facilities. Ownership of the vaccine will however, reside with AU-IBAR-PANVAC for immediate release within a confirmed rinderpest emergency situation.

3.6 Diagnostic Capacity Contingency Planning

It is assumed that FAO/OIE will put in place a global rinderpest contingency plan and will designate International BSL3 Reference Laboratory/ies able to confirm and identify as to likely source, any rinderpest virus recovered from a field situation.

In addition, AU-IBAR will designate two regional diagnostic reference laboratories for rinderpest, one in west and central Africa and one in east Africa. Each reference laboratory will be incorporated in the OIE twinning programme and will exist as a centre of excellence with respect to the diagnosis and differential diagnosis of diseases causing stomatitis-enteritis (the condition to be identified by syndromic surveillance).

The Reference laboratories will work in conjunction with a network of national laboratories that will work with national surveillance teams providing them with primary diagnostic assistance and a source of material to be submitted for confirmation by the regional reference laboratory.

3.7 Lessons Learnt

With the apparent success of the rinderpest eradication programme, there have been calls for a new international initiative to identify the next priority transboundary animal disease (TAD) for progressive control or eradication including suggested strategies and methodologies for control and/or eradication and pathways to monitor progress. While CBPP appears to be a candidate, among the stomatitis/enteritis group, PPR and FMD are strong candidates. All of these diseases are important with regard to international trade in livestock and their products.

There has been no meaningful review of the lessons that should be learnt in relation to rinderpest eradication and the different models that have been applied in different parts of the world as well as in Africa. At this point it would seem appropriate for the AU and development

partners to initiate a review of the major issues such as the need for increased reliance on a legislative approach to zoosanitary controls and more appropriate use of vaccination in relation to epidemiological understanding, modelling, limited time scales, socio-economic benefits and more flexible project management. The results of such a review should be in the form of a published report.

3.8 Generic national contingency plans

Generic national contingency plans should include early warning systems to alert veterinary services and track rumours of rinderpest re-emergence. Risk-based surveillance in ecosystems with former low incidence should be introduced and regional training on differential diagnosis of diseases causing stomatitis/enteritis syndrome should be undertaken to create and maintain expertise on diseases which include rinderpest so that experts can react in case of any outbreak.

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5. Appendix CASE DEFINITION EXAMPLE: STOMATITIS-ENTERITIS SYNDROME (which would capture rinderpest)

<u>Targeted Species:</u> Cattle, buffalos, yaks, small ruminants, wildlife and zoo animals of the order Artiodactyla.

<u>Suspect case:</u> A high morbidity outbreak in a herd or flock of the targeted species of a contagious disease in which fever is associated with ocular and nasal discharges, signs of drooling and lameness alone or with abortion and death of young animals. (per-acute rinderpest is able to cause the sudden death of bos taurus dairy cattle before clinical signs develop – apart from pyrexia)

<u>Probable case:</u> A group of a targeted species in which individual animals meet the suspect case definition and, in addition, have at least two of the following clinical signs: erosions in the oral cavity, diarrhoea/dysentery, dehydration, and death; and/or positive rapid (penside) field test results for viral antigen in one or more animals that meet the suspect case definition. Laboratory confirmatory tests might be conducted in country or at a regional or global level reference laboratory.

Confirmed case:

- Demonstration of viral antigen via immunocapture ELISA, or detection of viral RNA by PCR.
- If these tests are negative and animals have not been vaccinated, detection of rising titres of specific humoral antibodies in paired samples by competitive ELISA can be indicative of natural infection.

If all tests are negative, samples should be examined for other elements of the differential diagnosis.