Joint FAO/IAEA Programme
Nuclear Techniques in Food and Agriculture

The IAEA's contribution to the eradication of rinderpest

In the fight to control and eliminate rinderpest, the International Atomic Energy Agency (IAEA) supported its Member States through two mechanisms: Coordinated Research Projects (CRP) for the development, evaluation and validation of nuclear and nuclear related technologies, and Technical Cooperation (TC) projects for the transfer and sustainable implementation of these technologies. These early and rapid animal disease diagnostic mechanisms were implemented through the Joint FAO/IAEA Division of the Nuclear Sciences and Applications Department and the Department of Technical Cooperation.

To support the rinderpest control and eradication efforts in Africa and Asia, in 1987 the respective internationally funded programmes and IAEA's CRP and TC projects were launched. In order to maximize efficiency, these projects cooperated with the IAEA's laboratory in Seibersdorf in developing nuclear and nuclear-related immunological and molecular diagnostic tools. These capacity building efforts allowed 40 Member States to properly diagnose rinderpest and monitor the vaccination status of their national herds.

What is rinderpest?

Rinderpest, arguably the most devastating infection of cattle, was for centuries a major cause of famine and poverty. However, by 2010, some 176 countries and territories worldwide had been declared free from the disease and field operations discontinued. In 2011 the FAO and World Organisation for Animal Health (OIE) declared the disease officially eradicated from the world. This great achievement comes 30 years after the World Health Organization (WHO) declared that smallpox was eradicated, the only other viral disease to have been eliminated from the world.

Rinderpest (also known as cattle plague) is a highly contagious viral disease of cattle, buffalo, yak and several wildlife species, and has caused immense livestock losses throughout history. It was first described scientifically in Europe by Prof Bernardino Ramazzini in 1712. It caused major cattle losses in Northern Italy until Dr Lancisi, at the request of Pope Clement XI, suggested the 'stamping-out' policy, which meant the slaughter of all infected and exposed animals in order to control the disease. This remained the procedure of choice over the next three centuries. However, the advent of steam-powered ships enabled greater international trade in livestock and accelerated the spread of infectious diseases such as rinderpest. The most devastating effects of rinderpest were experienced in Africa in 1884, when cattle imported from India to Eritrea rapidly spread the disease into different parts of the continent, killing millions of cattle and wild animals and causing widespread starvation. Nevertheless, the stamping-out policy eventually controlled the disease.

Developing a suitable rinderpest vaccine and establishing an effective diagnostic capacity

The concept of preventing rinderpest was first attempted in the Netherlands in 1774 by using a rudimentary form of vaccination to induce immunity in at-risk livestock. The breakthrough, however, came in India in 1928 when a vaccine developed in goats was found to confer immunity in cattle. This vaccine was used extensively in Asia and Africa but occasionally caused the disease. In 1957, advances in virology allowed for a safer tissue culture vaccine, which was developed by Walter Plowright in Kenya.

This vaccine was cheap to produce and easy to assess for potency and safety. Granting life-long immunity through a single injection, it quickly became the vaccine of choice for controlling rinderpest globally. In 1990, the development of a heat stable version of the vaccine in Niger improved the efficiency of the vaccination campaign, especially in remote areas.

Historically, vaccination campaigns did not monitor the effectiveness of the intervention and thus the first major control campaign in Africa, the Joint Project 15 (JP 15), did not control the disease effectively. Central to a disease control campaign, is its diagnostic and vaccine strategies. The Joint Division brought evaluated and validated diagnostic tools to the Member States. The Pan African Rinderpest Campaign (PARC) requested that the vaccination's effectiveness be monitored using serological tools based on an indirect enzyme linked immunosorbent assay (ELISA) developed in 1985. Although superior to the laborious serum neutralization assay, its only shortcoming was that a country had to validate the ELISA for its specific cattle population. The development of a competitive ELISA in 1991 eliminated this problem and thus a common quality assurance procedure could be employed in all laboratories. In order to verify the absence of the rinderpest virus in the protected populations, an antigen detection ELISA (immunocapture ELISA) capable of screening large numbers of samples was validated and introduced to the veterinary laboratories. This monoclonal antibody (MAb) based test system uses a capture antibody, which recognizes both rinderpest and the peste des petits ruminants (PPR) virus and a second MAb specific for either to differentiate between them.

Controlling the disease by vaccination

In the 1930s, country-specific mass vaccination campaigns were used to reduce the incidence of rinderpest. The first internationally backed attempt to eradicate rinderpest from Africa - JP15, ran from 1962 to 1976 and was led by the Inter-Africa Bureau of Animal Resources of the Organization of African Unity (IBAR/OAU). This multi-donor campaign covered 22 countries at a cost of US $50 million. Although JP15 was highly successful in controlling outbreaks, the vaccinations stopped too early, leaving two foci of infection in Mali and Ethiopia. This led to a resurgence of the disease in the late 1970s and early 1980s. The disease quickly spread in West and East Africa and eventually over much of sub-Saharan Africa, peaking in 1983. The pandemic killed millions of cattle and wildlife and thousands of farmers and herders lost their livelihood.

PARC was initiated in 1987 by IBAR/OAU, mainly funded by the European Community. It covered 34 countries in sub-Saharan Africa with the goal to finally eradicate rinderpest from Africa. In order to ensure success PARC sought clear scientific evidence that national vaccination programmes were indeed effective and that sufficient animals were immune to the virus. Similar coordinated programmes were proposed for Asia – the West and South Asia rinderpest campaigns, respectively. The West Asia rinderpest campaign was supported by UNDP from 1989 to 1994 but left no coordination mechanism to take its place upon termination. The South Asia rinderpest campaign never materialised, although individual country programmes in Bhutan, India and Nepal achieved great success with support from the European Community. Following the success of these programmes in eliminating the virus, FAO launched the Global Rinderpest Eradication Programme (GREP) in 1994 in close association with OIE, IAEA and other partners to help eradicate rinderpest from the world.

Monitoring the efficiency of the vaccination campaigns

Central to the success of the rinderpest vaccination campaign was the sero-monitoring, using the internationally validated and standardized FAO/IAEA ELISA kit, which was supplied by the World Reference Laboratory for rinderpest, Pirbright, UK and the FAO/IAEA laboratories in Seibersdorf, Austria. Although vaccination was at the heart of eradication efforts, it would not have been as successful without the development and deployment of diagnostic tests to determine where the disease was, where it was spreading to, which animals were infected and/or at risk and, most importantly, to monitor the efficiency of the vaccination campaigns. Historically, an immune response to rinderpest vaccination was assessed by the virus neutralization test. This tissue-culture based test is relatively expensive, time consuming, and is not easily standardized, making it difficult to implement in many veterinary laboratories. Therefore, it was considered unsuitable for detecting antibodies to the virus in the blood samples required for monitoring vaccination campaigns or for use in epidemiological studies, and for detecting the virus itself.

The IAEA responded to diagnostic needs by introducing ELISA tests, to PARC and eventually all GREP countries, including those in West and South Asia. These nuclear related serological tests were initially developed using radioisotope labelling and tracing techniques, but were replaced with enzyme labelling and tracing to circumvent the disadvantages of the short half-life and higher technical proficiency requirements of radioisotopes. Additionally, the new generation ELISA tests could be used in relatively simple veterinary laboratories. For GREP, it was clear from the outset that the ELISA was an ideal tool for effective serological surveillance to confirm that sufficient animals were being protected by vaccination to ensure elimination of the virus from national herds.

Once the assay met these international requirements, it was adapted to a kit format linked to a quality assurance programme and provided with a standardised set of laboratory equipment for routine use. These kits (separate ELISA for the detection of antibodies and immunocapture ELISA for the detection of antigen of rinderpest virus and PPR virus) were developed, standardized and validated by the Joint Division and its associated laboratory at Seibersdorf working in close collaboration with Pirbright, UK and World Reference Laboratory for PPR at the Centre de coopération internationale en recherche agronomique pour le développement (CIRAD), Montpellier, France. These kits contained all the required reagents and a standardized protocol, making ELISA the prescribed test for international trade. The organizations also agreed on how to interpret the results and how these could be used to determine the effectiveness of vaccination. This required computerisation of the data collected and analysis of the results.

Support was provided to the laboratories and scientists working in rinderpest affected countries principally through CRPs and TC projects. The CRPs provided research contracts to scientists in veterinary laboratories in FAO and IAEA Member States, creating a network of laboratories and individuals that could test and assist in refining, validating and fully standardising the ELISA under different conditions and work situations. The first CRP (1987-1990) was funded by the Swedish International Development Authority (SIDA) and was mainly concerned with the introduction and routine use of an FAO/IAEA ELISA based system for rinderpest sero-monitoring. Research contracts were awarded to 17 laboratories involved in the diagnosis of rinderpest and the CRP was augmented by a number of IAEA TC projects. This pooling of resources optimized the support to the scientists carrying out rinderpest sero-monitoring. The Joint Division took the lead in developing and distributing fully validated and standardised indirect ELISA kits and materials to all participating countries in the network, and in providing the necessary equipment and training to African laboratories and staff to ensure a uniform approach throughout PARC countries. National and regional TC projects were implemented at the request of Member States to support government efforts in strengthening and enhancing veterinary laboratory diagnostic capabilities, training qualified staff and supporting networking and partnerships within the region.

A follow-up CRP (1991-1994), also funded by SIDA, saw the introduction of the competitive rinderpest ELISA test that was both more sensitive and that could distinguish between antibodies to rinderpest and those against the closely related PPR virus – attributes that meant it could be used as a surveillance tool within national rinderpest campaigns. The FAO/IAEA/SIDA/PARC CRP on rinderpest sero-surveillance phase II covered 17 African countries and included research agreements from Pirbright and the University of Reading in the UK and technical support from IEMVT in France. Quality assurance systems were also put in place, standardized sampling frameworks were designed, and computer software was developed for data management and analysis.

When support from SIDA ended in 1994, the capacity to monitor national rinderpest

Contribution of IAEA to rinderpest eradication

The IAEA has supported the programme to eradicate rinderpest for 25 years. The chart below highlights a few specific events over this timeframe. The Joint Division's contribution to the global effort included: developing a network of laboratories to diagnose the disease, organizing training workshops, supplying diagnostic kits and manuals, providing technical backstopping, producing international guidelines and technically supporting regional TC projects in Africa and Asia.

- **1986:** The Joint FAO/IAEA Division incorporates ELISA into its CRP on animal health. Technical cooperation support for the efforts to eradicate rinderpest commences in 20 national TC projects and seven regional projects in Africa and Asia to be funded over the next 25 years.
- **1987:** First research coordination meeting of the CRP on disease diagnosis using ELISA includes seven projects on rinderpest. PARC initiated with a central requirement for a suitable low cost diagnostic technique to monitor large numbers of samples.
- **1987-1990:** A CRP involving 14 countries, 'The Sero-monitoring of rinderpest in Africa', using ELISA initiated by FAO/IAEA in conjunction with PARC, and with financial assistance from SIDA.
- **1991-1994:** A CRP, 'Sero-surveillance of rinderpest and other diseases in Africa using immunoassay techniques, Phase II', initiated by FAO/IAEA/SIDA/PARC, establishing antibody monitoring facilities in 21 laboratories.
- **1997-2000:** A CRP, 'Rinderpest sero-monitoring and surveillance in Africa using immunoassay technologies' under FAO/IAEA/PARC established in 20 African countries.
- **2001:** Technical information document, 'Performance indicators for rinderpest Surveillance'.
- **2003:** Technical information document, 'Definition of technical guidelines and standard operating procedures for the surveillance and testing of rinderpest as part of GREP'.
- **2011 onwards:** Rinderpest virus sequestration.

Countdown of the eradication of rinderpest

1712: Rinderpest is described by Bernardino Ramazzini.
1715: Lancisi advocates the 'stamping-out policy' that is still valid today.
1762: The world's first veterinary school opens in Lyons, France to teach the Lancisi principle for rinderpest control.
1924: OIE is created as an intergovernmental body to combat rinderpest.
1928: J.T. Edwards discovers that vaccination with attenuated virus confers life-long immunity to rinderpest.
1950: Inter-African Bureau of Epizootic Diseases is founded to eliminate rinderpest from Africa.
1957: W. Plowright and R.D. Ferris develop a stable, safe and inexpensive vaccine against rinderpest.
1962: The JP15 is initiated in 22 African countries.
1987: PARC begins operations in 34 African countries.
1994: GREP is initiated by FAO and backed by OIE, IAEA and other partners to eradicate rinderpest by 2010.
2001: Last reported cases of rinderpest.
2006: Vaccinations stopped and provisional freedom from rinderpest announced.
2010: End of field operations. FAO declares end of GREP field operations.
2011: Joint FAO and OIE freedom from rinderpest declaration.

vaccination programmes by detecting antibodies had successfully been established in 17 countries of sub-Saharan Africa. This test proved to be more robust under field conditions than the indirect ELISA. The third CRP under the auspices of an FAO/IAEA/PARC epidemiology project was funded by the European Union and ran from 1997 to 2001. Its objectives were to consolidate support for the surveillance and diagnosis of rinderpest through the sero-monitoring network, which had by that time been established in 22 African countries, and to provide essential information on the epidemiology of rinderpest. Many of the institutes awarded research contracts also benefitted from IAEA support through national TC projects, and where national TC projects had ceased operation, support was provided through IAEA regional projects. One example was the large regional project in Africa which began in 1995, and throughout the duration of PARC provided regional experts, many opportunities for group and individual training courses and fellowships as well as critical laboratory equipment and infrastructure.

Similar regional projects in Asia proved indispensible for supporting GREP. In planning and implementing these projects, the high level of teamwork between counterparts and IAEA staff within the TC Department and the Joint FAO/IAEA Division ensured that inputs of hardware, reagents and guidance on technical issues were both appropriate and timely.

What next?

The OIE developed a set of recommended standards for epidemiological surveillance for rinderpest (the 'OIE Pathway') that governed the actions of Member States wishing to demonstrate that they are free from infection. A declaration of eradication will not put an end to the commitment of international bodies and veterinary authorities in fighting this or any other major transboundary animal disease. Now that rinderpest vaccination has ceased, laboratories are being requested to sequester their remaining virus stocks in order to eliminate any risk of laboratory 'outbreaks'. At the same time, it will be necessary to determine where rinderpest viruses, sera and vaccine banks can be contained. A surveillance strategy will also need to be devised so that early warning systems remain in place and laboratory capacities are sufficient to tackle other major transboundary diseases such as foot and mouth disease (FMD) and PPR. Indeed FAO, OIE and IAEA have already signalled their intention to assist countries to tackle FMD in a similar manner, and a programme for the progressive global control and elimination of FMD is currently under way.

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