VET nuus•news

Februarie / February 2026

The Monthly Magazine of the SOUTH AFRICAN VETERINARY ASSOCIATION
Die Maandblad van die SUID-AFRIKAANSE VETERINÊRE VERENIGING



THEME

Foot and Mouth Disease (FMD)

CPD

Behavioural disorders of backyard poultry

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February 2026

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Info: https://vetlink.co.za/saeva-congress-2026/

March 2026

Wildlife Group of the SAVA Congress 2026
12 - 14 March
Venue: 26° South Hotel , Muldersdrift, Gauteng
Info: https://vetlink.co.za/wildlife-group-2026/

NVCG: The Veterinary Masterclass: Neurology
17 - 18 March
Venue: Protea Hotel Stellenbosch (Techno Park)
19 - 20 March
Venue: Johannesburg, Midrand Premier Hotel
Vetlink: https://vetlink.co.za/nvcg-roadshow-march/
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April 2026

SAVA Oranje Vaal Congress
17 - 18 April
Venue: Khaya Ibhubezi, Parys
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May 2026

UP: Beyond Basics: Mastering the Cardio-respiratory Patient: A Structured Clinical Approach
11 - 12 May
Venue: Premier Hotel, Midrand, Gauteng
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June 2026

13th Int Crustacean Society Mid-Year Meeting
01-04 June
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Dear members,

The Work Begins



The moment we have been waiting for with bated breath has arrived. The Minister has finalised the Council process and announced the newly appointed Councillors. Congratulations to all.

Council carries a collective responsibility to provide strategic direction, safeguard professional integrity, and advance the interests of both the veterinary and para-veterinary fraternity in a rapidly evolving and highly pressured environment. We extend our confidence and trust to the newly appointed Councillors to exercise sound judgement, choose ethical leadership, and show courage in making decisions that serve the greater good of the profession and the country.

As this term of office commences, it is clear that the real work now begins—work that will require unity of purpose, principled engagement, and a steadfast commitment to science, transformation, and public service.

This edition of VetNews reflects on the lessons emerging from the Foot and Mouth Disease (FMD) response and highlights the critical importance of preparedness, collaboration, and trust. FMD continues to test our resilience as a profession and that of the livestock sector as a whole.

The Ministerial Task Team on FMD and Other Diseases has developed a Foot and Mouth Disease Vaccination Strategy, which seeks to provide a structured, risk-based, and scientifically defensible framework for the use of vaccination as a disease-control tool. In addition, the Minister has announced that he is pursuing the declaration of a national disaster. Such a declaration would enable the mobilisation of national resources, strengthen coordination across the security and economic clusters, and facilitate urgent measures to prevent further spread while mitigating the socio-economic impacts on the livestock sector and associated industries. We look forward to this possible declaration.

That said, veterinarians remain at the forefront of this response, from surveillance, diagnosis, and vaccination to movement control, compliance enforcement, and risk communication. This work is being undertaken under difficult conditions, with limited resources, intense public scrutiny, complex stakeholder dynamics, and the ongoing need to balance animal-health imperatives with socio-economic realities on the ground.

Of equal importance is the need to support the well-being and professional integrity of veterinarians and animal-health professionals who stand on the front line of this crisis. We must stand united, strong, ethical, science-driven, and kind to one another during this period.

One of the key areas of concern raised by colleagues, particularly within the small-animal clinician community, relates to negative perceptions created by certain pet-insurance advertisements and their impact on the veterinarian–client relationship. We are pleased to report that engagements have already taken place with some pet-insurance providers, with encouraging and constructive outcomes.

In addition, the Board has begun engaging with SAVA affiliates to collectively shape a fair and sustainable way forward. These discussions will be further strengthened during the upcoming Board of Directors Strategy Session later this month, with a clear emphasis on a coordinated, veterinarian-profession-led approach to affiliate engagement.

The past few months have been a profoundly difficult time for all of us at SAVA House. We mourn the loss of Elize Nicholas, one of our longest-serving colleagues, whose dedication and service left an indelible mark on the Association. A hybrid celebration of her life, hosted by SAVA, will be held at VetHouse on 18 February 2025. Further details, including the virtual participation link, will be shared in due course.

We also bid farewell to another deeply valued member of the VetHouse family, Jonas Mabaso. For many years, Jonas served as our gardener, handyman, security guard, and trusted all-round support. He was a constant and reassuring presence and will be remembered with great affection. He passed away on 21 January 2025 and will be sorely missed by all who knew him.

Colleagues, in closing, I wish to acknowledge concerns that have been raised regarding the moderation of posts originating from non-affiliated veterinary forums.

These actions are not intended to censor differing views, but rather to protect the rich legacy of SAVA and to ensure that the Association remains guided by its own mandate and objectives, as defined by and accountable to its members.

As we move forward, let us continue to engage constructively, with respect and purpose, as we strengthen our Association and advance the profession together.

Groetnis!
Ziyanda

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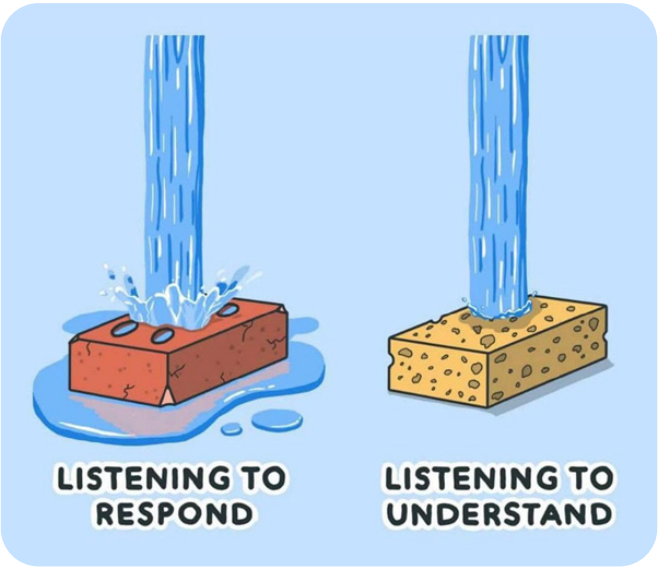
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Editor's notes / Redakteurs notas

The year with more than a bang.



2026 was declared by my daughter as the year of no comfort zones. Little did we know how the first month would turn out for us. Being in the upper North-east of the country, we are prone to the effects of tropical storm activities and, peculiarly enough, always around the time the schools are planned for opening. This year, the warning came for a deep low trough sweeping over Mozambique. No tropical cyclone. I keep an eye on several weather apps as well as a group on Facebook called Severe Weather and Information Centre South Africa (SWAICA). In the week leading up to the big rain, there were forecasts as many as there were forecasters. A quick 40mm on the Wednesday before the big rain pointed out a couple of water flow-off challenges. We spent the next two days clearing up and opening up spillways. Saturday, we stocked up on essentials, and on Sunday, the rain started. First slow, but then picked up. Our usually dry riverbed changed into a raging 2.5m deep watermass. We are lucky to be positioned over 4m from the sandbed and were never threatened with flooding through the house. But the power of the noisy water was something to behold. Lower in the same river system, a bridge was partially washed away, and many people, like us, were trapped. Eventually, after 2 weeks, we ventured off our property. The driveway was the first hurdle, as it was waterlogged and trapped vehicle tyres like a suction device. We had just less than 400mm in the week of the big rain. But the consistent rain even before that week soaked the soil, and it is still seeping out in many places. We were very blessed not to suffer any damage.

When the topic for this month was set more than a year ago, I would never have thought it would be in the middle of one of the biggest ruminant crises of the modern world in our country. It has turned into a bit of a civil war. All parties have very valid questions, suggestions, accusations, and some mud-slinging. Where does the veterinarian stand, and how can SAVA serve their members in this very sensitive time? There is the issue of vaccines. The shortage, the type, the availability and source are all contentious issues. The fact that the strain types were not submitted for a long time influenced the entire process.

Understandably, the veterinarians with clients affected by this outbreak of FMD want the best for their clients, including securing vaccines, quarantine measures and keeping the shelves in shops full. These animals are the lifeblood of the farmers. These animals are also the source of meat and milk that supply the consumers. On the other hand, there are the rural, informal and small-scale farmers who are looked after more by the state than by the private veterinarian. Both are important, and both need to be served in the best way possible.

It will take Solomon's wisdom to manage this outbreak. I can only pray that good judgment Is practiced and all possible different measures will be implemented. That there will be transparency, honesty, action and tolerance from all parties. May the flood of Foot and Mouth Disease run off sooner rather than later, be reduced to a trickle, and then dry up completely. Some documentation and views are shared this month.

Some very positive news is the appointment of the new Veterinary Council Board. Two of our SAVA presidents serve on the new Board, and many have before; obviously, SAVA is a good breeding ground for Veterinary leaders. We wish them all the best and wisdom for the difficult and important decisions that will come before them.

Please note that what I stated in these notes is just my observations from discussions and what I see on the news and social media. Included is a very funny piece about a dog and a rock monitor. Enjoy the giggles.

Have a good one!

Andriette

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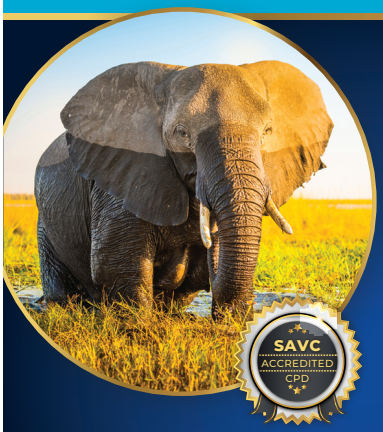
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Minister Steenhuisen announces the new South African Veterinary Council

The Minister of Agriculture, John Steenhuisen, has formally constituted the new South African Veterinary Council (SAVC).

The term of office of the newly formed council will commence on February 1, 2026 and will run until January 31, 2029.

Steenhuisen said the new council brings together a broad and diverse range of expertise drawn from across the veterinary and para-veterinary professions, academia, regulatory practice and law.

"I am confident that this council is fit for purpose and its composition reflects a careful balance between professional experience, technical expertise and independent oversight," said Steenhuisen.

The department said that views and representations were received from across the sector during this period, the minister applied his mind independently to the recommendations before him and was guided at all times by the requirements of the legislation and the long-term interests of the professions and the public.

The announcement of the council comes after a consent order was granted in the North Gauteng High Court last year after Steenhuisen had rejected the election of the new council in August and ordered that the election be rerun.

In terms of the consent order, the election results were allowed to stand, and the court instructed Steenhuisen to appoint a council in terms of agreed timelines.

The minister confirmed that the council is constituted as follows:

Ministerial Designees:

Officer of the Department of Agriculture (veterinarian): Dr Motsisi-Mehlape	**Veterinarians or veterinary specialists designated from elected members: Dr R Mulder; Dr B Lourens; Dr JA Fraser**
Person with knowledge of law: Adv. R Maruma	**Veterinarians or veterinary specialists designated from nominations: Dr NP Moswa-Kato; Dr L Kgatswetswe; Dr J van Deemter; Dr N Mnisi**

Non-veterinarian designated from nominations: Prof. S Willows-Munro	**University-nominated veterinarian (University of Pretoria): Prof. V Naidoo**

Appointees as nominated and/or elected:

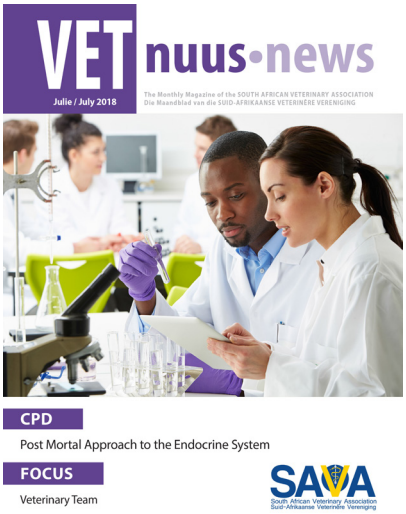
Veterinarians elected by their peers: Prof. JP Schoeman; Dr P van der Merwe; Dr J Basch	**Animal Health Technician: Mr T Serebolo**
Laboratory Animal Technologist: Ms B Mogodi	**Veterinary Technologist: Mr LS Mokami**
Veterinary Nurse: Sr E Bornman	**Veterinary Physiotherapist: Ms J Hager**

South African Veterinary Association nominee: Dr L de Bruyn

The minister expressed his confidence that the newly constituted council will execute its duties without fear or favour, and with the independence, integrity and professionalism required of a statutory regulator entrusted with safeguarding the standards of the veterinary and para-veterinary professions.

"The establishment of this council marks an important step in restoring stability, credibility and effective governance within the veterinary regulatory environment," said Steenhuisen.

The department said the induction and inaugural meeting of the new council will take place in February 2026, enabling the council to commence its work without further delay and to deal with outstanding matters inherited from the previous term in accordance with its statutory mandate.



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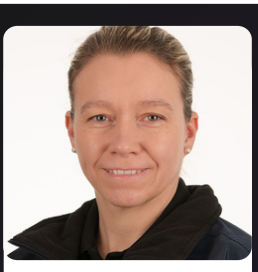
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SAVA Follow-Up Statement on Foot-and-Mouth Disease (FMD)

SAVA Calls for Stronger Ground-Level Coordination, Expanded Diagnostics and Welfare Measures to Strengthen National FMD Response

The South African Veterinary Association (SAVA), together with the Ruminant Veterinary Association of South Africa (RuVASA) and the SAVA Wildlife Group (WLG), welcomes recent steps taken towards the development of clearer national strategies to address the ongoing Foot-and-Mouth Disease (FMD) outbreak in South Africa. As a follow-up to its previous statement, the organisations reaffirm their support for a coordinated national response, while emphasising the urgent need to strengthen implementation, diagnostics, vaccination clarity, and animal welfare support at ground level.

SAVA, RuVASA and the WLG participated in a Foot-and-Mouth Disease (FMD) Information Day and Workshop held in Potchefstroom on 12 December 2025. The workshop was attended by more than 36 veterinarians in person and over 80 participants online, representing a broad range of stakeholders from the livestock and wildlife sectors.

The workshop underscored the complexity and seriousness of the current FMD situation and acknowledged the significant efforts of the Ministerial Task Team to develop and implement a National FMD Strategy. However, ongoing concerns remain regarding the growing disconnect between national-level decision-making and effective implementation at the ground level.

Participants highlighted inconsistent communication, limited consultation with key stakeholders, and the circulation of conflicting information as factors contributing to confusion, reduced compliance, and increasing frustration among livestock owners and veterinarians.
SAVA, RuVASA and the WLG expressed serious concern regarding laboratory capacity constraints, noting that delays in diagnostic testing are undermining effective surveillance, prolonging quarantines, exacerbating animal welfare challenges, and resulting in severe economic losses for affected producers. Particular attention was drawn to the urgent need for improved buffalo diagnostics, as limitations in current testing capacity and turnaround times pose significant risks to disease control efforts, wildlife management, and South Africa's FMD-free buffalo populations.

The organisations further emphasised the importance of ensuring that FMD vaccines are appropriately registered, available, and authorised for use across all affected cloven-hoofed species, including pigs, where vaccination options and clarity around usage remain limited.

In addition to disease control measures, the organisations raised serious animal welfare concerns. FMD causes significant pain, distress, and secondary complications in affected animals. Farmers are strongly urged to contact their veterinarians to assist with clinical assessment, symptomatic relief, pain management, wound care, and supportive treatment.

While vaccination remains an important component of FMD control, the organisations reiterate that it cannot replace effective local movement control, early detection, rapid response, strict biosecurity, and veterinarian-led implementation.

Issued by:
South African Veterinary Association (SAVA)

South Africa's Battle with Foot and Mouth Disease: Current Status, National Strategy, and Persistent Challenges



South Africa is in the midst of a deepening animal health crisis — one that threatens not only livestock health but also the stability of the country's agricultural economy, export markets and rural livelihoods. Foot and Mouth Disease (FMD), a highly contagious viral disease affecting cloven-hoofed animals, has persisted in multiple provinces and provoked an unprecedented multi-year response effort from government, industry and veterinary science stakeholders.

Timeline

South Africa has been dealing with a sustained Foot and Mouth Disease (FMD) crisis since losing its World Organisation for Animal Health (WOAH) free status in January 2019. Following widespread outbreaks originating in 2021/2022, the virus spread across multiple provinces (Limpopo, KZN, North West, Free State, Gauteng, Eastern Cape), with 274+ active, unresolved outbreaks reported by September 2025 and a 10-year vaccination strategy launched in early 2026.

Key FMD Outbreak Timeline in South Africa

2014 – 2019: Senzeni Zokwana serves as Minister of Agriculture.

January 2019: South Africa loses its WOAH-recognised FMD-free status, limiting international trade after Foot and Mouth Disease (FMD) was confirmed in cattle in the Vhembe district of Limpopo Province. The outbreak occurred in the high surveillance area of the FMD Free Zone, immediately adjacent to the protection zone. A total of five clinical cases were identified. The affected animals were cattle kept at rural villages with communal diptanks and grazing.

May 2019: Angela Thokozile Didiza is appointed as the Minister of Agriculture.

May 2021: An outbreak began when animals moved from Phalaborwa to KwaZulu-Natal.

Early 2022 – Oct 2024: A SAT 3 virus originated in Limpopo, causing a multi-province outbreak across Limpopo, North West, Free State, Gauteng, and Mpumalanga before being closed in Oct 2024.

May 2024: The same 2022 SAT 3 virus strain was identified in East London and Humansdorp areas of the Eastern Cape.

July 2024: John Steenhuisen is appointed as Minister of Agriculture.

July 2025: 270 FMD outbreaks confirmed across five provinces, with 249 remaining unresolved.

May - September 2025: New outbreaks emerge in previously cleared areas, with 274 active, unresolved outbreaks reported by early September 2025, primarily in KZN, Gauteng, Free State, North West, and Mpumalanga.

Nov 2025: First confirmed case in a commercial piggery (Free State), signalling an escalation and the jump to species other than cattle.

Where Things Stand:

Widespread Outbreaks and Continuing Spread

Since mid-2025, FMD outbreaks have been confirmed across several provinces, including KwaZulu-Natal, Gauteng, Free State, North West and Mpumalanga. In July 2025, the Department of Agriculture confirmed a new outbreak on a commercial farm in the Free State,

triggering quarantines, surveillance and containment measures within a 10 km radius of affected properties. As of that time, South Africa had reported **270 outbreaks across five provinces**, with **249 unresolved** and only 21 declared resolved.

Earlier in 2025, Agriculture Minister **John Steenhuisen signalled the severity of the situation**, announcing that intensified control efforts, including lockdowns of Disease Management Areas (DMAs), vaccination, surveillance and vaccine procurement were underway. (Government of South Africa). These persistent outbreaks follow long-standing outbreaks in KwaZulu-Natal and the Eastern Cape, which in previous years had already necessitated disease-management zones and strict movement controls. (SAnews)

Farmers and veterinarians describe the current crisis as among the most serious in recent memory, warning that FMD outbreaks continue to damage industry confidence and could have **long-term consequences for food security and market access**. (BusinessTech)

The Shift in Strategy: "FMD-Free with Vaccination"

In late 2025, South Africa announced a **decisive shift in national policy** for tackling FMD when Minister Steenhuisen outlined a **ten-year, science-based national strategy** to control the disease and move the country toward a recognised disease-free status.The government's approach is now centred on **vaccination as a core pillar**, rather than using movement restrictions alone.

This strategy — often referred to as **"FMD-Free with Vaccination"** — aims to **restore confidence in export markets, stabilise the R80 billion livestock sector, and align South Africa with the World Organisation for Animal Health's (WOAH) Progressive Control Pathway.** (IOL)

Under this framework:

- **Mass vaccination** will begin first in high-risk provinces like KwaZulu-Natal and Gauteng before expanding to Limpopo, Mpumalanga, North West and beyond. (Government of South Africa)
- Government and industry aim for **90 % vaccination coverage in target populations** in high-risk zones, and **100 % coverage in dairy and feedlot herds**, reducing outbreaks by over 70 % in priority areas within the first 12 months. (The Mail & Guardian)
- A phased rollout is planned, starting in early 2026, with support from both international vaccine suppliers and domestic production capacity through the Agricultural Research Council (ARC) and Onderstepoort Biological Products (OBP). (Government of South Africa)
- Strategic tools such as a **Livestock Identification & Traceability System**, developed with the Council for Scientific and Industrial Research (CSIR), are set to help monitor vaccinated animals and inform control decisions. (Business Day)

Notably, governments have procured millions of doses from external partners like the Botswana Vaccine Institute (BVI), which is supplying roughly 1 million doses per month beginning in early 2026. (African Farming)

The Ministerial Advisory Task Team, appointed to finalise implementation details, is also working on a **Section 10 scheme under the Animal Diseases Act, 1984**, aimed initially at regulating vaccination parameters within industries such as dairy and feedlots. (Government of South Africa)

Controversy and Calls for Faster Action

While industry bodies such as the **National Red Meat Producers' Organisation** have welcomed the vaccination-led strategy, expressing support for steps that could curb the outbreak, there has been notable scepticism from some farmers and analysts about the pace and implementation of the plan. (IOL)

A group of farmers and livestock stakeholders has raised concerns that declaring FMD a **national state of disaster** may be necessary to unlock additional resources, coordinate enforcement more effectively and expedite response actions. (BusinessTech)

Delays in vaccine roll-out, logistical challenges and concerns about supply reliability have also been flagged by producers, with some citing **vaccine shortages and operational inefficiencies** as ongoing obstacles in controlling spread. (Food For Mzansi)

Biosecurity, Movement Controls and Animal Welfare

Central to all FMD control strategies are **strict movement controls, enhanced biosecurity and early detection**. The Animal Diseases Act obliges owners and managers of cloven-hoofed animals to take all reasonable steps to prevent infection and spread, such as limiting animal movements, maintaining secure boundaries, and reporting suspected clinical signs immediately. (Government of South Africa)

Movement restrictions — including quarantines and controlled slaughter at designated abattoirs — remain in place in affected DMAs, and farms are urged to adopt rigorous surveillance and reporting practices. (SAnews)

Economic and Trade Impacts

FMD is not dangerous to humans, but it has **devastating economic implications** for livestock producers and export markets.

Because FMD-affected animals cannot be certified for international export, South Africa's access to lucrative markets in the EU, Asia and the Middle East has been constrained by ongoing outbreaks. (The Mail & Guardian). Loss of "FMD-free" status resulted in reduced export certifications and trade restrictions that have directly impacted farmers, feedlots and meat processors, with implications for jobs and food price stability. The national strategy aims to recover these certifications by achieving freedom with vaccination — a recognised status that could allow phased re-entry to export markets once risk is sufficiently mitigated. (IOL)

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Looking Forward: Science, Compliance and Cooperation

The success of the national strategy will hinge on:

- **Rapid and widespread vaccination**, backed by reliable vaccine manufacturing and procurement;
- **Robust enforcement of movement controls and traceability systems**;
- **Animal owner compliance with reporting and biosecurity protocols**; and
- **Continued coordination between government agencies, industry and research institutions.**

While implementation challenges remain — including logistic bottlenecks, farmer scepticism, and the complex biology of the virus across multiple serotypes — the integrated strategy represents a **more comprehensive and science-based approach** than earlier, more fragmented efforts. (The Mail & Guardian)

If effectively executed, South Africa could not only reduce the incidence of new outbreaks but also set a path toward the eventual restoration of its **FMD-free status**, stabilising the livestock sector and securing its place in international markets.

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Minister John Steenhuisen briefs the media on the national strategy on Foot and Mouth Disease containment

14 January 2026

Good morning to members of the media, our social partners, and most importantly, our farmers.

Today, I address you with a clear roadmap for the protection of our national livestock herd and the restoration of South Africa's international standing in the agricultural sector. Since losing our Foot and mouth disease (FMD) free status in 2019, our farmers have faced unprecedented challenges.

I have received many pleas for help - from commercial to communal farmers, who have borne the heavy burden of the recent FMD outbreaks in the country. We see your struggles. We understand the financial and emotional toll that the outbreaks have had on your families and your livelihoods. We remain deeply sympathetic to the hardships you have endured, however I want to assure you today that we have a plan that is both realistically achievable and technically sound. I must be frank with the nation: achieving FMD-free status is a monumental task that will not happen overnight. Our strategy will be phased over ten years, beginning with stabilisation and consolidation, before moving toward the eventual withdrawal of vaccination and final recognition of national freedom through vaccination by the World Organisation for Animal Health (WOAH). This is a long-term commitment to the health of our economy and the security of our food supply. I need to emphasise that vaccination is not a silver bullet to eradicate or manage this disease. It is merely one of the tools that can and should be used to combat FMD.

At the AFASA Leadership and Strategic Partnership Conference in November, I announced this initiative of vaccinating the national herd – starting with those areas where the biggest and most severe cases of FMD has occurred. These areas are identified through a scientific process also referred to as a heatmap. This is why it is important that outbreaks are reported to ensure that we know where the biggest areas of concern is. The Ministerial Advisory Task Team on Animal Disease Prevention and Control, led by Dr Emily Mogajane was tasked with translating the vision of "FMD Free through Vaccination" into a high-impact, actionable strategy.

This task team brings together the nation's foremost authorities in veterinary science, biosecurity policy, and livestock management to ensure a resilient and secure agricultural economy.

Representing the government:

- Dr Emily Mogajane - Chief Director: Biosecurity Coordination (Chairperson and convener)
- Dr Botlhe Modisane - Chief Director: Animal Health and Production, DoA Dr Nomsa Mnisi - Director: Biosecurity Support Services DoA
- Dr Themba Sikhakhane - Chief Director: Veterinary Services, KwaZulu-Natal Dr Bheki Cele - Chief Director: Veterinary Services, Mpumalanga
- Dr Wynton Rabolao - Director: Veterinary Services, Gauteng Dr Baratang Lubisi - Research Team Manager, ARC
- Dr Moses Mabunda - Director: Veterinary Services, Limpopo Dr Marietta Swanepoel - Deputy Director: Secretariat Support Dr Oseke Ngoveni - State Secretariat Support

Representing the private sector, we have the following specialists to provide technical depth across the entire value chain:

- Prof. Dietmar Holm - University of Pretoria, Bovine Herd Health (Academic/Beef)
- Dr Dirk Verwoerd - Specialist in infectious diseases of intensive production systems, with emphasis on vaccine development, surveillance, and diagnostics Dr Jacque Marais - Dairy industry
- Dr Anthony Davis - Milk processors Dr Adriaan Olivier - Ostrich industry
- Dr Amanda Botes - Specialist in FMD and African Swine Fever (ASF) diagnostics and molecular epidemiology
- Dr Mark Chimes - Dairy, Chairperson of the Brucellosis and Tuberculosis Steering Committee
- Dr Pieter Evans - Specialist in eradication of PRRS and ASF outbreak management Dr Shaun Morris - Feedlot Specialist

- Dr Baty Dungu - Member of the World Organisation for Animal Health (WOAH) Scientific Commission, African Union Pan African Veterinary Vaccine Centre (AU PANVAC) Steering Committee, and African Union – InterAfrican Bureau for Animal Resources (AU-IBAR) expert panel on animal health and disease control

- Dr Danie Odendaal - Ruminant Veterinarian Specialist Dr Gerhard Neethling - Export and Abattoir Specialist

- Dr Francois Maree - Specialist in vaccine design, testing, and diagnostics and Dr Livio Heath - Diagnostics, Epidemiology, and International Trade Relations.

To maintain transparency and cross-sector alignment, this task team reports directly to the Value Chain Round-Tables. This structure ensures that every stakeholder - from local producers to international trade partners - is represented in the decision-making process.

A Technically Rigorous Strategy

The strategy we are employing is not a temporary patch; it is a comprehensive control and eradication programme designed to interrupt virus transmission and protect our national herd. It is important to emphasise that the success of this strategy will strongly rely on urgent review of the legislative framework, that has to be adapted to the current emergency situation. Our plan is built on world-class technical principles:

Targeted Vaccination: We are prioritising high-risk zones, with the goal of reaching at least 80% coverage in targeted cattle populations especially the communal areas and up to 100% in feedlots and dairy cows. The objective is to reduce outbreak incidence within 12 months by more than 70% in the high-risk provinces through systematic vaccination and preserve FMD-free provinces through buffer vaccination and strict movement controls.

High-Quality Vaccines with high-potency will be used during the campaign especially, trivalent vaccines of SAT 1, 2, and 3 currently circulating in South Africa. Partnerships with global leaders like Biogénesis Bagó in Argentina will ensure that we have a reliable supply, with one million doses ready to be sent as soon as the necessary permits are issued. The company indicated that as soon as the permits are issued, they are able to supply the vaccine in the coming two weeks. We are currently preparing the application for authorisation by the South African Health Products Regulatory Authority (SAHPRA) to use an unregistered medicine under Section 21 of Act 101. The application will be filed by Monday. Biogenesis will also be able to supply an additional five million doses by March 2026.

Since the outbreak we have been procuring vaccine from the Botswana Vaccine Institute (BVI) and will continue sourcing vaccine from this institute. The BVI and the ARCI will look into the existing memorandum and complement one another to ensure that we reach the maximum vaccine coverage. Last year we received confirmation from the BVI that they can supply us with one million doses per month. Unfortunately, due to the closure of their factory for cleaning purposes they could not deliver on time. The delegation of Botswana was in South Africa yesterday and the have confirmed that they have the bulk antigen of SAT 2. This bulk antigen will be formulated to produce SAT 2 vaccine to be used in arears where SAT 2 is prevalent.

We have also secured the one necessary permit to import Dollvet vaccine from Turkey. As indicated earlier it will take us some time to contain the disease.

Locally, we are activating a local production line through the ARC and OBP, which will initially produce 20 000 doses per week , scaling up to a capacity of 960 000 doses. The ARC indicated on Monday that they can bring forward their production – which will add 12 000 doses to our vaccine pool by mid-February.

Pirbright Institute – Many calls have been made, and assumptions that we have not sent our latest strains to the Pirbright Institute. However, I can confirm I instructed the ARC to send the field strains to Pirbright as a matter of urgency.

The ARC confirmed they are currently preparing the strains to be sent to the institute.

All FMD vaccines to be used in South Africa will have full antigenic matching at Pirbright against South Africa's current field strains to allow comparison of the various vaccines; this will allow South Africa to select the best vaccines to contribute to the control of this devastating disease.

Enhanced Surveillance & Movement Control: We are strengthening our laboratory network, led by the Agriculture Research Council – Onderstepoort Veterinary Research (ARC-OVR), which will work with existing state laboratories to ensure that results are received timeously. We have started with increasing capacity at the OVR. We will implement a digital livestock and traceability system to ensure that animal movements are safe and tracked. Other simplified mechanism will also be looked into. We are currently working with the Council for Scientific and Industrial Research (CSIR) and RMIS traceability platform to implement the Livestock Identification and Traceability System (LITS) which will enhance our traceability.

With the integration of advanced technology, we are no longer fighting this disease in the dark. Through the Red Meat Industry Services (RMIS) Operational Centre, we now utilise a real-time digital heatmap to track verified cases and suspected outbreaks within a 10km radius. This work is done together with Epidemiologists from SAEHP, using resources from the equine industry.

Outbreaks

It is important to note that the current outbreak started in 2021 when animals moved from Phalaborwa to KwaZulu Natal.

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Minister John Steenhuisen briefs the media..... <<< 17

The Northern Cape is currently the only province that never reported an outbreak of FMD. Up to date we have vaccinated almost two million animals since the recent outbreaks occurred.

Details of the outbreaks :

- SAT2 FMD outbreak in KwaZulu Natal, Mpumalanga, North West, Gauteng and the Free State;
- SAT1 FMD outbreak in KwaZulu Natal;
- SAT3 FMD and SAT2 FMD outbreak in the Eastern Cape;
- The Western Cape reported one outbreak - there is a targeted active surveillance which commenced in May 2025;
- Limpopo had SAT3 FMD outbreaks on 8 properties in 2021 and recently they had three outbreaks.

I want to turn the focus now to what actions we will take in each province.

As already indicated, Kwazulu-Natal, Gauteng, Free State and North West were identified as the hardest hit provinces. Interventions include the immediate mass vaccination across affected districts, that will be repeated within three months – 100% vaccination of feedlots and dairy cows; 90% commercial and 80% of communal animals.

Areas where recurring infections occur like parts of Mpumalanga and Limpopo, where Buffalo farming is increased there will be- biannual campaigns to be launched at these border hotspots and vaccination will continue in the protection zone.

Biannual campaigns will be held in Nkomazi and Bushbuckridge with vaccination of 85% of the communal and 90% of the commercial animals. Joint wildlife surveillance and targeted vaccination near reserves will also be implemented.

Eastern Cape (Moderate–High risk) – Biannual vaccination will take place in hotspots and the establishment of a protection zone will be implemented.

In addition, we will increase surveillance in markets and slaughterhouses.

A Call for National Support

The success of this strategy relies on the cooperation of every citizen. We need our farmers to work hand-in-hand with state veterinarians, to report clinical signs immediately, and to strictly adhere to movement controls.

I want to make it clear that the detailed plan will be shared with MEC's, provincial veterinarians, Cabinet Ministers and Industry leaders. We will be depending on industry, including private veterinarians together with government to ensure implementation of the plan is executed country wide.

By protecting our national herd, we are protecting our future. I ask for your patience, your partnership, and your unwavering support as we implement this scientifically-backed plan to restore South Africa to its rightful place as a leader in global livestock trade.

Together, we can ensure a resilient and FMD-free South Africa!



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Steven De Decker graduated from Ghent University in Belgium. After graduation, he performed a rotating internship there and undertook a PhD studying 'wobbler syndrome' in dogs. This was followed by a Residency in Neurology and Neurosurgery at the Royal Veterinary College. He is
Senior Lecturer and the Head of Service of the neurology and neurosurgery team at the Royal Veterinary College. Although he is interested in all aspects of veterinary neurology, most of his research and publications focus on spinal disorders and neurosurgery.

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Foot-and-Mouth Disease Vaccines in South Africa: What's Available Now and What's Coming

South Africa continues to respond to ongoing Foot-and-Mouth Disease (FMD) outbreaks through targeted vaccination programmes and expanded vaccine access aimed at protecting livestock health, producer livelihoods, and international trade.

Current Vaccine Supplies

In recent outbreak responses, South Africa has relied primarily on emergency FMD vaccine supplies sourced from the **Botswana Vaccine Institute (BVI)**. These vaccines are formulated against the **Southern African Territories (SAT) serotypes**, which are most relevant to the regional epidemiological situation.

The vaccines currently in use are **water-based FMD vaccines**, which provide effective but relatively short-term protection, typically lasting around **four months**. This makes them suitable for outbreak control and for animals destined for slaughter in the short term, such as those in feedlots, but less ideal for long-term protection of breeding and dairy herds.

Distribution of these vaccines has been tightly controlled by the Department of Agriculture, with priority given to outbreak zones and high-risk provinces including KwaZulu-Natal, Limpopo, Mpumalanga, Gauteng and North-West. Both state-led campaigns and limited private sector access have been used to support rapid disease containment.

Limitations of Traditional FMD Vaccines

While conventional FMD vaccines play a critical role in outbreak response, they have an important limitation: once animals are vaccinated, it becomes difficult to distinguish between animals that have been **vaccinated** and those that have been **naturally infected**. This complicates disease surveillance, prolongs movement restrictions, and can delay the recovery of disease status for trade purposes.

These limitations have been a long-standing challenge for countries such as South Africa, where effective disease control must be balanced with the need to maintain transparency, confidence, and access to export markets.

What Are DIVA Vaccines – and Why Do They Matter?

DIVA vaccines (Differentiating Infected from Vaccinated Animals) are designed to overcome this challenge. They protect animals against Foot-and-Mouth Disease while still allowing veterinarians and authorities to reliably identify animals that have been exposed to the live virus.

Unlike traditional vaccines, DIVA vaccines exclude certain viral components. This means diagnostic tests can clearly distinguish between antibodies produced through vaccination and those produced through infection.

For **South African livestock management**, DIVA vaccines are particularly important because they:

- strengthen **disease surveillance and early detection**, even in vaccinated populations;
- allow for **more targeted outbreak control**, reducing unnecessary restrictions;
- support **international trade**, where proof of disease freedom is essential; and
- enable vaccination strategies that do not undermine confidence in disease reporting.

In a country managing both endemic risk and trade sensitivity, DIVA vaccines offer a practical way to improve transparency, trust, and long-term resilience in the livestock sector.

What's Expected in 2026

South Africa is preparing for the introduction of **oil-based, DIVA-compatible FMD vaccines**, expected to become available in **early 2026**, subject to regulatory approval. These vaccines are anticipated to provide **longer-lasting immunity** than current water-based formulations, making them more suitable for breeding herds and dairy operations.

The availability of DIVA vaccines is expected to be a significant step forward for the livestock industry, enabling more strategic vaccination programmes while maintaining robust surveillance and supporting the country's efforts to regain and protect market access.

Strengthening Long-Term Vaccine Capacity

Beyond immediate vaccine supply, government has indicated plans to strengthen **domestic vaccine production capacity** as part of a broader national biosecurity strategy. Expanding local manufacturing and diversifying vaccine options will be key to improving South Africa's preparedness for future outbreaks and reducing reliance on emergency imports.

Conclusion

While current vaccines remain essential for outbreak response, the introduction of DIVA-compatible vaccines will significantly strengthen South Africa's ability to manage FMD, protect trade, and build a more resilient livestock sector.

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Live-attenuated foot-and-mouth disease virus vaccine engineered by codon deoptimization induces a strong protective immune response in cattle

Sarah E. Attreed, Christina Silva, Monica Rodriguez-Calzada, Ryan D. Heimroth, Michael Oldakowski, Carolina Stenfeldt, Paul Azzinaro, Edward Spinard, Aishwarya Mogulothu, Steffen Mueller, Bruce Taillon, Jonathan Arzt, Elizabeth Rieder, Teresa de los Santos, Fayna Díaz-San Segundo & Gisselle N. Medina. **We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note that there may be errors present which affect the content, and all legal disclaimers apply. If this paper is published under a Transparent Peer Review model, then Peer Review reports will be published with the final article.**

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ABSTRACT

Foot-and-mouth disease (FMD) is a fast-spreading, economically devastating veterinary viral disease. While inactivated vaccines have contributed to FMD control worldwide, recent outbreaks in Europe and Asia highlight the need for new control strategies. Live-attenuated virus vaccines (LAV) provide strong and long-lasting protection. We previously demonstrated that deoptimization of various viral coding regions results in attenuated foot-and-mouth disease virus (FMDV). Here, an FMDV A24Cruzeiro LAV with codon-deoptimized P2/P3 regions (A24-P2/P3Deopt) and markers differentiating infected from vaccinated animals (DIVA) was tested for safety/efficacy in cattle. Animals inoculated intradermal-lingually (IDL) with 10^6 or 10^7 pfu of A24-P2/P3Deopt for safety testing exhibited no clinical signs, viremia or viral shedding for 28 days post inoculation (DPI). To assess efficacy, cattle were subcutaneously inoculated either once with 10^5 pfu or twice (0- and 14-dpi) with 10^4, 10^5 or 10^6 pfu A24P2/P3Deopt. No animal developed signs of disease post-inoculation. All vaccinated animals developed strong neutralising antibody responses that were protective against challenge with WT FMDV A24 prime-boost groups. Moreover, vaccinated sera showed strong cross-reactivity against several A strains and serotype Asia1. Our work demonstrates that codon deoptimization is a viable technology to derive novel LAV candidates that are safe, immunogenic and efficacious against FMD in cattle.

INTRODUCTION

Foot-and-mouth disease (FMD) is a highly transmissible disease of even-toed ungulates, characterised by the development of vesicles on the mouths, feet and teats of affected individuals [1]. FMD is known to affect over 70 wild and domestic species such as swine, cattle, sheep, goats and cervids [1]. Given the host range of the disease, it is of great agricultural interest around the world, particularly in pig and ruminant agriculture. FMD is one of 26 multi-species reportable terrestrial diseases for the World Organisation for Animal Health (WOAH) [2].

While mortality from FMD is low, the disease is of great economic importance as it is highly transmissible and there are restrictions on the movement and export of animal products from FMD-endemic countries. Therefore, maintenance of FMD-free status is a valuable economic asset for all countries worldwide. Foot-and-mouth disease virus (FMDV) is the causative agent of FMD and is a member of the *Picornaviridae* family along with enteroviruses such as Poliovirus. FMDV is a single-stranded, positive-sense RNA virus of approximately 8.5 kb composed of a single open reading frame (ORF), flanked by 5' and 3' untranslated regions (UTRs). The ORF is divided into four main regions: Leader proteinase (Lpro), P1, P2 and P3. Upon translation, the immature polyprotein is processed by 2A (a non-canonical protease that cleaves immature proteins by translational ribosome skipping) as well as the classical viral proteinases Lpro and 3Cpro into structural proteins—1A (VP4), 1B (VP2), 1C (VP3), and 1D (VP1)—as well as nonstructural (NS) proteins—2A, 2B, 2C, 3A, three distinct 3B genome-linked proteins (Vpg) [3], 3Cpro and RNA-dependent RNA polymerase 3Dpol.

Current control measures in FMD-free countries include culling of infected and contact animals, movement restrictions of infected and contact animals and sometimes prophylactic ring vaccination with an adjuvanted inactivated vaccine [4], which, when combined with Montanide ESSAI IMS D 12802 VG PR aqueous adjuvant, can confer protective immunity within 4 days [5]. Another candidate vaccine under conditional license in the US employs a replication-defective adenovirus 5 (Ad5) encoding only the P1 capsid, 2B and 3C protease domains [6].

While the Ad5-FMD vaccine has been shown to confer immunity in approximately 7 days, similar to the commercially available inactivated vaccine, neither confers long-lasting immunity, which is often a function of strong T cell engagement during the post-vaccination period. To address the desire for more durable immunity as well as to possibly broaden the cross-neutralisation potential of the vaccines available for FMD, other methods of vaccine preparation are being employed. One of the most successful methods for vaccination against viral infections

involves the use of live attenuated viruses (LAVs), which can replicate in the host, eliciting a more robust B and T cell response. Some of the most successful vaccination campaigns against viral pathogens have utilised LAVs, including smallpox [7] and Rinderpest [8], which were both eradicated, and the oral polio vaccine that is still part of the eradication strategy [9,10]. However, LAVs may be prone to recombination and random mutation events that can result in reversion to virulence, increasing awareness about vaccine safety. One method that has been devised to simultaneously reduce viral virulence as well as the risk of replication-driven recombination is codon deoptimization of the viral genome. Codon deoptimization (CD) and codon pair deoptimization (CPD) are strategies for virus attenuation built upon the concept that, while multiple codons exist for many common amino acids, these codons and codon pairs are not evenly employed. Rather, genomes show bias in the employment of some codons over the use of others in a species-specific manner. In CD and CPD, selected genomic regions can be rewritten in such a way as to swap out "preferred" codons or codon pairs for those less commonly encountered in the given genome. While the precise mechanisms of attenuation are unknown, it has been shown that synonymous codon substitutions can alter the co-translational protein folding mechanisms, which can increase degradation of these proteins in the cell [11].

To date, CD/CPD have been utilised in the development of a number of LAV vaccine candidates. Vaccinia virus (VV), a DNA poxvirus—which serves as the backbone to many poxvirus vaccines—was found to be strongly attenuated *in vivo* by CD and to confer strong immunity to an otherwise fatal challenge of VV [12]. When applied to the Zika virus, a positive-sense ssRNA virus of the *Flaviviridae* family, CPD viruses exhibited reduced virus replication fitness and some induced sterilising immunity in a mouse model, protecting against lethal challenge as well as vertical transmission during pregnancy [13]. An engineered deoptimized respiratory syncytial virus (RSV), a negative-sense ssRNA virus of the *Pneumoviridae* family, resulted in minimal viral shedding when administered to African green monkeys that then produced a strong humoral and cellular immune response [14]. A construct with CPD targeted only to the surface glycoprotein G and F ORFs showed reduced viral replication fitness and temperature sensitivity. However, some viral fitness was regained over several passages, along with defective helper particles [15].

A 2021 paper by Chen et al. also found that a CPD RSV virus regained replication fitness under many serial passages, particularly through mutations in the phosphoprotein gene [16]. A more recent RSV vaccine candidate with CPD applied to seven of the virus's eleven ORFs demonstrated retained temperature sensitivity over many passages and strong humoral immunogenicity in hamsters and protective efficacy as measured at three days post-challenge (dpc) [17].

CPD has also been utilised in other picornaviruses, such as poliovirus. In one such study, where the capsid region was CPD, highly modified viral clones exhibited lower RNA yield and specific infectivity [18]. Furthermore, the authors found that reduced fitness was well-maintained over up to 25 serial passages, or about 50 viral replication cycles. In a separate study, Mueller et al. found that, for equal doses of viral particles, pathogenicity to the brain was significantly decreased in CPD infectious clones with the most replication-deficient phenotype [19]. In a study of Enterovirus A71, a picornavirus that causes hand-foot-and-mouth disease, CD of the P1 region, along with a high-fidelity 3D polymerase, resulted in a genetically stable viral clone with decreased virulence and maintained antigenicity [20]. Finally, work from our own lab has consistently revealed slower growth kinetics and reduced virulence in CPD and CD

FMDV across several serotypes and strains. When CPD was applied to the capsid (P1) region of FMDV A12 and the resulting attenuated strain tested *in vivo*, mice were able to tolerate inoculation doses up to 10,000 times higher than the WT dose needed to cause disease, yielding a safety margin of at least 4 logs, while the safety margin of A12 WT virus was only a single log [21]. In a study by Medina et al., where CPD was applied to the P1 region of A24 and Asia1, attenuated virulence and growth kinetics were observed in a serotype-independent manner both in mice and swine, though protection against later parental challenge was not observed in swine [22]. In another study, various strains were derived where CD was applied to one or both of the P2 and/or P3 regions of the FMDV A24Cruzeiro genome, then tested for safety and efficacy in mice and swine [23]. The P2-deopt and P2/P3-deopt strains were found to have reduced virulence in mice and elicited strong neutralising antibody titers in both mice and swine. While the A24-P2/P3Deopt strain was also found to have reduced virulence in swine, as was found with the CPD A12-P1Deopt, A24-P1Deopt and Asia1-P1Deopt strains [22], inoculation was found not to confer protection against later homologous challenge.

In the current study, we evaluated the FMDV A24Cruzeiro with P2/P3 CD region strain (heretofore A24P2/P3Deopt) for both safety and efficacy as an LAV vaccine candidate in dairy cattle according to WOAH requirements. We demonstrate that the margin of safety in cattle for this strain is at least 3 logs, with a prime-boost schedule of 10^4 pfu/animal conferring protection against later homologous challenge, while an intradermal-lingually (IDL) dose of up to 10^7 pfu (the highest dose tested) resulted in neither clinical disease nor viremia or shedding in safety-tested cattle. Additionally, sera from inoculated cattle displayed broadly neutralising capacity against a range of A topotypes and even the Asia1 serotype, suggesting the potential of such a vaccine during an outbreak scenario.

RESULTS

Safety Study

We decided to pursue the use of A24-P2/P3Deopt as an LAV in cattle after observing significant attenuation during prior *in vivo* routine titration according to WOAH standards. To first test the safety of this candidate LAV, we inoculated cattle with A24-P2/P3 Deopt intradermal-lingually (IDL). The WOAH requires that for inactivated virus vaccine potency assays, all control animals must develop typical FMD lesions in 3 out of 4 feet within 8 days of inoculation with 10,000 median bovine infectious dose (BID_{50}) of WT FMDV [24], equivalent to 2.36 x 10^4 pfu of our WT A24 strain. In the present study, none of the animals IDL inoculated with either 10^6 or 10^7 pfu of A24-P2/P3Deopt virus developed vesicular FMD lesions or fever (Fig 1). Mild, transient lymphopenia—a characteristic feature of FMD [25]—was observed in three out of four control (wild-type inoculated) cattle at 2 dpi (#74, 75 and 76) and in one out of four cattle in the 10^7 pfu dose group at 1 dpi (#02).

During FMD progression in cattle, FMDV is typically shed in abundance as early as one day after infection with the WT virus, which can lead to the rapid direct contact spread of the virus in both wild and domesticated herds of susceptible animals. In our study, following inoculation with FMDV A24 WT, we studied viral shedding (Fig 2) by analysing viral burden of nasal swabs by virus isolation, observing a peak at 10^4 to 10^7 pfu/ml and by RT-qPCR up to 10^8 to 10^9 genome copy particles (GCP)/ml. By contrast, no viral shedding was detected via either method following inoculation with either IDL dose of FMDV A24P2/P3Deopt. When we assessed viremia by virus isolation in A24-WT inoculated animals, we found peak titers of about 10^3 to 10^4 pfu/ml and 10^5 to 10^7 GCP/ml when assessed by RT-qPCR. By contrast, we were unable to isolate infectious virus from the sera of cattle inoculated with either dose of FMDV A24P2/P3Deopt virus. Rather, we observed only "RNemia" ranging between 10^2 and 10^5 GCP/ml in 3 out of 8 A24-P2/P3Deopt-inoculated animals (#61, 64 and 04), while RNemia was below the lower limit of detection for the remaining 5/8 FMDV A24-P2/P3Deopt- inoculated animals.

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FMD vaccination prevents disease through the elicitation of a strong neutralising antibody response in cattle. We observed that, following inoculation with the highest doses of A24-P2/P3Deopt, cattle in the 10^7 pfu dose group developed neutralising antibody titers at about the same rate as those animals administered the WT virus, with both groups reaching the protective threshold of 1.2 for cattle by 4 dpi (Fig 3A). Meanwhile, those animals administered 10^6 pfu of A24-P2/P3Deopt developed neutralising antibody titers more slowly, reaching a protective threshold by 7 dpi and reaching a maximal titer somewhat lower than the other two treatment groups.

A two-way ANOVA mixed effects model revealed highly significant effects for treatment group (P<0.0001), time point (P=0.0001) and treatment group x time point interaction (P<0.0001). Post-hoc comparisons by timepoint revealed significant differences between WT and 10^6 pfu administered cattle at 7DPI (P=0.0225), 14 (P=0.0009) and 21 dpi (P=0.0068). A statistically significant difference was also detected between WT and 10^7 pfu administered cattle at 14 dpi (P=0.0359). Additionally, significant differences were detected between 10^6 and 10^7 pfu inoculated cattle, at 7 (P=0.0192), 14 (P= 0.0213) and 21 dpi (P=0.0025).

To determine the DIVA compliance of this vaccine, we next tested the sera at 0 and 21 dpi for antibodies against FMDV nonstructural (NS) proteins $3B_2$ and $3D^{pol}$ (PrioCheck®ELISA, Applied Biosystems), which had been mutated to serve as a DIVA marker in A24-P2/P3Deopt as in Uddowla et al (2012) [26]. We found that while 10^6 pfu A24-P2/P3Deopt-administered animals remained free of any such antibodies, one animal from our maximum safety dose, 10^7 pfu dose group, developed these antibodies, leaving the DIVA status of this vaccine in doubt (Fig 3B). Prior to inoculation, however, the virus was sequenced, and the presence of the DIVA marker previously described [26] was confirmed.

Our safety assessment of the FMDV A24-P2/P3Deopt strain reveals a virus that is safely administered even via IDL at high doses in cattle without risk of development of clinical disease, though its DIVA compliance needs further investigation.

Efficacy Study

Having confirmed the safety of FMDV A24-P2/P3Deopt at high doses in cattle, we then moved on to assessing the effective dose range for preventing clinical disease upon homologous challenge. For this efficacy study, we utilised four groups of four Holstein heifers each and subcutaneously (SQ) administered FMDV A24-P2/P3Deopt as either a single dose (10^5 pfu) or a two-dose series administered at 0 and 14 dpi (10^4, 10^5 and 10^6 pfu). A fifth group of 4 heifers was subcutaneously administered PBS at 0 dpi (Fig 4A). Animals in groups 1 through 4 were sampled daily through 7 dpi for blood and nasal secretions, then weekly thereafter for blood. Animals in group 5 were sampled weekly to check for the absence of virus prior to challenge. At 28 dpi, all animals were challenged with $2.36x10^4$ pfu (equivalent to 10^4 BID_{50}) of homologous FMDV A24Cruzeiro WT via the IDL route. Following challenge, cattle were clinically examined daily and again sampled daily for blood and nasal secretion up to 7 dpc, then weekly thereafter for blood.

To corroborate results obtained during safety studies, cattle were assessed for signs of clinical disease following primary SQ inoculation with FMDV A24-P2/P3Deopt. As expected, they were found to remain free of fever, lymphopenia and the development of FMD vesicles (data not shown). Similar to the IDLinoculated safety dose groups, shedding was absent via both virus isolation as well as RT-qPCR following inoculation (Fig 4B). Additionally, viremia was absent by virus isolation, while variable amounts of circulating viral RNA (10^2-10^7 GCP/ml) were detectable—generally only for one day per animal—by RTqPCR from timepoints ranging from 1-4 dpc.

Following challenge at 28 dpi, all animals in the control group developed clinical FMD with elevated temperatures starting at 2 dpc and with maximum disease scores by 3 dpc (Fig 5). On the contrary, all animals in the two-dose inoculation groups were found to be protected from the development of clinical FMD (Fig 5). One heifer in the 10^5 pfu single dose A24-P2/P3Deopt vaccinated group exhibited delayed fever (3-4 dpc) with a peak clinical score reached at 5 dpc, while the other 3 animals in this group were protected from disease after parental challenge.

When cattle were assessed for viremia and shedding following challenge, a trend was observed in the inverse relationship between the dose (PFU) of vaccine received and the likelihood and amount of virus detected in both the blood and nasal secretions. (Fig 6). Animals in the control group exhibited viremia and nasal shedding detected by both virus isolation and RT-qPCR starting as early as 1 day after challenge. Viremia peaked at titers of about 10^4-10^5 pfu/ml by virus isolation and 10^8 GCP/ml by RTqPCR, while shedding peaked at 10^5-10^7 pfu/ml by virus isolation and 10^7-10^{10} GCP/ml by RT-qPCR. By contrast, none of the cattle inoculated with two doses of A24-P2/P3Deopt prior to challenge showed any viremia or RNemia. In parallel, shedding was observed in only 1 out of 4 heifers by RT-qPCR at concentrations of about 10^4 GCP/ml among the two groups vaccinated with the highest A24P2/P3Deopt doses (two doses of 10^5 or 10^6 pfu). Amongst the two-dose 10^4 pfu efficacy group, 4/4 heifers displayed shedding by RT-qPCR, with 1/4 also positive for shedding by virus isolation. Finally, among the single-dose 10^5 pfu dose group, the same animal that showed clinical FMD development also became viremic by 1 dpc by both RT-qPCR as well as virus isolation. Similarly, this animal began to shed by 2 dpc when assessed via virus isolation and RT-qPCR. All other heifers in this dose group were only positive for shedding by RT-qPCR and were negative for viremia.

Having established that a two-dose prime-boost vaccination strategy with FMDV A24-P2/P3Deopt can prevent clinical FMD at doses ranging from 10^4-10^6 when administered SQ, we next assessed the development of neutralising antibody titers. We found that while all dose groups achieved a protective titer—as defined by a $\log_{10}$ serum dilution of ≥1.2 determined experimentally in our lab for other vaccine candidates [27]—on average by 7 dpi, the 10^6 pfu dose group achieved that titer by 4 dpi (Fig 7A). All vaccine dose groups maintained a protective titer leading up to challenge, at which point their serum neutralising antibody titers increased again due to the boost effect of the challenge. A two-way ANOVA mixed effects model revealed significant effects for treatment (P<0.0001), timepoint (P=0.0016), and the interaction effect (P=0.0047) between the two were all significant. Pre-challenge statistical comparisons against the vaccinated groups were not assessed for controls, as blood samples were not collected from control cattle between 4 and 21 dpi. during the pre-challenge period. At 4 dpi, the neutralising antibody titer of animals in the two-dose 10^6 pfu treatment group was significantly higher than those from the single 10^5 pfu dose and the two-dose 10^4 pfu (Ps<0.0001 for both) treatment groups. At 0 dpc, the neutralising antibody titer of the cattle in the two-dose 10^6 pfu treatment group (P=0.0135), along with those in the two-dose 10^5 pfu treatment group (P=0.0023), was found to be significantly higher than that of the control animals, whose titer remained at 0. At 4 dpc neutralizing antibody titer of the cattle in the two dose 10^5 pfu treatment group (P=0.0156) along with those in the one-dose 10^5 pfu treatment group (P=0.0065) were found to be significantly higher than the control animals, and at 10 dpc, neutralizing antibody titers of the cattle from the two dose 10^4 pfu treatment group were found to be significantly higher (P=0.027) than that of the control group. As with the safety study, we again looked to assay for the presence of anti-NSP antibodies in vaccinated cattle to determine the DIVA compliance of this LAV candidate (Fig 7B).

Curiously, we found that all animals remained anti-NSP antibody negative following vaccination except for two heifers from the two-dose A24-P2/P3Deopt 10^4 pfu dose group. By 14 dpc, all animals from the control, two-dose 10^4 and one-dose 10^5 A24-P2/P3Deopt dose groups were anti-NSP antibody positive, while 3/4 heifers were positive from the remaining two-dose 10^5 and 10^6 dose groups. The results at 0 dpc again cast doubt on the DIVA compliance of this vaccine candidate as formulated and with the current available tests, and indicate that further tweaking of the sequence may be necessary for true DIVA compliance.

Finally, we were interested in assessing the broadly neutralising capacity of the antibodies elicited by animals inoculated with the LAV candidate. To that end, we tested the sera of two-dose 10^5 and 10^6 pfu A24-P2/P3Deopt inoculated cattle from 0, 7, 14 and 21 dpi against six other serotype A strains, and two different serotype strains, Asia1 and O1Manisa (Fig 8A) and used the resulting titers to calculate the r1 value (defined as the quotient of the titer against the heterologous strain over the titer against the homologous strain) for each strain. In general, sera from the two-dose 10^5 pfu dose group consistently performed as well or better than samples from the two-dose 10^6 pfu dose group against a variety of serotype A strains, both in the aggregate and over time. Titers continued to rise or remain steady up to 21 dpi in all A strains except A12, where a slight decline in average titer was observed at 21 dpi, though the titer and r1 value continue to exceed the threshold for protection. In contrast, the sera from the two-dose 10^6 pfu A24-P2/P3Deopt inoculated cattle showed a decline in neutralising capacity by 14 dpi (A22 Iraq and A Iran) or by 21 dpi (A27) in three of six A strains tested. Additionally, when tested against A79, sera from the two-dose 10^6 pfu A24-P2/P3Deopt inoculated animals took longer to achieve an average protective r1 value of 0.3 (14 dpi vs 7 dpi) than the two-dose 10^5 pfu A24-P2/P3Deopt dose group. While no titer was obtained against O1Manisa at any timepoint (data not shown), the sera of the two-dose 10^5 pfu dose group reached a neutralising titer as well as an R1 value greater than 0.3 against serotype Asia1 by 7 dpi, though the titer returned to 0 by 21 dpi. Phylogenetic analysis of VP1 (Fig 8B, S1 Fig) from the strains used for the cross-protection neutralisation assay reveals low correlation with the r1 values obtained by this assay. However, while r1 values remained strong over the various timepoints tested (7, 14 and 21 dpi) for all serotype A strains, particularly among the A24-P2/P3Deopt 10^5 pfu dose group, r1 values fell to just above zero by 21 dpi for the more distantly related Asia1 strain.

DISCUSSION

Our work demonstrates that the A24-P2/P3Deopt strain is a highly effective live attenuated vaccine candidate with a broad safety margin and ability to elicit a strong, cross-protective neutralising antibody response when administered in cattle, improving current vaccine strategies. Specifically, we have demonstrated that A24-P2/P3Deopt is safe at IDL doses as high as 10^7 pfu and effective at a prime-boost dose of 10^4 pfu, establishing a safety margin in cattle of at least three logs.

LAVs are generally understood to be the most successful type of vaccine, not only because they typically induce stronger protection, but also because they bring other advantageous qualities that make them easier to deploy than other vaccine types commonly applied to viral illnesses. For example, all commercial LAVs—with the exception of the oral polio vaccine—are lyophilised, a process of freeze-drying that results in significantly improved stability, sterility of the end-product and reduced reliance on cold chain [28]. This reduced reliance on cold chain also significantly reduces the cost of producing these vaccines and improves their distribution to remote and low-resource areas for field application. In addition to cost savings from reduced cold chain reliance, LAVs also require less viral material per dose.

For example, the commercially available FMD vaccine formulation is administered at 10 µg/dose, an amount equivalent to about $2 \times 10^{\wedge 8}$ pfu (using FMDV A12 for demonstrative purposes, which has a molar mass of $8.6 \times 10^{\wedge 6}$ g/mol and a viral particle-to-pfu ratio of 5000 VP/pfu [21]). By comparison, while the viral particle-to-pfu ratio of the present A24-P2/P3Deopt LAV is 27,000 VP/pfu, at the lowest effective dose schedule investigated—two doses at $1x10^4$ pfu each—the viral material administered in a commercially inactivated vaccine is still 3 logs higher than for A24-P2/P3Deopt. Production cost of codon deoptimized FMD vaccines could also be further reduced if the CD strain were delisted on the United States Select Agent Program regulations and able to be grown outside of BSL-3 facilities, as has happened for other FMD attenuated vaccine strains such as FMDV A24 Leaderless [29].

Another benefit of LAVs is their ability to confer early, long-lasting and broad-spectrum immunity by recruiting both humoral and cellular arms of the immune system. In the past, while several attenuated strains tested in cattle were not capable of inducing protective levels of immunity, swine inoculated with FMDV SAP mutant were protected against WT homologous challenge as early as 2 days after inoculation [30]. In the present study, animals inoculated with the highest dose in the efficacy study (10^6 pfu), showed systemic protective antibody titer by 4 dpi, at least as rapidly as the adjuvanted inactivated FMD vaccine formulation [5], suggesting the present LAV vaccine could be an effective substitute and may be protective even at this early time point, though a challenge study should be conducted to confirm this hypothesis.

While the precise mechanisms of attenuation conferred by CD or CPD are not well-understood, particularly in the context of FMDV, many well-supported hypotheses exist. First, CPD has been shown to increase CpG and UpA dinucleotide frequencies in the resulting viruses (as reviewed in [31]). These dinucleotide pairs are far less frequent in mammalian hosts, and many innate immune-sensing molecules exist that target them, triggering an antiviral response that slows virus growth and spread among cells. Additionally, the increase in these uncommon dinucleotide pairs is attended by increasing frequency of "near-stop" codons, which are more prone to random mutation into stop codons, leading to evolutionary dead-ends. It has been long established that tRNA concentrations for uncommon codons tend to be lower, which may contribute to a reduced rate of translation [32]. CPD is also understood to have effects on RNA secondary structure folding, which can result in changes in translation initiation and stalling and can further lead to misfolding of the amino acid chain (as reviewed in [33]). All these putative mechanisms of attenuation result in viruses that are slow growing, which presents a drawback for large-scale production. Given the slower growth rate, CPD viruses are more time and resource-intensive than WT viruses. However, the cell lines used in virus propagation could be modified to make them more permissive to the replication of these CPD viruses with reduced fitness. For instance, the host factor variously known as zinc-finger antiviral protein (ZAP) and poly(ADP-ribose) polymerase 13 (PARP13), among others, is a viral nucleic acid sensor and a component of the innate immune system. ZAP targets and binds CpG dinucleotides in RNA and targets them for destruction [34]. In the future, cell lines with knock-outs or RNA-binding domain mutations in antiviral proteins such as ZAP could be developed to improve CPD vaccine strain production. On the other hand, CD viruses showed a reduced translation efficiency because rare tRNAs are limiting, causing the ribosome to stall or pause, ultimately reducing protein yield and therefore influencing viral fitness [18,1935]. CD also affects viral protein folding kinetics due to slowed translation [36]. Therefore, both methods of deoptimization ultimately cause viral attenuation.

In the present study, we observed a lack of detectable circulating virus by virus isolation and only low levels by PCR in some cattle, consistent with our previous findings in swine [23].

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It was proposed in the previous swine study that the lack of detectable circulating virus following vaccination likely contributed to the suboptimal humoral immune response. However, the robust humoral immune response observed in vaccinated cattle despite the recapitulation of the viremia results seen earlier in swine suggests that the cause of the reduced humoral immunogenicity of this virus in swine is likely more complex and multifactorial than a lack of circulation and may instead be related to swine immunology or the tropism of the A24-P2/P3Deopt strain. Immunological divergence has been observed between cattle and swine. For example, while IgA+ B cells—a critical contributor to mucosal immunity—are found circulating only in small numbers in swine [37], an analysis of the frequency of expressed sequence tags in GenBank suggests that IgA+ B cells may account for as many as 15% of the circulating B cell population in cattle (unpublished data).

A robust circulating double-positive CD4+CD8+ T cell population has also been observed in suids and seems to play a role in immune response to certain pathogens, such as African Swine Fever Virus [38-40] and Japanese encephalitis virus [41], while this population circulates at a much lower frequency in cattle, though may still be relevant to pathogenesis in certain diseases [42].

Additionally, the frequency of regulatory T cells (Treg) in cattle has been observed at high levels relative to many other mammalian species [43], while this cell population represents a smaller subset of porcine CD4+ T cells [44,45]. Tregs are well known to play a role in virus-host détente and persistence [46], and it has been proposed that they may be important to virus ecology in cattle in the context of FMDV [47]. Many differences in FMDV immunity have also been observed over the years. For example, while a strong neutralising antibody titer reliably correlates with a protective immune response in cattle, this is not the case in swine [48-50]. In cattle immunised with the adenoviral vectored FMDV O1Campos vaccine, the proportion of CD4+ and CD8+ cells expressing IFNγ upon *ex vivo* restimulation significantly increased following a homologous challenge against which they were protected [51].

Similarly, PBMCs isolated from cattle inoculated with the inactivated FMD vaccine either with or without Montanide adjuvant produced significant quantities of IFNγ at 4- and 7-days post-vaccination [5]. While the present LAV platform has not demonstrated protective efficacy—even serotype specific—in swine, it is possible that this could be achieved through formulation with adjuvants or using alternative routes of vaccination. While our group found that a preparation of Asia1 Shamir CPD formulated with Montanide did not result in protective efficacy when administered to swine (data not published), novel adjuvants could be assayed. Analogously, novel routes of vaccination that increase potency and safety might be considered, such as microneedle inoculation [52].

In addition to demonstrating a strong humoral immune response and excellent efficacy against the parental A24Cruzeiro WT strain, sera from the two-dose 10^6 and 10^5 pfu A24-P2/P3Deopt vaccinated groups demonstrated broad neutralisation capacity both within the A serotype and even across serotypes against Asia1. This is consistent with what has been shown historically with a wide variety of live attenuated vaccines [53,54], underscoring the vaccine's potential for application in ever-evolving outbreak situations. For many of the other strains assayed by serum microneutralization, the amino acid sequence identity of VP1—particularly in hypermutable regions such as the G-H loop and AA43-49, both regions known to interact with integrin during receptor binding and internalisation—did not necessarily concord strongly with the r1 value of the assay. This suggests that other immunodominant epitopes in the capsid may be responsible for driving the broadly neutralising response observed early after vaccination or that successful neutralisation may be more dependent on microhomology within these hypermutable regions, such as the RGD sequence in the G-H loop.

When considering O1Manisa, it is possible that the incorporation of charged and polar amino acids well-suited to electrostatic interactions in the G-H loop contributed to the lack of cross-reactivity of the serum antibodies. In addition to the broadly neutralising antibody response elicited by this LAV vaccine, the vector from which the A24P2/P3Deopt virus was derived was engineered with restriction sites flanking the P1 capsid domain, allowing for easy sequence swapping to quickly derive additional vaccine candidates against other serotypes and strains [26]. As a result, this platform has the potential to be rapidly adapted to meet local needs in outbreak situations.

Currently, the predominant trend in FMD vaccination strategy is to utilise vaccines incorporating purification steps in the production chain or incorporating DIVA markers. Unfortunately, it remains unclear why the DIVA marker included in A24-P2/P3Deopt [26] is not fully effective. Given the error-prone RNA polymerase of this virus, however, it is conceivable that random mutations over serial passage resulted in some reversion to the parental sequence. In their work on a CPD RSV vaccine strain, MIN AL, Levy et al. found significant accumulation of mutations over serial passage, though most were missense mutations that did not result in reversion to virulence [17].

However, in their work with MIN AL, they found that reintroduction of a few point mutations was sufficient to reverse virus temperature sensitivity and return growth curves to the levels seen in WT RSV. Conversely, Yeh et al. [55] was able to introduce significant genetic stability over many passages to the Sabin[2] live attenuated poliovirus— vaccines notorious for rapid genetic evolution and reversion to virulence—by introducing a small number of mutations in 3 regions of the genome, including mutations in the 5' UTR to stabilize a temperature sensitivity mutation and move a cis-acting replication element (*cre*), several synonymous mutations in 2C to disrupt the secondary structure of a *cre* site and single amino acid substitutions in 3D.

For the present FMD vaccine candidate to be attractive for licensing, the issue around DIVA marker stability must be further investigated. Reversion to virulence is always a concern with LAVs, and while recombination events could be initiated in the UTRs or non-deoptimized 3D region of A24-P2/P3Deopt, we have previously shown that the risk of such recombination events is low [56].

Additionally, such recombination events would require the presence of the WT virus. Mutations to the 3Dpol gene that increase replication fidelity, such as replacement of W237 with phenylalanine, have resulted in mutants with similar *in vitro* growth kinetics to WT virus, while achieving a more attenuated *in vivo* phenotype [57].

Such mutations could also be incorporated into future infectious clones, although it has been observed that the non-deoptimized region (conserved because of a proposed RNA structure at this site [58]) of the 3Dpol in A24-P2/P3Deopt served as a recombination initiation site when the WT virus was present *in vitro* [56].

While genetic stability over many passages should be assessed, both *in vitro* and *in vivo*, recombination events such as this in the field with the WT virus would not result in more virulent strains of virus than the currently circulating WT.

The present study demonstrates that our A24-P2/P3Deopt vaccine candidate shows strong promise in cattle as an LAV vaccine. Not only have we established a minimum 3-log safety margin for this strain and a lack of shedding, but A24-P2/P3Deopt also induced full protection and elicited broad cross-neutralising antibody protection.

Given these factors and the engineering of this live attenuated virus, this platform could provide an agile tool for outbreak prevention and control.

METHODS

Virus and Cells

Porcine kidney cells (LFPK) were obtained from the Foreign Animal Disease Diagnostic Laboratory (FADDL) of the Animal & Plant Health Inspection Service (APHIS) at the Plum Island Animal Disease Center (PIADC). A porcine kidney cell line overexpressing specific integrin receptors (LFPK-αVβ6) was developed in-house as previously described [59]. BHK (Baby hamster kidney cells, strain 21, clone 13, ATCC CL10) were purchased from the American Type Culture Collection (ATCC, Manassas, VA). All cells were maintained as previously reported [60].

Stock of FMDV A24-WT was generated from the full-length serotype A24 Cruzeiro infectious clone (pA24-WT) and amplified in BHK-21 cells as previously reported [61]. Stock of FMDV A24-P2/P3Deopt was generated as described by Diaz-San Segundo et al. [23] and amplified in LFBK- αVβ6 as previously reported by the same group. Specifically, the P2 and P3 regions of the A24 WT genome were codon deoptimized and antigenic markers at 3B and $3D^{pol}$ were abolished through an $RQKP_{9-12}$ ->PVKV substitution in $3B_2$, along with $H_{27}Y$ and $N_{31}R$ in $3D^{pol}$ [26] to serve as a DIVA marker.

Animal Studies

All animal experiments were performed under agricultural biosafety level 3 at Plum Island Animal Disease Centre (PIADC) and were approved by the PIADC Institutional Animal Care and Use Committee of the U.S. Department of Agriculture and the U.S. Department of Homeland Security (USDA/APHIS/AC Certificate number: 21-F-0001; Protocol #: 244.00-23-R).

Furthermore, all experiments were completed in compliance with the Animal Welfare Act (AWA) (2011); Guide for the Care and Use of Laboratory Animals; the 2002 Public Health Service Policy for the Humane Care and Use of Laboratory Animals; U.S. Government Principles for Utilisation and Care of Vertebrate Animals Used in Testing, Research and Training (IRAC, 1985); as well as specific animal protocols reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of the Plum Island Animal Disease Centre (USDA/APHIS/AC Certificate number: 21-F-0001; Protocol 244.01-19-R).

A total of 32 Holstein heifers (n = 4 heifers/treatment group) of about 450 lbs each were used for the current study. In a preliminary safety study, 2 groups were intradermal-lingually inoculated with either 10^6 or 10^7 pfu of A24-P2/P3Deopt, and a control group was inoculated with 2.36 x 10^4 pfu [equivalent to 10^4 50% bovine infectious dose (BID_{50})] wild-type A24Cruzeiro (A24-WT) virus. Heifers were then followed for up to 21 days post-inoculation (dpi). In a follow-up efficacy study, four efficacy groups were subcutaneously inoculated/vaccinated either only once with 10^5 pfu A24-P2/P3Deopt or twice at 0 and 14 dpi with 10^6 10^5 or 10^4 pfu, plus a control group inoculated with PBS. At 28 dpi, all cattle were challenged with 2.36 x 10^4 pfu (equivalent to 10^4 BID_{50}) A24-WT intradermal-lingually IDL and followed out to 14 days postchallenge (dpc).

Clinical evolution in both the safety and efficacy studies was followed daily for 7 days after inoculation and after challenge, with temperature recorded every day and clinical score assessment at 0, 3, 5 and 7 dpi/dpc. Clinical score is calculated as the sum of the number of feet and the snout that present with vesicular lesions, with a maximal score of 5. Nasal swabs were collected daily from 0-9 dpi/dpc. The blood collection schedule is detailed below.

For intradermal-lingually inoculation as well as clinical evaluations of the snout and feet occurring on 0, 3, 5 and 7 dpi/dpc, animals were sedated with IM xylazine at 0.66 mg/kg and reversed by IV tolazoline at 2 mg/kg. At the conclusion of the study, animals were humanely euthanised by IV pentobarbital sodium overdose at 85 mg/kg followed by exsanguination.

Blood

Processing lood samples were collected daily from 0-9 dpi/dpc, then weekly at 14 and 21 dpi/dpc in serum or EDTA Vacutainers (BD, Franklin Lakes, NJ). Serum tubes were allowed to coagulate for at least 30 min and centrifuged at 2100 xg for 10 min at RT before aliquots were collected.

Half the aliquots were heat-inactivated at 56 °C for 30 min, and all samples were stored at -70 °C until analysis. Blood from EDTA tubes was analysed on a Hemavet (Drew Scientific, Miami Lakes, FL).

Anti-NSP ELISA

In order to test the DIVA compliance of this vaccine, serum samples from 0 dpi and 21 dpi in the safety study, and 0 dpi, 0 dpc and 14 dpc in the efficacy study were assayed for presence of anti-nonstructural proteins (NSP) antibodies targeted to viral genes 3B and 3Dpol by PrioCHECK™ competitive ELISA (Applied Biosystems, Waltham, MA) according to manufacturer's instructions.

Serum Neutralisation Assay

Serum neutralisation assays were performed on heat-inactivated cattle sera samples by end-point titration according to the Kärber method 62 on BHK cells. Antibody titers were expressed as the log10 value of the reciprocal of the dilution that neutralised 100 TCID50 WT A24Cruzeiro in 50% of the wells.

Detection of Virus in Sera and Nasal Swabs

Cattle sera and nasal secretion were examined for the presence of virus by plaque assays on BHK-21 cells for post-inoculation samples and on LFPK-αVβ6 cells for post-challenge samples to account for differences in virus strain susceptibility of the two cell lines. Virus titers were expressed as log_{10} pfu/ml of serum or nasal swab secretions.

The minimal detection level for this assay is 5 pfu/ml. In addition, FMDV RNA was detected by real-time quantitative PCR (RT-qPCR) as previously described [63]. Cycle threshold (Ct) values were converted to RNA copies per millilitre using the equation derived from analysis of serial 10-fold dilutions of *in vitro* synthesised FMDV RNA of known concentration and expressed as the genome copy number per ml of serum or nasal swab [64].

For Phylogenetic Analysis, Statistics, Data-Availability, Acknowledgements, Author contributions, Competomg interest, Citing, References and Figures, please follow the link to the full article

https://www.researchgate.net/publication/400055982_Live-attenuated_foot-and-mouth_disease_virus_vaccine_engineered_by_codon_deoptimization_induces_a_strong_protective_immune_response_in_cattle

https://doi.org/10.1038/s41541-025-01368-7

THE CATHETER

Steve Wimberley



Parvovirus is a terrible disease. It usually affects puppies and causes severe repeated vomiting, bloody diarrhoea and dehydration. It requires intensive treatment, and there is no guarantee that the patient will survive. The disease appeared, as if from nowhere, in 1979. It resulted in the deaths of thousands of dogs before an effective vaccine could be produced. Today, unvaccinated dogs are still very much at risk of contracting the dreaded "cat flu", as it is called in layman's terms.

I was a final year student doing two-week rotations through the various departments. It was my last day in small animal medicine, and I was looking forward to moving on. We had been nursing a litter of beagle puppies from the gynaecology department that had somehow contracted parvovirus. It was soul-destroying work cleaning the endless vomit and diarrhoea and replacing the drips. It was after 10 pm, and I was ready for bed. Just as I was leaving, I noticed that one of the pups had pulled its drip out. Better replace it quickly, I thought.

I placed the miserable little creature on the treatment table. We were using jugular catheters (placed in the neck) as opposed to cephalic catheters (placed in the foreleg), as the jugular catheters stay in longer and don't kink as easily. However, they are more difficult to insert. I shaved and prepped the neck and gently inserted the catheter. I was quite pleased with myself for having found the vein so easily. I threaded the catheter carefully through the needle and down into the vein. Suddenly, the puppy gave a little yelp and tried to get up. I held him down and focused on the catheter. To my horror, there was no sign of it. During the little struggle, the needle had sliced right through the catheter, and it had fallen into the vein – GONE.

I needed some whiskey to steady my nerves, but there was none available. The meths weren't appealing enough either. After a few deep breaths, I took stock. Well, the pup was still alive, there was no exterior evidence of the catheter and the puppy and I were the only ones who knew what had happened. I wasn't going to talk, and the puppy couldn't. Also, there was the very real possibility that the poor puppy would die and take the evidence with him. Quite calmly, I inserted a second catheter, hooked the puppy to his drip and left for the night. I was to begin a new rotation the following day.

A few months passed, and I was now on the small animal surgery rotation. One morning, when I got to the surgical department, there was a buzz going around amongst the students. Word had it that the professor was going to do open-heart surgery on a dog that morning. We finished our duties as quickly as possible and all piled into the theatre to watch. The patient was already fully draped, and the professor had already opened the chest. The students were in awe.

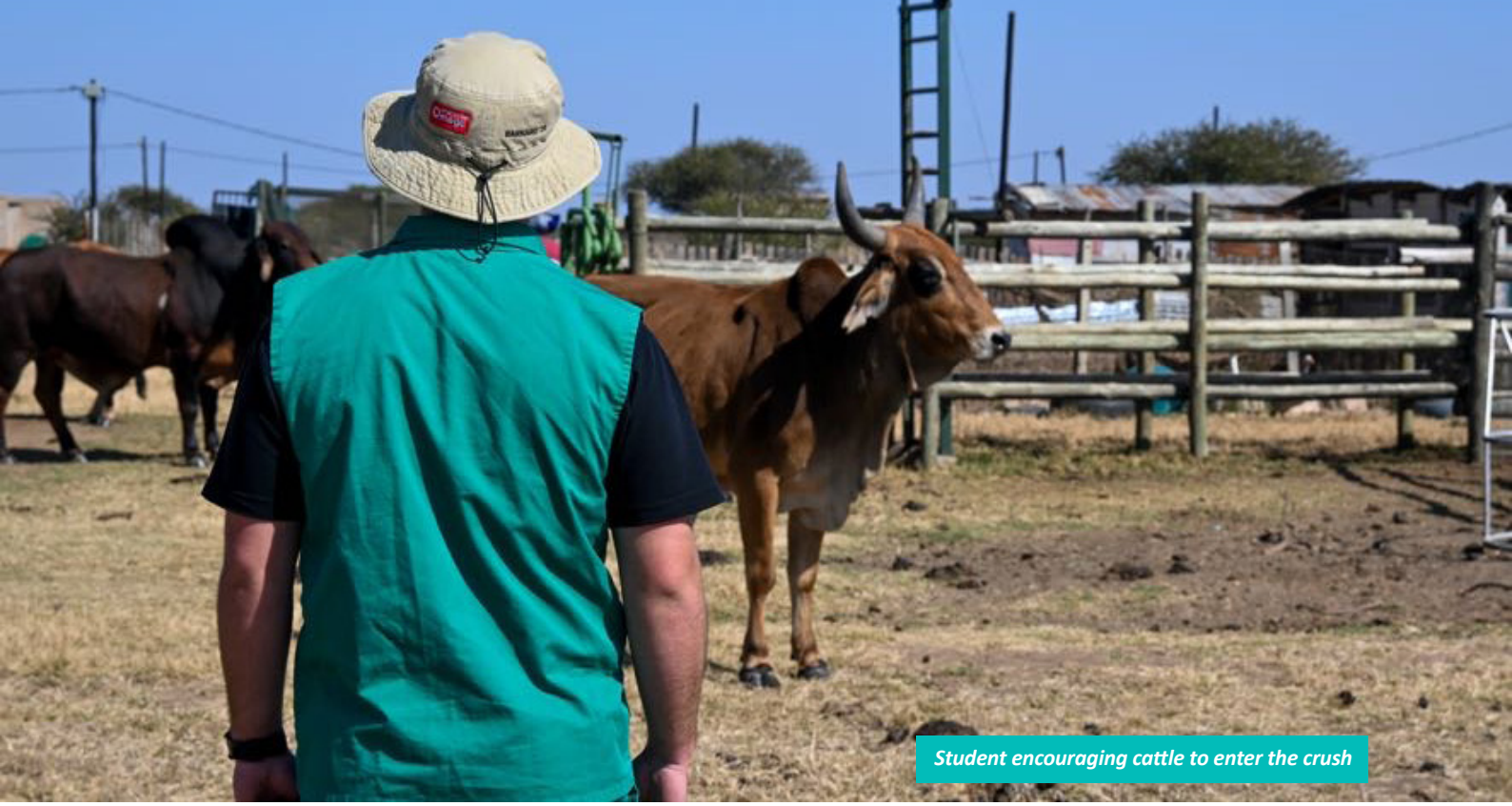
"What are you doing, Prof?" asked a student.

"Some idiot student somehow managed to drop a jugular catheter into this poor dog's vein. It moved from there and is now sitting in the right ventricle of the dog's heart. I'm going to try and get it out."

I pulled my theatre cap down low over my eyebrows and raised my mask as high as possible, and slowly eased my way over to the door. As I ran, I glanced back over my shoulder and saw the X-ray of the puppy on the viewing box. The catheter showed up bright and white in the right ventricle for all the world to see.

I never did find the courage to ask if the operation was a success. I suspect it was, as the talk for days afterwards was not so much about the operation but how the catheter got there in the first place.





Student encouraging cattle to enter the crush

Production Animal Mobile (PAM) Outreach Clinic

The Production Animal Mobile (PAM) Outreach Clinic is the Community Engagement part of the final clinical year Veterinary Core Practice (VCP) modules for veterinary and veterinary nursing students.

Over the course of their eighteen-month clinical time, each student goes out once or twice to the communities of Ratjespane and Makopanstad and their surrounding villages with a fully equipped mobile clinic. PAM outreach works alongside and through the tribal authorities in these areas to implement animal health and welfare.

Farm visits entail addressing any sick animals and advice on management of herds using a complete health approach (nutrition, welfare, preventative medicine), all in the hope of increasing the value and productivity of the animals to benefit their human partners. Companion animal care focuses on primary care – vaccination, deworming, nutrition, welfare, the human animal bond and population control.

Over the past few months, the students have experienced treating and advising on a range of animals from geese and kittens to mules and prize village breeding bulls. They have assisted with formulating information sheets on small and large livestock vaccination and supplemental feeding, and information on sterilisation of pets and control of certain diseases such as rabies, distemper and transmissible venereal tumours. Students have learnt to interact with the communities and provide solutions with the means available to these communities on improving not only the lives of animals but of the citizens as well.

Amongst the citizens of the villages, we have seen a shift in their outlook regarding their animals. The weekly requests for vaccinations and parasite control have increased as people learn the benefits of preventative medicine. Spin-offs from PAM Outreach are the implementation of the sterilisation project for cats and dogs, and vaccination days organised for livestock in the area.

PAM outreach is extremely rewarding, weekly the number of animals that are seen is growing as the community understands the importance of investing in the health of their animals. The clinicians and students find it an extremely rewarding learning experience. To quote a final year student – "Our job doesn't get much better than sitting under a tree with a village elder discussing the communal herds and chatting about life in general…."



Student drawing up cattle vaccines at the mobile clinic



Vaccinating dogs against rabies







Marmaduke and the likkewaan

Ag, nee man, you won't believe what happened here by us this afternoon. It was enough to make a goat laugh.

So there I was, just trying to drink my rooibos in vrede on the stoep. But nee wat. Pietie, that rooster of mine, he starts with his nonsense. "Kukelé-koo! Kukelé-koo!" Like a doring in his broek. His best hen's eggs were gone, you see. Weer eens.

My hondehond, Marmaduke, heard the opskudding. Ag, he's a good brak. Not the sharpest mes in the drawer, but loyal like an old veldskoene. He trots off to investigate, his ore flapping like two gebreekte parachutes. He snuffel around the hok, and I can see his neus twitch. He's got the spoor.

It leads him right to the ysterhout pile. And there, lag my dood, is the skelm. A dik likkewaan, lui soos 'n slang in the sun. You could see its maag was vol, twaalf eiers, easy.

Now, Marmaduke, his brain works simple: "See a problem? Put it in your bek." He gives a little grom, and then, whap!, he goes for the lizard's stert.

Sjoe. Bad move, boetie.

That vervelige likkewaan didn't even try to run. He just opened his grote bek and... O k#k, man.

It was a vloed of half-verteerde egg. Geel, snotterige k#k. It covered Marmaduke's whole kop and bors. He stumbles back, skok tot in sy pootjies. He looks at me like, "ma, what in the naam of grondboontjiebotter was that?"

And then the reuk hits. Jislaaik! You know how a likkewaan smells like a dood thing on a good day? Multiply that by ten, add a rotten egg from hel itself, and you're close. Vieslik.

Pietie shut up dadelik. Even the vlieë seemed to hover for a second, confused.

Marmaduke, the poor dog, tries to shake it off. He rubs his face in the grass. He rolls in the sand. Now he's not just stinking, he's a gesmeerde, stinking mess. Like a omgekeerde malva pudding.

"Bliksem, Marmie! Bly daar!" I shout.

But the jammerte comes aangeslof towards the house, smelling like Satan's ontbyt. I had to bos him down with the hose. Three times with Sunlight soap, and nog steeds he smelled like möre.

He spent the rest of the middag under the perskeboom, a broken spirit. Every now and then he'd lift his head, snuffel at his own skouer, and let out a soft "Moer..." of pure wanhoop.

The likkewaan? Natuurlik long gone. Probably smiling a krokodil smile somewhere.

That evening, clean but with his trots in the stof, Marmaduke wouldn't leave the stoep. When Pietie strutted past, throwing him a look, he just dropped his head on his pote.

Lesson learned, I suppose. Don't baklei with something that can opgooi its lunch on you. Maar truly, you won't believe the smell. It's hanging in the lug still. 😂😂😂

Rustic Rooster (Facebook)

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Dr. Dave Miller



Dr. Rowena Watson

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CALL FOR NOMINATIONS FOR SAVA AWARDS AND HONORARY MEMBERSHIP 2026

Nominations for the SAVA Awards are invited. These awards are conferred on persons who have made exceptional and significant contributions in the fields of Veterinary Science, or the Veterinary Profession and they serve as a prestigious form of recognition of distinguished service. They require sufficient but concise justification for the nomination in the category selected, as outlined in the criteria listed for each category. The presentation of awards will be made at a suitable venue and occasion identified by SAVA and this usually occurs every second year to coincide with the Gala Dinner of the SAVA Biennial Congress. Please adhere to the nomination guidelines as set out below.

1. GOLD MEDAL OF THE SAVA

Awarded to any person, in recognition of outstanding and sustained scientific achievement, with a major impact in the field of veterinary science in South Africa. The medal will only be awarded once to a particular person, and there will be one award per year. The award requires a very comprehensive curriculum vitae and motivation.

2. PRESIDENT'S AWARD

Awarded to any veterinarian registered with the SAVC in recognition of outstanding service to and advancement of the veterinary profession in South Africa. The award will only be bestowed once on a particular person, and there will be one award per year. The award requires a very comprehensive curriculum vitae and motivation. .

3. BOSWELL AWARD

Awarded to any member of the SAVA for eminent service rendered to the profession through the SAVA. The award may be bestowed upon more than one person in a particular year.

4. CLINICAL AWARD OF THE SAVA

Awarded to any veterinarian or group of veterinarians who are registered with the SAVC and have excelled in applied veterinary practice. There is a limit of one award per clinical discipline per year. Past recipients become eligible for another award after a period of five years, for a different contribution.

5. RESEARCH AWARD OF THE SAVA

Awarded to one or more veterinarians for a body of research related to Veterinary Science, and published in scientific journals, that has made an important contribution to a particular field of study. Recipients of this award may be eligible for nomination for new original research. Submission to the Awards Committee may be made by candidates themselves.

6. YOUNG VETERINARIAN OF THE YEAR AWARD

Awarded to one veterinarian registered with the SAVC per year, younger than 35 years of age or who has not been registered for longer than 10 years and who has made a significant contribution to veterinary science in his / her work sphere.

7. SOGA MEDAL

Awarded in recognition of exceptional community service rendered by a veterinarian registered with the SAVC or a veterinary student enrolled at a South African veterinary faculty. In addition to veterinary-related services, other forms of community service may be considered to support the nomination.

8. CITATION OF THE SAVA

The SAVA may bestow a citation upon one or more persons, including non-veterinarians, in recognition of specific achievements and / or meritorious contributions to the veterinary profession or the SAVA. More than one citation may be bestowed per year.

9. HONORARY LIFE MEMBER

Any SAVA member who has rendered long and outstanding service to the veterinary profession may be awarded Honorary Life Membership. Honorary Life Membership will not be granted to more than three people in one year.

10. HONORARY ASSOCIATE LIFE MEMBER

Any person who is not a veterinarian and who has rendered outstanding service to veterinary science, or the veterinary profession may be awarded honorary associate life membership. Honorary Associate Life Membership will not be granted to more than three people in one year.

All nominations must be supported by:

- Submissions must be made on the official nomination form available from the SAVA office.
- A brief motivation in terms of the conditions of the specific award, including the impact the work of the nominee has had. Evidence supporting the motivation, such as testimonials, may be included.
- A full *curriculum vitae* of the nominee, including a list of publication(s) where applicable and all the contact details of the nominee.
- Copy (ies) of the relevant publication(s) in the case of the Research Award.
- It should be clearly understood that all SAVA Awards are conferred for contributions that have been made specifically in a South African context and not elsewhere.

Please note that:

- Any member of the SAVA may submit nominations, while others making nominations must include the support and signature of a SAVA member. Nominators are encouraged to channel their nominations via a SAVA Group or Branch.
- Non-SAVA members may be nominated for all categories except the Boswell Award and Honorary Life Membership.
- Unsuccessful nominations of previous years may, at the discretion of the Awards Committee, be held over for consideration in the following year.
- Where the nominator and seconder have indicated their permission, award categories of nominations could be changed by the Awards Committee.
- Members of the Awards Committee are permitted to propose or second candidates for awards, on condition that they recuse themselves when such nominations are discussed.

The onus is on members to submit appropriate nominations by the due date.

Failure to comply with the above will lead to disqualification of the nomination.

All nominations, in electronic format, marked for the attention of Prof G Bath, Chairperson, Awards Committee of the SAVA, must reach the SAVA office, Sonja Ludik by

FRIDAY, THE 31ST JULY 2026

Nomination forms may be obtained from Ms Sonja Ludik

012 346 1150 or please send an email to sonja@sava.co.za

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We look forward to connecting with our members on this community platform!

CREDO

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Suid-Afrikaanse Veterinêre Vereniging

We, the members of the Association, resolve at all times:

- To honour our profession and the Veterinary Oath
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- To use our professional knowledge, skills and resources to protect and promote the health and welfare of animals and humans
- To further the status and image of the veterinarian and to foster and enrich veterinary science
- To promote the interests of our Association and fellowship amongst its members.

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Members can also contact one of our mentors:

Ken Pettey: 082 882 7356, ken.pettey@gmail.com

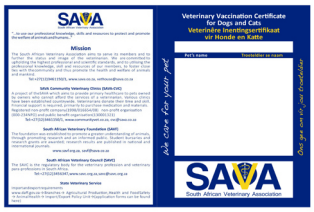
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Praktykbestuurder
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In Memoriam

Dr Bruce Irvine-Smith

27 June 1943 – 30 October 2025



Bruce Irvine-Smith was the elder of 2 sons born to Charles and Winifred, both architects. His birthplace was Nigel, and schooling was at King Edward VII Preparatory School and King Edward VII School, both in Johannesburg. Bruce's grandfather, James Irvine-Smith, was also a veterinarian; he graduated from the Veterinary Faculty at Glasgow University in Scotland. He came to South Africa from Britain in the late 1800s as a veterinarian in the British Army. He was elected the first President of the Transvaal Veterinary Medical Association in 1903. This body was the forerunner of the South African Veterinary Association, where James also served a term as President from 1921 to 1924. Bruce, his brother Craig, and Bruce's eldest son Gregory also became veterinarians.

After matriculation, Bruce enrolled at the University of Natal in Pietermaritzburg and then the University of Pretoria, where he graduated with a BVSc at Onderstepoort in 1965.

Subsequent to spells as the after-hours vet at Sandown Veterinary Hospital, Bruce went to Europe before deciding to study ruminant physiology and obtained a bursary to study at Cornell University in the USA. However, his exposure to the challenges of companion animal practice saw him change course, and in 1970, together with his brother Craig, the Bryanston Veterinary Hospital, designed by their parents, was established. Bruce has a shared distinction of being one of the first three private practitioners to graduate MmedVet, in small animal surgery in 1976. The Hospital has since expanded over 50 years to employ more than 80 members of staff. Following on from Bruce's example, multiple vets have gone on to complete residencies at Bryanston Veterinary Hospital and become registered specialists in Small Animal Surgery and Medicine. Bruce was a visionary in private practice, always striving to improve small animal practice. He was available, approachable and happy to help younger colleagues at any time. Bruce served as a mentor to many vets over his veterinary career.

In 1969, Bruce married Lindsay Grant Stuart, a champion diving athlete who competed for the then Rhodesia at the Commonwealth Games in 1962 and the Olympic Games in 1964. They had four children, 3 boys and a daughter who qualified as a physiotherapist but sadly passed away in 1989 from pneumonia. Greg qualified as a veterinarian in 1993 and furthered his qualification with an MMed Vet. in small animal surgery in 2002. He is now a senior partner at Bryanston Veterinary Hospital. Ian too works at BVH in an administrative role. Grant, the third son, lives in the UK and works in Asset Management. The Irvine-Smith family has since expanded, with Bruce and Lindsay sharing 9 grandchildren from their three sons.

Bruce was a professional who was looked up to by the veterinary profession – and despite his immense contributions and commitments to the field, his priority was his family, and he spent as much of his time as possible with them – hiking, joining in on his kids' sports, and making memories with the people he loved most. Some of his favourite memories involved countless trips to Botswana and Kruger Park – a tradition he has passed down to his children and grandchildren. When time allowed, Bruce enjoyed playing squash, cycling and wildlife photography. His favourite photos grace the walls of BVH today.

Bruce's brother Craig left the practice in 1978 to pursue a career in Britain, but Bruce continued in full-time practice until 2015, and after that, often visited BVH to the delight of staff. His example and determination to deliver only the best service to clients and animals have inspired staff and made the BVH a byword for excellence. He will be remembered as an exemplary veterinarian, surgeon, and gentleman. Beyond that, he leaves a legacy as a family man and an inspirational father, grandfather, and devoted husband. V

Greg Irvine Smith & Gareth Bath

MEMORIES OF ROBERT PATERSON



I met Robert in January 1970 when we both arrived at Onderstepoort, all bright-eyed and bushy-tailed, ready to embark on our journey as Veterinarians. Robert arrived, as those of us who did have vehicles, in an antiquated Morris Minor which his family nicknamed "Miranda".

As those of my vintage will remember, we were a relatively small group and had to line up before dinner outside the "Old Hostel" and be introduced to the seniors.

This lasted for a week, after which we were tested on our ability to remember the seniors. Depending on the result, we were then awarded OP colours and the right to wear an OP blazer! In typical Robert fashion, he accepted this process with much muttering!

During our limited vacations from OP, we shared trips to the Drakensberg and Fannies Island, Lake St Lucia. Great time of camaraderie! These outings were usually preceded by an overnight with Robert's parents at Western Agricultural College, where his father was the principal.

After we qualified, Rob had a short stint with the State Vet in Estcourt. I remember having lunch with him there on the eve of his marriage to Lyne. Being naïve in matters of the heart, I asked him how he knew he had made the right choice. He answered that he had absolutely no doubt that Lyne was "the one", and so it was. Their marriage, which started in the unlikely town of Dannhauser, Natal, lasted for well over 50 years. The Patersons had an "open house", and we seldom visited Natal without spending a night or two with Rob, Lyn and their sons, Gareth and John.

True to his Scottish heritage, Robert loved a good argument, and we would be up late into the night arguing about something to the ninth degree. I remember evenings, usually after a vet meeting, when Rob, who loved to tell jokes, would tell one after another. Robert was one of the most non-materialistic people I knew. He was a true Natalian who was not impressed with the trappings of life in the Fastlane!

After a short stint as State Vet in Estcourt, Rob started a mixed Practice in Greytown, where he was based until an unfortunate embolism during a canoe race left him unable to continue private practise.

He returned to State service before retiring to Howick.

Lala kahle, my friend.

Eddie Lee

In loving memory of
Jonas Mabaso

Jonas was a dedicated father, and he always spoke about his children with pride. In his home area, he was a preacher and voiced his love for the Lord. He always found opportunities to bring warmth and quality to everything he did by sharing jokes and stories. He will be remembered for his sense of humour, positive spirit and dedication.

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Greetings everyone, and hope that it has been a wonderful and re-energised start to 2026!

Last month, we looked at moving past misperceptions and the cycle of change that you can bring about for yourself by taking action. Working towards your goals should always remain a top priority. It is a New Year, with New Momentum - Reclaim Your Path With Purpose.

For many professionals, the start of a new year can feel less like a fresh beginning and more like a pile-up—returning to work, school fees, credit card balances, and the never-ending list of responsibilities that compete with your personal goals. If you're struggling to get going, you're not alone. And more importantly, you have more within you than you might realise. Here's your reframing guide to step into the year with clarity, courage, and consistent action.

You do have what it takes. It is not just the tough that get going. The cliché "when the going gets tough, the tough get going" can make success feel reserved for the superhuman. But real progress isn't about being invincible—it's about being intentional. You don't need to be fearless; you need to be willing. Willing to start small. Willing to persist through imperfect days. Willing to ask for help, adjust your approach, and keep moving. Confidence isn't a prerequisite—it's a byproduct of courageous, consistent action. Every small step is evidence that you can do hard things, even when life's pressures are real.

Take ownership of your time, life, and days. Ownership is empowerment. Instead of waiting for the perfect conditions, create them with boundaries and structure. Define your non-negotiables: an hour for deep work, 20 minutes for movement, 10 minutes for reflection. Guard them like appointments with your future self. Batch tasks, block distractions, and align commitments with your values. Remember: if you don't prioritise your time, someone else's priorities will. Own your calendar so your goals don't get squeezed into the margins of your life.

The opportunities are multiple—take them consistently toward your success. Opportunity rarely arrives gift-wrapped. It shows up as emails, conversations, incremental improvements, and daily decisions that compound over time. Instead of searching for the one big break, build momentum through small wins: reach out to a mentor, refine your pitch, update your portfolio. With consistency, little doors open into bigger rooms. Success is less about luck and more about showing up often enough to be present when luck knocks.

We can learn a lot when things do not work according to the plan—take the lessons. Detours aren't dead ends—they're data. When something doesn't go as planned, ask: What did this teach me about timing, approach, assumptions, or skills? Turn setbacks into feedback. Document what happened, identify one change for next time, and keep the experiment alive. The most resilient professionals are not those who avoid failure, but those who harvest it for insight. Make learning your default response to difficulty.

Be committed all the way—it has always been up to you. Commitment means deciding in advance how you'll behave when motivation dips (it is if you get demotivated sometimes; it makes you human). It's a choice to honour your goals even when the mood isn't there. Build commitment with clarity: write a simple, measurable plan, share it with someone you trust, and set checkpoints. Your progress doesn't belong to external circumstances; it belongs to your daily choices. When you commit fully, you stop negotiating with your excuses and start negotiating with your future.

We can manage risk. Risk is not the enemy—unmanaged risk is. De-risk your goals by starting smaller, testing faster, and gathering evidence. Use pilot projects, pre-orders, prototypes, or simulations. Diversify efforts so one setback doesn't sink the ship. Build buffers—time, savings, energy—so you can absorb volatility. And remember that the biggest risk is often inaction; the cost of waiting is missed opportunities, stalled learning, and momentum lost.

It is possible to fail forward. To fail forward is to let outcomes refine your strategy rather than define your identity. You are not your results—you are your response.

When things fall short, translate that experience into skill: iterate your approach, sharpen your message, improve your systems. Celebrate attempts, not just wins. The person who fails forward accrues wisdom and resilience that the perfectionist never earns.

We owe it to ourselves to try our absolute best and go all in. Going all in doesn't mean reckless overcommitment. It means wholehearted engagement—showing up fully for the things that matter most.

Give yourself the dignity of effort. Replace half-hearted attempts with focused intensity. When you go all in, you honour your potential, inspire others, and build evidence that you are the kind of person who follows through. Your best effort is not just a strategy; it's a statement of self-respect.

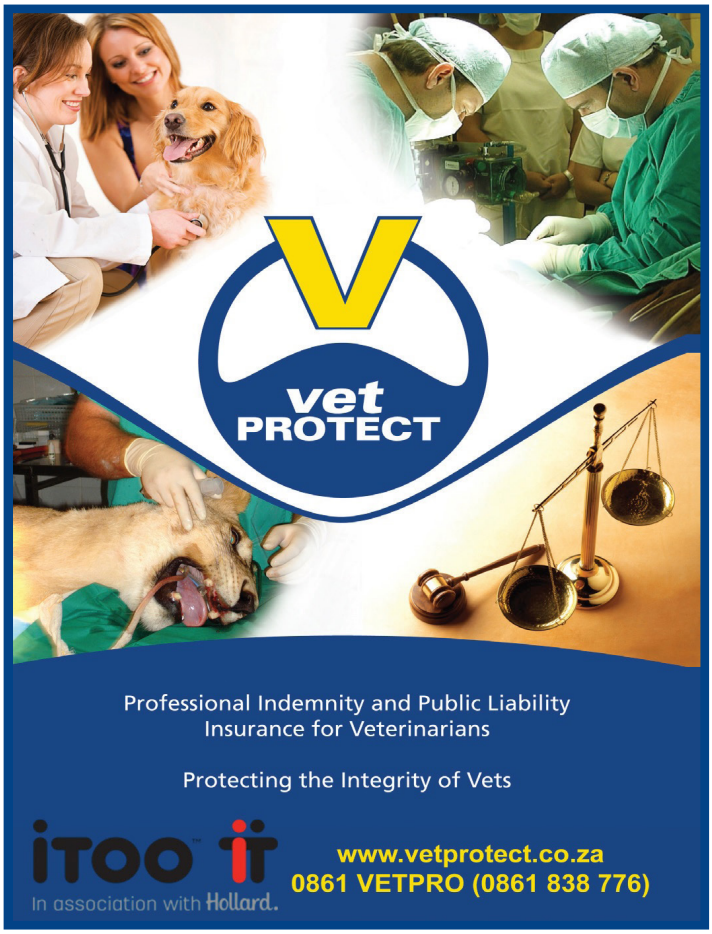
Be better than you were yesterday. Progress is personal. Measure your growth against your own baseline, not someone else's success. Aim for marginal gains: one better decision, one improved habit, one more quality conversation, one extra rep of courage. Over weeks and months, these small edges compound into meaningful change. When you commit to being a little better than yesterday, you transform ambition into a sustainable practice.

A closing word to carry into the year: You are capable of more than your current circumstances suggest. Your responsibilities are real—and so is your agency. Start where you are, with what you have, and move one step at a time. Own your days.

Take the small opportunities. Learn from every misstep. Manage risk with wisdom. Fail forward with grace. Go all in on what matters. Be better than you were yesterday.

When doubt whispers, remember this: momentum is built by ordinary people who choose consistent action over perfect conditions. This year is not waiting to be great—it's waiting for you to show up. Keep going. Your future self is already cheering you on.

Next month, we will continue looking at more ideas for improving our quality of life and overall performance, both at work and at home.



The SAVA Stress Management Hotline

The following SAVA members are available on the SAVA stress management hotline. If required, they will refer you to professionals.

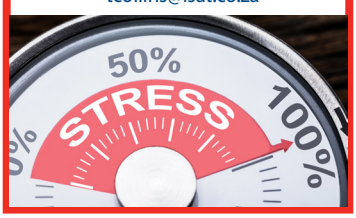
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Fungal Keratitis in horses

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The cornea is a highly specialized structure that act as the barrier between the intraocular environment and the, quite often, hostile external environment of the equine world. The eye has developed a complex and dynamic system of ocular surface defenses that protects against potentially vision threatening disease. Physically this is represented by the corneal epithelium which acts as a physical barrier and the tear film which traps debris and microorganisms in the tear fluid which is removed by the blinking action.

Additionally, the tear film contains multiple antimicrobial- and epitheliotropic molecules, and the cornea has a highly developed innate and adaptive immune defense system. Together these create a surveillance system of the ocular surface which maintains the normal commensal (and necessary) microorganism population of the ocular surface and detects and eliminate potential pathogenic microorganisms.

Pattern recognition receptors of the innate immune system will recognize and bind to highly conserved microbial molecules (pathogen-associated molecular patterns or PAMP's), which include bacterial flagellins and cell wall lipopolysaccharides, viral DNA/RNA fragments, and fungal zymosans. Activation of this system ultimately results in gene transcription for predominantly pro-inflammatory cytokines.

The adaptive immune system, via immune surveillance by the conjunctiva and conjunctival-associated lymphoid tissue, responds through various antigen-presenting cells, T-cells and B-cells. Simply put, and depending on the exact nature of the trigger, T-cells will mature into various cell lines (CD4+, T-helper cells, T-regulatory cells, etc.) and B-cells will produce appropriate immunoglobulins

Fungi are defined as any member of the broad kingdom of eukaryotic organisms which includes mushrooms, molds and yeasts. They are typically filamentous and multicellular, and they do not contain chlorophyll.

Fungal organisms are considered normal inhabitants of the equine ocular surface although many (Fusarium, Aspergillus) have a significant keratopathogenic potential. They are ubiquitous in the equine environment and existing geographic environmental differences will account for significant variation in the prevalence of different species in specific areas. For this reason, it is always advisable to culture corneal ulcerations, the insight gained is invaluable in the clinical setting.

Fungi are heterotrophic organisms that secrete digestive enzymes into their environment to acquire nutrients. This may suggest a mechanism for their pathogenicity in the equine cornea. Fungal hyphae have a definite cell wall made up of chitins glucans and mannins.

Chitin is absent in vertebrates and can activate the innate immune system and the adaptive immune system. In some instances, the immune response can clear the chitin and its associated organism, but the immune response can also become pathological.

The disruption of the ocular surface and tear film instability usually precedes the onset of ulcerative fungal keratitis. Foreign bodies and plant material can also seed the organism. Stromal penetration with vertical posterior movement results from release of proteases and other enzymes released by the fungi, chemoattracted leukocytes and reactive keratocytes in cases of highly pathogenic fungal infection.

Lateral or horizontal movement in the corneal stroma occurs with low pathogenic fungi, this is related to lower local concentrations of proteases and leukocytes. Some fungi (Fusarium spp and Candida spp) form biofilms which makes eliminating the organism especially difficult. Some of the more pathogenic fungi appear to have an affinity for the Descemet's membrane collagen, this deep invasion can easily lead to liberation of fungal organisms into the anterior chamber, iris, and lens with resultant endophthalmitis.

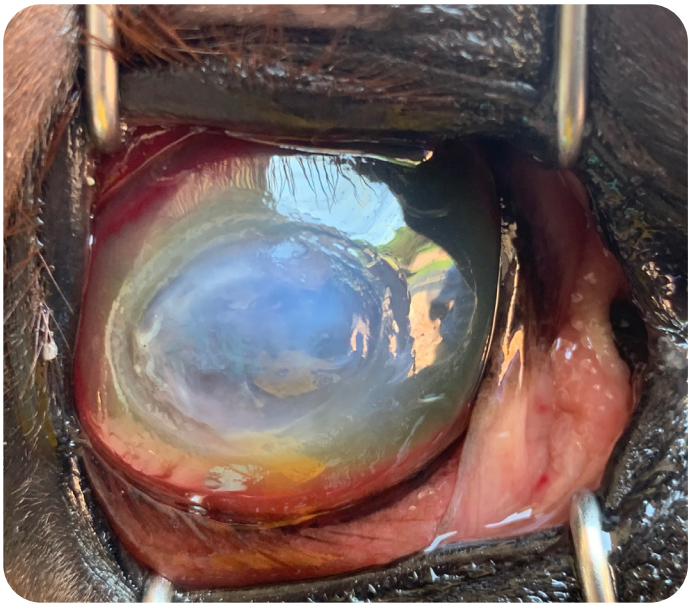
The use of topical corticosteroids has been implicated in predisposing the cornea to fungal infection, enhancing fungal replication and reducing the efficacy of antifungal agents. Previous use of topical antibiotics may have as great an influence on the occurrence of fungal keratitis as corticosteroids. Topical antibiotics could create and environment favourable to fungal replication by altering the overall balance of the commensal microbiota population.

The mainstay of treatment remains topical antifungal drugs, but treatment is notoriously difficult. Complicating factors include the usually delayed diagnosis plus the limited and deficient ability of the medication to penetrate deep into the cornea.

Treatment must be aggressive considering the potentially devastating visual outcome. Topical use of diluted intravenous antifungal agents provides enough medication to eradicate the organism while being tolerated by the eye. Treatment must be directed against both the fungi and the corneal- and inflammatory responses occurring as a consequence of fungal replication and hyphal death. Removal of the dead fungal hyphae by the neutrophil-dominated innate ocular defense mechanism is a slow process which results in protracted inflammation and delayed healing. The fungicidal activity of most antifungal agents is concentration dependent, and it is difficult to achieve these concentrations in the cornea, thus they are generally considered to be fungistatic only.

Azole antifungal agents (miconazole, ketoconazole, fluconazole, itraconazole, and voriconazole) bind to fungal-specific enzyme in the P450 system, inhibiting ergosterol synthesis, increasing membrane permeability and altering fungal cell enzyme systems.

Surgical intervention is indicated when the stromal loss is greater than 1/3'rd of the corneal thickness, corneal perforation has occurred, the anterior uveitis is uncontrolled and the response to medical treatment has been limited to poor.





The main goals of surgery are stabilizing of the weak cornea and removal of the infectious organisms & inflammatory cells.

Surgical options include superficial or lamellar keratectomy with conjunctival grafting, amnion grafting and corneo-conjunctival transposition.

Early recognition of potential equine ulcerative keratitis, together with culture and appropriate treatment is vital to improve the outcome of this potentially vision threatening disease.

Reference:

Equine Ophthalmology, 4'th edition, Brian C Gilger, Wiley Blackwell, 2022

Eye COLUMN

Managing the Vomiting Cat - A Practical Approach

Adapted by:
Dr Angeliki Kaldelis (BSc, BVSc, MRCVS)

Vomiting is a frequent and often challenging clinical sign in feline practice. It can indicate anything from a minor dietary indiscretion to a serious systemic illness. A structured and methodical approach is essential to effectively diagnose and manage vomiting in cats, ensuring better patient outcomes and client satisfaction.

This article adapts key clinical insights from the Royal Canin Academy's expert guidance on managing vomiting in cats, emphasising diagnostic strategies, therapeutic interventions, and nutritional management.

For the full article, references, and detailed clinical protocols, please visit the Royal Canin Academy at How I Approach the Vomiting Cat, *written by Dr Ivan Montanes-Sancho and Dr Silke Salavati (Sep 13, 2023)*

Understanding Vomiting in Cats

Vomiting is a complex reflex involving the gastrointestinal tract and central nervous system. It is important to differentiate vomiting from regurgitation and other causes of oral expulsion, such as coughing or retching. Vomiting can be acute or chronic, and its causes are diverse, including dietary indiscretion, infections, inflammatory diseases, metabolic disorders, toxins, and neoplasia.

Cats are particularly sensitive to prolonged anorexia or fasting, which can lead to hepatic lipidosis, making timely nutritional management critical.

Clinical Approach: History and Physical Examination

A thorough history is the foundation of diagnosis. Key aspects include:

- Signalment (age, breed)
- Duration and frequency of vomiting
- Characteristics of vomitus (presence of food, bile, blood)
- Appetite and water intake
- Weight changes
- Exposure to toxins or new foods
- Previous medical history and medications

Physical examination should assess hydration status, abdominal palpation for masses or pain, oral cavity inspection, and systemic evaluation for signs of systemic illness.

Diagnostic Workup

Initial diagnostics typically include:

- Complete blood count and serum biochemistry to evaluate organ function and detect inflammation or infection
- Urinalysis
- Faecal examination for parasites
- Abdominal imaging (radiographs or ultrasound) to identify structural abnormalities
- Specific tests as indicated (e.g., pancreatic lipase immunoreactivity, thyroid function tests)

In regions with high parasitic prevalence, ruling out parasitic infections is essential.

Nutritional Management: A Cornerstone of Therapy

Nutrition plays a pivotal role in managing vomiting in cats, both as a therapeutic intervention and a preventive measure.

Acute Vomiting

For cats with acute vomiting but no systemic illness, dietary modification is often the first step.



The goals are to support the gastrointestinal tract, reduce inflammation, and provide easily digestible nutrients.

- **Fasting:** A *short* fasting period (12-24 hours) *may* be recommended to allow gastric rest. However, prolonged fasting is contraindicated in cats due to the risk of hepatic lipidosis.
- **Hydration:** Maintaining hydration is critical, with intravenous or subcutaneous fluids administered as needed.
- **Diet:** A gradual introduction of a highly digestible, moderate to low-fat diet is recommended. Therapeutic diets formulated with hydrolysed proteins and prebiotics can support gut healing and reduce antigenic stimulation (such as Royal Canin Gastrointestinal diets, or Hypoallergenic diets)
- **Feeding frequency:** Small, frequent meals reduce gastric workload and improve tolerance.

Chronic Vomiting

Chronic vomiting often indicates an underlying disease such as inflammatory bowel disease (IBD), food intolerance, or neoplasia. Nutritional strategies include:

- **Novel protein or hydrolysed protein diets:** To minimise immune-mediated reactions in the gut.
- **Highly digestible diets:** To improve nutrient absorption and reduce gastrointestinal irritation.
- **Fat restriction:** Particularly in cases with pancreatitis or fat malabsorption (It must, however, be noted that cats are not as fat sensitive as dogs).
- **Prebiotics and probiotics:** To support a healthy gut microbiome, which plays a critical role in gastrointestinal health.

Tailoring nutritional plans based on diagnostic findings and patient response is essential.

Therapeutic Management

Clinically stable cats with acute vomiting often have self-limiting gastroenteritis, especially once foreign bodies are ruled out. Treatment typically involves feeding a gastrointestinal diet for a few days, administering probiotics, and using antiemetics depending on the severity. Maropitant is the most commonly used antiemetic in cats, but should be avoided in kittens under 16 weeks due to the risk of bone marrow hypoplasia. Other options include metoclopramide (less effective in cats), ondansetron (effective but costly and unlicensed), and phenothiazines like chlorpromazine or prochlorperazine, which are often more cost-effective.

As mentioned, nutritional support is critical to prevent complications such as hepatic lipidosis, especially in cats with prolonged anorexia. Appetite stimulants may be used, though not all are licensed for cats.

If oral intake remains inadequate, feeding tubes—either naso-oesophagal for short-term or esophagostomy for longer-term support—should be considered once vomiting is controlled.

For cats with suspected food-responsive chronic enteropathy (CE) or inflammatory bowel disease (IBD), an elimination diet trial using a hydrolysed or novel protein diet is recommended. Most cats respond within 2–3 weeks, but a full response may take up to 6–8 weeks. If the first diet trial is only partially successful, a second trial with a different diet is indicated. Additional treatments for IBD can include probiotics or glucocorticoids, ideally after obtaining gastrointestinal biopsies. High-grade or large granular lymphomas require chemotherapy protocols.

Extra-gastrointestinal causes of vomiting should be managed according to their specific underlying aetiology.

When to Refer and Consider Advanced Therapies

Persistent vomiting despite initial management warrants further work-up or referral for advanced diagnostics such as endoscopy or biopsy. Nutritional support remains important in these cases, often requiring specialised diets or feeding tubes.

Conclusion

Vomiting in cats can signal a wide range of underlying problems, making a thorough history, signalment, and clinical examination essential before developing a diagnostic plan.

Acute vomiting cases should be triaged for emergency or surgical intervention and assessed for the need for nutritional support before pursuing extensive diagnostics.

Chronic vomiting allows for a more measured approach, with diet or symptomatic drug trials often preceding advanced testing.

While supportive care is important in most cases, identifying and addressing the specific cause is crucial for effective, targeted treatment and improved patient outcomes.





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GAUTENG
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We are looking for a qualified veterinarian to join our team! Well-established practice in Centurion, Pretoria. Half- or full day, Mondays to Fridays. Contact Charlotte on 072 242 6982 or send an email to charlottevdijken@gmail.com Ref26FE03

RANDBURG

Jukskei Park Vet Clinic has recently become substantially busier, and our 2-vet clinic needs to be expanded. We are looking for a qualified veterinarian to join our team. We believe in hard work combined with adequate time off. The candidate will work every 2nd weekend, alternating with a 3-day long weekend. No after-hours duties and a 3-hour lunch break make this an attractive prospect. Candidates should send their C.V. to both drjdmckenna@gmail.com and lesterjackson73@gmail.com Ref26FE04

KYALAMI, JOHANNESBURG

Northrand Animal Clinic in Kyalami, Johannesburg, is looking for a qualified equine veterinarian. Please contact Dr Mike Ross on 011 468 3100 or email mike@nrac.co.za Ref26FE06

AUCKLAND, NEW ZEALAND

The Veterinary Hospital Group, based in Auckland, New Zealand, is a privately owned group practice currently recruiting for experienced mixed or companion animal vets.
Candidates must be able to register with the New Zealand Vet council (info linked here: https://vetcouncil.org.nz/Web/Web/1.Support-and-Information/Vets/Registration.aspx).
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Contact: Dr Daleen Erasmus
Tel or WhatsApp 082 416 9592
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Dr Georgina Crewe BVSc, MSc(Wits)
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115 9th Ave., Fairland, Johannesburg 2195
Telephone: 011-678-3121
Cell: 082-492-6247
E-mail: crewegeorgina@gmail.com
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Prof. Dr. med. vet., Dr. habil. Hartmann, Katrin, Prof., Dipl. ECVIM-CA (Internal Medicine)

Katrin Hartmann graduated from the College of Veterinary Medicine at the LMU Munich, Germany, in 1987, completed her Doctoral Thesis in 1990 and her Habilitation Thesis on antiviral treatment of feline immunodeficiency virus infection in 1995. She worked as Clinical Instructor and Assistant Professor at the Clinic of Small Animal Medicine until 2001. From 2001 to 2003, Katrin was as Associate Professor of Internal Medicine at the Department of Small Animal Medicine at the College of Veterinary Medicine, University of Georgia, Athens, USA. In 2003, she returned to Germany as Full Professor and Head of the Clinic of Small Animal Medicine at the LMU Munich, Germany. From 2009 until now, she additionally served as Director/Vice Director of the Centre for Clinical Veterinary Medicine at the LMU Munich.Katrin's major research area is infectious diseases in cats and dogs, with a special interest in feline virus infections. She is author of more than 400 research papers, in addition to proceedings, abstracts, and book chapters. She also has lectured at numerous international meetings worldwide.

Prof Ralf S Meuller

Prof. Dr.med.vet. Ralf S. Mueller, DipACVD, FANZCVSc (Dermatology), DipECVD

Prof. Ralf S. Mueller graduated in Munich/Germany, completed his doctoral thesis in 1987, and worked in several large and small animal practices before completing a residency in veterinary dermatology at the University of California/Davis in 1992. In 1992 he moved to Melbourne/Australia to work with his partner and wife Dr. Sonya Bettenay. Together, they created the first, purpose-built specialist practice in Australia. During that time, Dr. Mueller was concurrently consulting and teaching at the Veterinary Teaching Hospital/University of Sydney. Ralf and Sonya established (and continue to conduct) the Distance Education Program in Veterinary Dermatology of the Centre for Veterinary Education of the University of Sydney. In 1999, Ralf became Assistant Professor in Veterinary Dermatology at the College of Veterinary Medicine and Biomedical Sciences/Colorado State University. In 2004, he accepted a position as chief of the veterinary dermatology service at the University of Munich/Germany. His main research interests are allergies and ectoparasites. He has published over 250 studies, articles, book chapters and books and given more than twelve hundred seminars, lectures and talks all over the world.

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