

EVALUATION OF INTRAOCULAR BRUCELLOSIS VACCINE AND ITS POTENTIAL BENEFIT IN AN ENDEMIC SETTING: A COMPREHENSIVE REVIEW

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INTRODUCTION

Brucellosis is an infectious, contagious bacterial zoonotic disease caused by various *Brucella* species, containing several biotypes, such as *B. abortus*; *B. melitensis*; *B. suis*; *B. ovis*; *B. canis*; *B. neotomae*, which mainly infect cattle, small ruminants, pigs, rodents and carnivores, as well as humans. Livestock infections are highly contagious resulting in abortions in the last stages of pregnancy followed by retention of fetal membrane and infertility in succeeding pregnancies.

The detrimental economic impact of animal brucellosis is felt mostly in the dairy and meat industries, especially in low-income countries including South Africa (SA), as the disease not only causes production losses (from abortion, stillbirth, sterility, a longer calving interval, and lower milk yields), it also constitutes a barrier to trade in the affected regions.

In SA, bovine brucellosis is classified as a controlled disease in animals in terms of the Animal Diseases Act 35 of 1984. As such, there is frequent serological surveillance of high-risk farms, especially dairy and Stud herds suspected of having brucellosis, combined with compulsory vaccinations of 4-8 months old heifers with 5×10^{10} organisms of *B. abortus* S19 live attenuated vaccine (LAV).



PROBLEM STATEMENT

B. abortus S19 LAV is effective in the prevention of brucellosis in cattle and provides good immunity for animals against brucellosis. It causes the shedding of the organism in milk leading to the persistent circulation of brucella in a herd. The persistent serological response post-vaccination with the *B. abortus* S19 LAV is one of the main problems associated with the use of this vaccine in endemic settings, as it interferes with screening and hinders trade.

This raises the need for the development of improved vaccines against bovine brucellosis, and research to inform best practices for cattle health and vaccination strategies for disease control.

AIMS AND OBJECTIVES

- To review the literature on *B. abortus* S19 LAV administered intraocularly at a reduced dose in endemic settings.
- To evaluate the protective response induced by intraocular *B. abortus* S19 LAV, in comparison to the normal route of vaccination.
- To ascertain the potential benefit of a reduced dose of *Brucella* S19 LAV administered by the intraocular / conjunctival route.

METHODS

- A literature review search was conducted on the Google Scholar database to identify all *Brucella abortus* S19 live attenuated vaccine studies on the reduced *B. abortus* S19 LAV dose
- The search was limited to 'English articles only' with Search terms: Endemic area *Brucella abortus* S19 vaccine AND "live attenuated" AND "Cattle".
- Search was narrowed to publications from the last 10 years, that is from 2014 to 2024
- Publications were reviewed based on title, abstract, and methods, and Exclusion criteria were applied
- The relevant articles were selected and reviewed

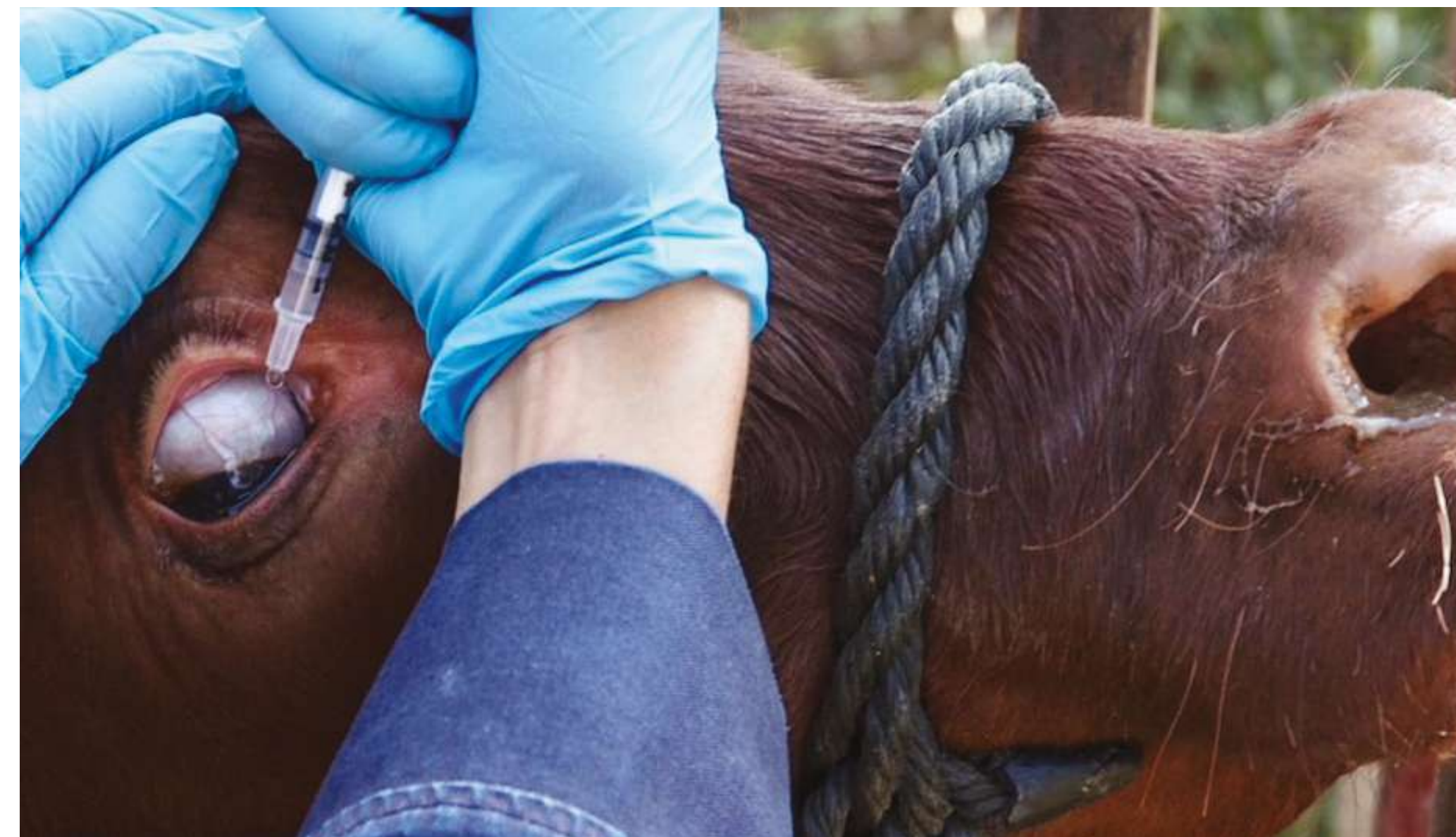


Photo: University of Saskatchewan/Vaccine and Infectious Disease Organization

RESULTS

Figure 1: Flow diagram of selection steps after search filtering procedures with Google Scholar.

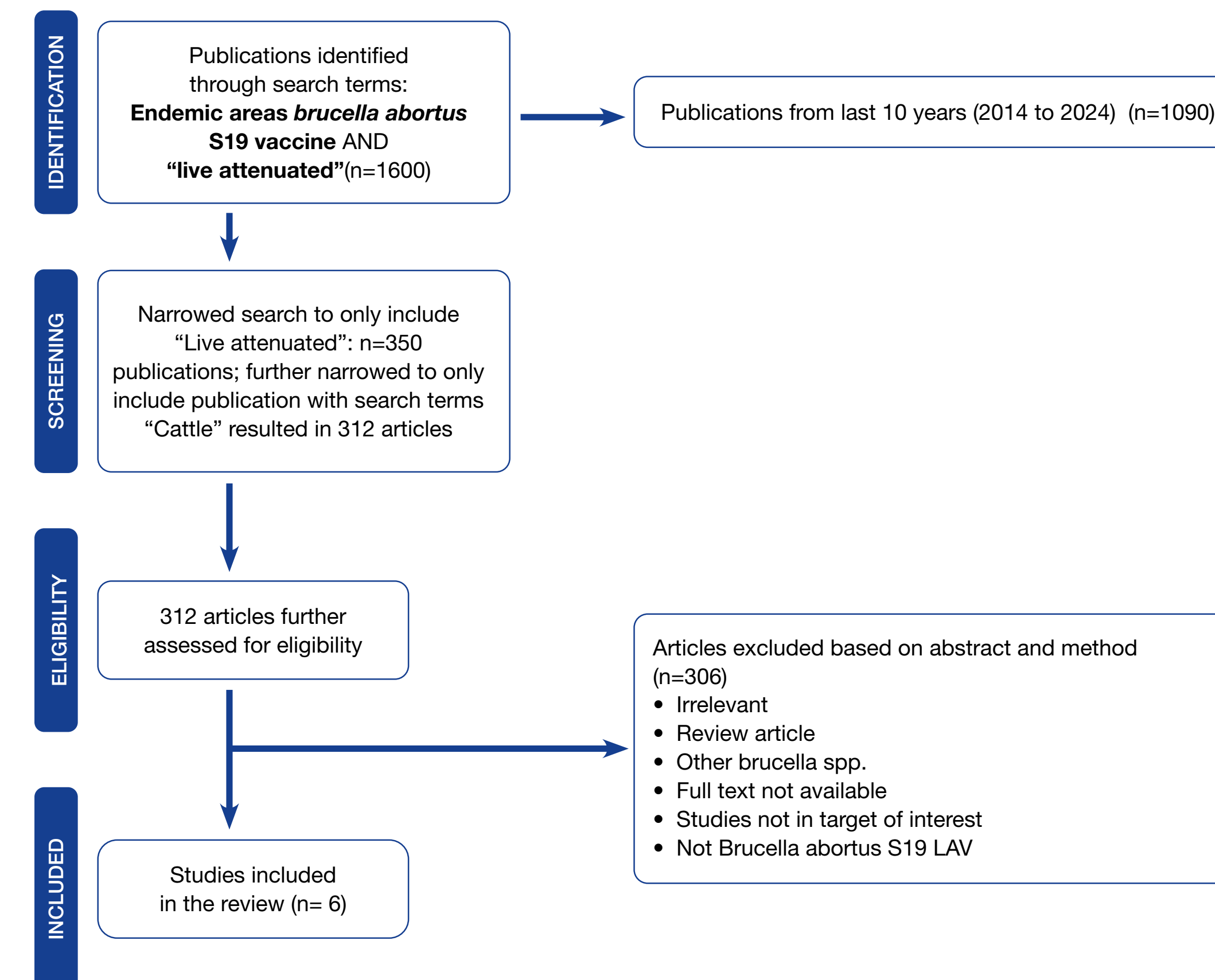


Table 1: Studies reviewed and summary of experimental data.

PUBLICATION	BRUCELLA VACCINE EVALUATED	VACCINATION ROUTE	CRU / DOSE	BOOSTER	NUMBER OF ANIMALS*	PRE-VACCINATION SCREENING TEST; POSITIVE CASES EXCLUDED	POST-VACCINATION IMMUNOLOGICAL ASSESSMENT DONE			ADVERSE RESPONSE MEASURED		
							IELISA / C-ELISA	RBT	IFN-γ RESPONSE	SHEDDING	ABORTION	
https://doi.org/10.1007/s11258-014-0678-2	<i>B. abortus</i> S19 LAV	Cj	$5.00E+09$	At 4 months	911	IELISA; RBT	Yes	Yes	Not tested	Weak antibody response, which disappeared within 9 to 12 weeks	Not tested	12 animals
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Cj	$5.00E+09$	At 4 months	10	IELISA; SAT; RBT	Yes	Yes	Yes	12 weeks on RBT	10% in milk IgGCF at 17 weeks	Not tested
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Sc	$5.00E+09$	No	10	IELISA; SAT; RBT	Yes	Yes	Yes	17 weeks on RBT	60% in milk IgGCF at 17 weeks	Not tested
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Sc	$5.00E+10$	No	58	IELISA; RBT	Yes	Yes	Not tested	59 weeks on RBT, 7 cases remained positive 4.5 years PV	Not tested	Not tested
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Sc	$4.00E+10$ $4.00E+09$ $4.00E+08$ $4.00E+07$	No	13 13 13 13	RBT	Not tested	Not tested	Not tested	Antibodies still detected at 34 weeks PV	Not tested	Not tested
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Sc	$5.00E+10$	At 4 months	30	IELISA; SAT; RBT	Yes	Yes	Yes	17 weeks, comparable antibody response	pCt=10% at 17 weeks PV pCt=60% at 17 weeks PV	Not tested
https://doi.org/10.1016/j.livsci.2022.104932	<i>B. abortus</i> S19 LAV	Cj	$5.00E+09$	At 4 months	24	C-ELISA; RBT	Yes	Yes	Yes	Antibodies still detected at 25 weeks PV	Not tested	Not tested

* Different age groups (young, old heifers & milking cows); RBT refers to "Rose Bengal test"; Cj refers to the Conjunctival route; Sc refers to the Subcutaneous route.

CONCLUSION

- Antibody response persists in subcutaneous immunization compared to intraocular immunization
- Intraocular administration of *B. abortus* S19 LAV resulted in reduced shedding of organisms in milk
- Intraocular administration of *B. abortus* S19 LAV offers several potential benefits, especially in endemic settings where brucellosis is prevalent
 - The intraocular route of vaccine administration offers several advantages that can enhance vaccine efficacy; Such as:
 - The vaccine directly interacts with immune cells at the site of entry. By stimulating mucosal immune responses, which are crucial for protection at mucosal surfaces (such as the eyes, respiratory tract, and gut).
 - Antigen-presenting cells (such as dendritic cells) in the conjunctiva capture the vaccine antigen. These cells then activate T cells and B cells to migrate to Lymph nodes, leading to specific systemic immune responses
 - Induces the production of secretory IgA antibodies locally, which helps prevent pathogen attachment and neutralizes them at mucosal surfaces.
- Activated B cells produce antibodies (including IgG) that provide systemic protection
- Further research is needed to optimize the effectiveness of intraocular administration of *B. abortus* S19 LAV. Extensive research is needed to fully characterize the nature of the protective immune response stimulated by this route.
- An understanding of the shedding patterns is essential for successful vaccination strategies.
- Of note:** Two eye drops *B. abortus* S19 LAV are licensed in Europe for the control and eradication of Brucellosis (BRUDOLL-A Conjunctival and B19 CZV Ocular). Similar products are not yet available in SA.

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