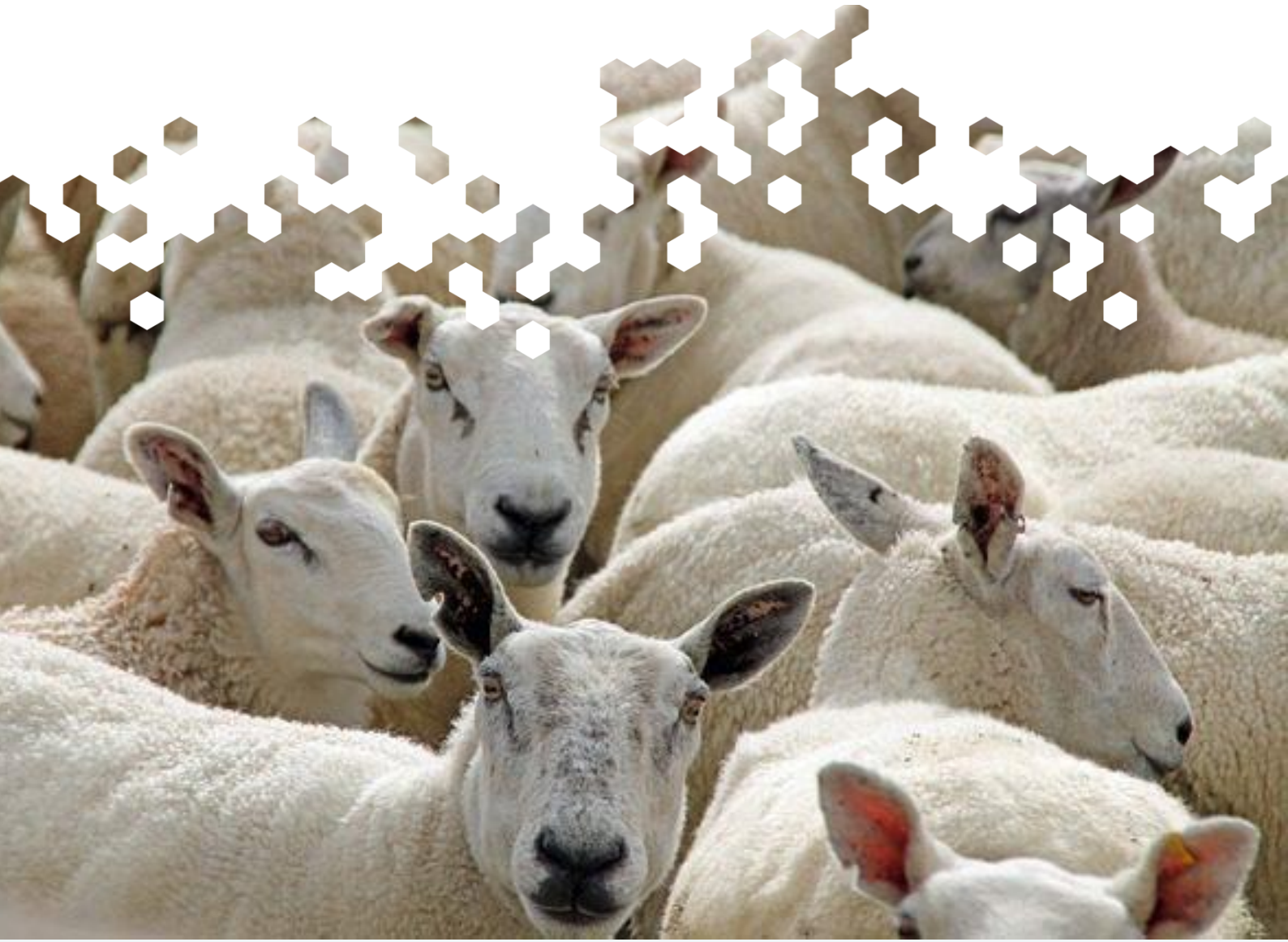
STAR IDAZ International Research Consortium on Animal Health

STAR IDAZ Brucellosis Vaccine Workshop Report

3 November 2025



STAR IDAZ IRC is the 'Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses - International Research Consortium'. It is a global consortium that brings together funders and programme owners for research on animal health to maximise funding for coordinated animal health research. To achieve its aim, STAR IDAZ facilitates networking among funders, researchers, industry experts, policymakers and other stakeholders to collaborate on research and innovation in the field of infectious animal diseases. This document was produced by SIRCAH, the Scientific Secretariat of the STAR IDAZ IRC.

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More information on STAR IDAZ IRC can be found at www.star-idaz.net

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STAR IDAZ IRC Brucellosis Vaccine Workshop: Format overview

Purpose:
To identify, prioritise, and address key gaps in global brucellosis vaccine research through two dedicated plenary sessions:

1. Session 1: Plenary Presentations
2. Session 2, Round 1: Identification and prioritisation of needs and gaps.
3. Session 2, Round 2: Discussion of strategies and research actions to address the identified gaps.

Expected outcomes:

- Consensus on the most urgent vaccine research priorities.
- Clear input for updating the STAR IDAZ Brucellosis Vaccine Research Roadmap.
- A consolidated set of recommendations for follow-up activities and collaborative initiatives.

Format:

- Plenary discussions facilitated by designated topic leaders.
- Each topic included approximately 30 minutes of discussion followed by 10 minutes of summary preparation.
- Topic leaders delivered a 5–10 minute synthesis of their discussions during the final plenary wrap-up.

Introduction

Brucellosis remains one of the most consequential zoonotic diseases globally, impacting livestock productivity, rural livelihoods, and human health. Despite existing vaccines, significant gaps persist regarding safety, species coverage, stability, and applicability in diverse epidemiological and socioeconomic contexts.

The STAR IDAZ IRC convened this workshop to:

- Identify and prioritise critical gaps in brucellosis vaccine research.
- Discuss strategies to address these gaps.
- Generate inputs to update the STAR IDAZ Brucellosis Vaccine Research Roadmap.
- Strengthen global collaboration among leading researchers and institutions.

Workshop Objectives

Brucellosis remains one of the most consequential zoonotic diseases globally, impacting livestock productivity, rural livelihoods, and human health. Despite existing vaccines, significant gaps persist regarding safety, species coverage, stability, and applicability in diverse epidemiological and socioeconomic contexts.

- Review current brucellosis vaccine performance, gaps, and needs.
- Discuss feasibility and scientific rationale for next-generation vaccine platforms.
- Analytically assess challenges in LMIC implementation.
- Integrate perspectives from DISCONTOOLS gap analysis, the STAR IDAZ Roadmap, and the GALVmed Brucella Vaccine Prize.
- Identify priority research areas for coordinated investment.

Participants

The workshop gathered leading experts from more than 18 institutions and from more than 12 countries, representing academia, WOAH reference centers, national governments, and global research programmes.

A full participant table is provided in **Annex 1.**

Workshop Setup

The workshop followed the following facilitation structure:

- Plenary presentations on state-of-the-art gaps and priorities.
- Two rounds of structured breakout discussions across six topics (A–F).
- Moderated plenary synthesis to consolidate research recommendations.
- Additional expert consultations conducted during the Brucellosis International Conference to integrate broader perspectives.

A full participant table is provided in **Annex 2**.

Executive Summary

The STAR IDAZ IRC Brucellosis Vaccine Workshop brought together leading global experts in veterinary microbiology, vaccinology, epidemiology, immunology, and public–animal health to identify priority gaps in brucellosis vaccine development and to formulate actionable research directions for the update of the STAR IDAZ Brucellosis Vaccine Research Roadmap.

Discussions during the workshop, as well as follow-up expert consultations with researchers present at the Brucellosis International Conference reinforced the urgency of accelerating vaccine innovation while strengthening evaluation capacity, basic immunology research, biosafety infrastructure, and country-adapted vaccination strategies, particularly in endemic regions.

Key scientific and operational conclusions include:

(1) Live attenuated vaccines remain the most feasible and effective tools, though improvements in safety, stability, and quality control are essential.

(2) Non-living vaccines have significant scientific interest but remain impractical for LMIC mass-vaccination programs due to high cost, multiple doses, and insufficient efficacy in target species.

(3) There is an urgent need for vaccines and diagnostics tailored to camels, buffaloes, yaks, infected with either *B. abortus* or *B. melitensis*, and for sheep infected with *B. ovis*, and wild and domestic pigs infected with *B. suis..*

(4) BSL-3 facility scarcity is a major global bottleneck, requiring harmonised evaluation SOPs and international collaboration.

(5) Better understanding of *Brucella* biology, host immune responses, correlates of immunity, and vaccine-induced protection mechanisms is essential for next-generation vaccine design.

The workshop produced strategic research recommendations for STAR IDAZ and its international partners, focusing on feasibility, scientific impact, and realistic implementation in endemic countries.

Session Summaries

1. Plenary presentations discussions

1.1 Gaps and Priorities for brucellosis vaccines – STAR IDAZ 2018 Roadmap and current perspectives

Professor J.M. Blasco

- There are new *Brucella* species identified in recent decades, but these are not considered important as a threat to domestic animals or humans.
- The most important species for affecting livestock and human health is *B. melitensis*. It is the major cause of human brucellosis, small ruminant infections and cattle infections in mixed breeding systems. This species, while identified primarily as a pathogen of sheep and goats, also infects "non-typical" domestic hosts as camels, water buffalo and yacks in many countries.
- Second in importance is *B. abortus* as it infects not only cattle as a primary host but also humans and the above "non-typical" domestic hosts.
- So, *B. melitensis* and *B. abortus* are priorities for vaccine development.
- *B. suis* could be also a target because biovars 1 and 3 cause human and pig disease in parts of the world and thus is important. But in general, *B. suis* infection in intensive pig farming can be controlled through biosecurity measures. In continental Europe *B. suis* biovar 2 is the major problem. In selective extensive breeding conditions in Portugal, Spain, France and Italy pigs are in close contact with wildlife reservoirs that can infect pigs. For these conditions there is space for *B. suis* vaccine development.
- *B. canis* is not an important human pathogen but it can be a problem in kennel breeding, so it may be interesting to produce a vaccine.
- *B. ovis* is non-zoonotic but causes abortion and infertility in sheep and thus is an important problem in developed and developing countries, needing a specific *B. ovis* vaccine.
- Some wild species can be a carrier of various *Brucella* species but it is not important enough to justify developing a vaccine for these species. Only 2 cases have been well documented for which wildlife is a reservoir (French alps and Yellowstone National Park in the USA), but both cases were the consequence of anthropogenic interventions in wildlife management.
- Brucellosis is not a problem any more in wealthy countries because it has been eradicated by vaccination and testing and culling. However, the disease is a major health problem in Low- and Middle-Income Countries (LMIC) (in the context of brucellosis, LMIC are better described as

resource-limited countries, which is more appropriate for rich countries like China where brucellosis is important).

- It would be feasible to control brucellosis in 2 generations (10-20 years) in countries where it is still prevalent. In these countries it is neither possible to identify individual animals within the whole populations nor to control animal movements and they lack the economic resources required for eradication. Thus, the only feasible control program is mass vaccination, which makes safety of vaccination essential. Other vaccination options are currently explored (for example in India (Holt et al, 2023).

1.2 DISCONTOOLS Report 2024

Professor J.M. Blasco

1. DISCONTOOLS did a gap analysis score of WOAH recognized brucellosis vaccines (December 2024).
2. For all WOAH vaccines interference wanes in a few months when applied before sexual maturity.
3. The *B. abortus* vaccine RB51 interferes in some diagnostic tests (ELISA, FPA, LFIC) while the vaccines strain S19 and Rev 1 interfere in all tests using S-LPS or O-PS as antigens.
4. S19 and Rev1 vaccines have been proven effective in eradication programmes but while the RB51 vaccine in combination with S19 has proven effective in preventing abortions (de Oliveira MM et al, 2022).
5. S19 is cross protective against *B. melitensis* infection in cattle but RB51 has not been proved effective.
1. The 3 vaccines have low virulence in humans, but infections occur and there is no diagnostic test for RB51 in humans, and Rev 1 and RB51 are resistant to streptomycin and rifampicin, respectively.
2. There are WOAH quality control protocols for S19 and Rev 1 but not for RB51.
3. For S19, bull vaccination is not recommended because of safety issues. Safety in pregnant cattle is improved when the vaccine is administered conjunctively (safety not assessed in bulls).
4. For RB51 the manufacturers instruct that it is not to be used in adult cattle and its safety in bulls is unknown.
6. In the DISCONTOOLS scores for WOAH-approved brucellosis vaccines, RB51 scored as poor in cattle, and its usefulness is questionable. It is considered a DIVA but there are gaps regarding

immunity duration and safety issues and RB51 is not a DIVA vaccine when vaccinated cows are exposed to field S brucellae.

5. In the DISCONTOOLS analyses Rev 1 scored very good for immunity but poor for safety. (Note: it should be used between 3-6 months of age, as its application in pregnant sheep induces abortions. The vaccination of young lambs with Rev 1 is a suitable method for the prophylaxis of *B. ovis* infection too. Using Rev 1 for sheep against *B. ovis* was scored very good.
7. There are 2 non-WOAH approved vaccines (Delta *pgm* and the influenza-vectored vaccine [Flu-BA; only registered in Kazahkstan]) but they have not been assessed properly for efficacy and safety.
8. *B. abortus* Delta *pgm* is only registered in Venezuela and Argentina. No advantages to it, since it needs revaccination and interferes in S-LPS-based diagnostic tests. Safety and efficacy were not assessed for this vaccine.
6. Marker (DIVA) vaccines are not important in developing countries in which eradication is not feasible while could be useful in brucellosis-free conditions, in which vaccination is not currently necessary.
9. China, Russia and others favour their non-WOAH approved vaccines but for most data on safety and effectiveness are not available, and the only one tested in Europe (vaccine S2) was found not satisfactory.
10. There is a huge gap in developing vaccines for non-typical domestic species like buffaloes, yacks and camels. *B. ovis* vaccine may be needed in both LMIC and rich countries. Obstacles are many: (1) it takes 10 years to develop a vaccine; (2) few teams are remaining that know how to evaluate a vaccine, and this skill is non-existent in resource limited countries; (3). there is no SOP for evaluating vaccines; and (4) BSL3 facilities are lacking in all these countries.
11. The minimum product profile for new vaccines is focused on safety.

1.3 GALVMED $30 million Brucella Vaccine Prize

Gwynneth Clay

- This competition is using a milestone-based approach. Some Milestones 1 and 2 awards have been made but no vaccine is registered yet. The rules of the prize do not include getting the product into the market once it is registered.
- *AgResults* goals are reducing food insecurity, improving nutrition and health, and increasing livestock productivity.

- She could not reveal the number of groups participating in the competition, but it predominately generated academic interest. It has been a long development phase but still are many groups in the competition.
- The deadline is 2028 for the vaccine to be registered. There are a limited number of groups that are likely to achieve this. No proof of principle has yet been accomplished.
- Strength of this type of funding structure (pull mechanism) is that you can get many more groups involved and many more innovations being involved.
- There is a lack of policy to control the disease in goats and sheep and the process to develop a better vaccine is long and there is a lack of BSL3 facilities for the testing phase.

2. Breakout discussions

2.1 Session 1: Identifying and prioritising needs and gaps

Topic A – Countries' needs and vaccine characteristics

Leader: Gabriela Hernández, Unidad de Microbiología Médico Veterinaria, Servicio Nacional de Salud Animal (SENASA), Ministerio de Agricultura y Ganadería, Heredia, Costa Rica

Main question: Which countries need brucellosis vaccines, and how do local conditions influence vaccine use and desired characteristics?

Sub-question: Are there universal characteristics for an ideal vaccine applicable across developing countries?

Guiding points for discussion:

1. Feasibility: Mass vaccination vs. test-and-slaughter.
2. Practicality: Number of doses, cold chain, DIVA interference, and safety.
3. Barriers: Lack of awareness, weak infrastructure, insufficient training.
4. Capacity building: Training approaches, reference laboratories, field-based learning.

Facilitator focus: Encourage participants to share examples of country-specific challenges and successful approaches to vaccine implementation.

Main points of the discussion

5. We have already designed ideal characteristics so do not need to "reinvent the wheel".
6. Vaccines must be free of costs to farmers to get them to use in LMICs, which are those that require vaccines.
7. Who decides where vaccines are needed in the world?
8. Several things are lacking regarding brucellosis in many countries including awareness of the disease/infection, diagnosis, veterinary services in resource-limited countries; need to push international agencies about the need for these things.
9. May achieve awareness by going through the human infection arena; that is, the zoonotic potential of the disease and impact on public health.
10. Some farmers and veterinary health workers are missing information about how to apply S19 vaccination properly.
11. Because S19 is not patented no incentives for manufacturers to push its use.
12. Need to push mass vaccination programs.
13. Training is more important than generating new vaccines.
14. S19 cost not a problem but quality control is a problem.
15. To reduce vaccination costs, there is a need to explore combining brucella vaccines with other vaccines that are already accepted and used (e.g., FMDV).
16. One option to encourage vaccination is for the government not to give compensation for infected animal if the animal was not vaccinated (e.g., Kuwait) – need to target policy makers.
17. Illegal vaccines also imported into some countries, which is a problem.
18. test and slaughter cannot be used in countries without traceability even in those with diagnostic tests.
19. Are false diagnostic test results provided to farmers, and they show these to the inspectors. How do we create a culture that overcomes this corruption?
20. Training manual needed to train people in countries.
21. The vaccine alone cannot solve the problem but rather need training, diagnostic tests, sanitary conditions.
22. For mass vaccination need 100% vaccination coverage to be successful.
23. Can brucellosis ever be considered as important as other diseases (trypanosomiasis, FMD, etc.) by funders and policy makers?
24. More important in LMIC to control the disease than to eradicate it.
25. Animal movement across international borders can reintroduce the infection to a country that has eradicated it.

Key findings:

- Mass vaccination is the only feasible strategy in most LMICs; test-and-slaughter is unrealistic where traceability is weak.
- S19 and Rev1 remain effective but require strong quality control and proper administration protocols.
- Lack of awareness, weak veterinary services, illegal vaccines, and missed cold-chain constraints undermine success.
- Training and capacity building are more urgently needed than novel vaccines for many countries.
- Combining brucellosis vaccines with existing vaccination programs against other diseases (e.g., FMD) may reduce vaccination costs and increase uptake.
- Policy levers (e.g., compensation conditional on vaccination) could drive adoption.

Conclusion: We need better awareness, training, control policies and reference labs placed in representative resource limited countries affected by the disease. What are realistic expectations for a vaccine? Strategies must include political resources.

Topic B – Priority *Brucella* species and host targets for vaccine research

Leader: Gamal Wareth, Faculty of Veterinary Medicine Benha University, Egypt

Main question: Which *Brucella* species and host animals should be prioritized for vaccine research and development?

Sub-question: How can existing or new vaccines be adapted to meet the needs of different species and production systems?

Guiding points for discussion:

1. *B. melitensis* as the top priority.
2. Safety and efficacy issues with S19 (especially in bulls and adult cattle).
3. Extending vaccine coverage to yaks, camels, and buffaloes.
4. Economic justification for *B. ovis* and *B. suis* vaccines.
5. Balancing resources among *Brucella* species and production systems.

Facilitator focus:

Guide the discussion toward prioritization—identify which *Brucella* species or hosts should be targeted first and why.

Main point of the discussion

7. What comes next after cattle and goats and sheep? We need vaccines for non-typical domestic species that serve as reservoirs (camels, yacks, buffaloes).
8. Regionally the priority is different: should base it on public health cases and economic impact. For example, people drink milk directly from camels so in some countries it is an important public health problem.
9. Some people felt the most important *Brucella* species are those that infect humans; mostly *B. melitensis* but in countries without it, then it is *B. abortus*.
10. What about vaccinating males? Do so in small ruminants but studies in bulls S19 vaccinated by the standard subcutaneous method resulted in genital lesions. The safety of S19 applied by conjunctival route in bulls is unknown and should be investigated as a priority.
11. What about wildlife? Low (if any) priority.
12. If we are going to develop a new vaccine, ideally it should be multivalent for *B. abortus*, *B. suis* and *B. melitensis*.

Key findings:

- *B. melitensis* remains the highest global priority due to human health burden.
- *B. abortus* (and also *B. melitensis* in some areas) remain essential for cattle programs.
- *B. suis* and *B. canis* require targeted vaccine development.
- Urgent vaccine developments are needed for camels, yacks, and buffaloes.
- Regional differences must guide prioritization.
- Brucellosis vaccines associated to other animal vaccines are desirable for mixed-species systems to reduce vaccination costs.

Conclusion: Small ruminants and cattle are the target for control; Other economically important species (buffaloes, camels and yacks) but not wildlife should be a target for vaccine development. Recently, the appearance of canine brucellosis cases caused by *Brucella canis* has left many pet owners struggling to choose between euthanizing their pets or facing high treatment costs. We must prioritize effective vaccine solutions to protect both pets and their owners.

Topic C – Vaccine evaluation

Leader: Jaques Godfroid, Arctic University of Norway

Main question: How should brucellosis vaccines be evaluated in countries lacking high-containment facilities?

Sub-question: How can safety and efficacy be reliably assessed in low-resource settings while maintaining appropriate biosafety standards?

Guiding points for discussion:

1. Realistic biosafety levels and containment requirements.
2. Harmonization of evaluation protocols across laboratories.
3. Minimum field trial conditions for validity.
4. Key influencing factors: breed, gender, pregnancy, nutrition, parasitism.
5. Human–animal interaction and product safety.
6. Adapting global biosafety frameworks for endemic contexts.

Facilitator focus:

Encourage exchange on existing evaluation constraints and practical solutions for conducting trials safely in endemic areas of resource limited countries.

Main point of the discussion

7. First need to define precisely what want to achieve and remember there are also cultural differences to respect (e.g., India)
8. Need guidelines to assess progress as can be a long-term program (takes decades)
9. Policies in many countries require new vaccines to be tested in high containment facilities for the first development stages and experimental studies, that is under BSL-3 conditions and to not be done in countries without those facilities.
10. Whenever adequate biosafety standards are fulfilled, case-control studies in endemic areas can be of value for vaccine evaluation. Otherwise, experiments essential for poor countries (i.e., development of vaccines for camels), could be conducted only by wealthy countries that may not be willing to invest in the subject.
11. A recognized vaccine (e.g., WOAH certified) can be tested in LMIC but not other vaccines that aren't "certified".
12. Need to assess risk and safety for animals and humans when setting up field trials in LMICs.

13. Review/revise the international biosafety regulations to adapt experimental vaccination and challenge to common sense SOPs.
14. International organizations should develop a SOP for vaccine safety and efficacy evaluation.
15. Need to ensure we don't develop sub-standard vaccines by lowering testing standards.

Key findings:

- International biosafety rules and BSL-3 facilities scarcity limit global vaccine development and evaluation.
- Harmonised SOPs for challenge models, endpoints, and vaccine safety and efficacy evaluation are urgently needed.
- Avoid lowering standards to accelerate the development of substandard vaccines.

Conclusion: Evaluation bottlenecks significantly delay vaccine development.

2.2 Session 2: Addressing the identified needs and gaps

Topic D – Feasibility and characteristics of non-live vaccines (Groups 4–7)

Leader: Jean-Jacques Letesson, Namur, Belgium

Main question: What is the potential role and feasibility of non-living brucellosis vaccines (e.g. subunit, RNA, DNA, or vectored vaccines) in controlling the disease?
Sub-question: Can these vaccines provide effective and lasting protection under the practical conditions of developing countries?

Guiding points for discussion:

1. Antigen composition: How many and which antigens are required for effective protection?
2. Cross-species consistency: Are protective antigens conserved among Brucella species and across host species?
3. Vaccine platforms: Which delivery systems (e.g. subunit, RNA, DNA, vectored) appear most promising?
4. Immune mechanisms: What immune components do these vaccines stimulate (humoral, cellular, or both)?

5. Feasibility: Can non-living vaccines be realistically deployed in mass campaigns in resource limited countries given their need for booster doses?
6. Research priorities: Should effort focus on adjuvant innovation or on other vaccine types better suited to endemic contexts?

Facilitator focus:

Guide participants to weigh scientific promise versus practical feasibility. Encourage realistic recommendations, what investments are justified now and what should remain long-term research.

Main point of the discussion

7. The consensus was that a non-living vaccine will not work because *Brucella* is an intracellular bacterium and there are many research papers showing this.
8. OMPs, LPS, etc. have been tried with various adjuvants, and while are effective in mice to some extent, do not work in the target domestic species.
9. We have technology to cultivate live attenuated vaccines in bulk so can be produced at low cost.
10. Do we need LPS in the vaccine? Yes, for sheep and goat vaccines seems to need some LPS while in cattle the rough strain RB51 may be effective in specific settings although there is some low level of O-polysaccharide expressed. It is important to note that Discontools gave RB51 a negative rating.

Key findings:

- Some subunit, RNA, DNA, and vectored vaccines show protection in mice, but consistently less than the reference live vaccines; hence they are predicted to fail to protect adequately in livestock.
- Booster requirements make them impractical for LMIC mass vaccination programs.
- Protective antigen identification remains a challenge.
- A killed vaccine is not a priority for resource limited countries.
- Bacterins and subcellular vaccines have demonstrated minor protection in animals.

Conclusion: Non-living vaccines are a long-term research line, but not an immediate solution and of no priority for resource limited countries.

Topic E – Feasibility and characteristics of non-live vaccines (Groups 2–3)

Leader: Henriette Van Heerden, University of Pretoria, South Africa

Main question: What is the feasibility of developing and deploying live brucellosis vaccines in endemic regions?
Sub-question: How can modern molecular tools improve the safety, stability, and practicality of live vaccines for large-scale use?

Guiding points for discussion:

1. Vaccine selection: Should development rely only on reference strains to ensure openness and comparability?
2. Cold-chain independence: Potential for freeze-drying or stabilizing media to extend shelf-life.
3. DIVA feasibility: Are differentiating vaccines still a realistic goal under endemic conditions?
4. Identification alternatives: Use of ear tags, tattoos, or digital records to mark vaccinated animals.
5. Field applicability: How to ensure safety in pregnant animals and during mass vaccination.
6. Regulatory and biosafety: What international standards or criteria should guide approval and deployment?

Facilitator focus:

Promote debate on balancing innovation and practicality. Aim to identify the most promising approaches for field-ready live vaccines and any regulatory barriers to address.

Main point of the discussion

7. All new vaccines should address the question of deleting genes seen in naturally attenuated mutants to make new engineered mutants.
8. We need to redefine and harmonize the criteria for the evaluation of efficacy and safety of living vaccines in animals.
9. We need to continue testing candidate genes to make a double-attenuated live vaccine.
10. When considering host responses, how do you avoid skewing of a particular T cell response that makes the animal more susceptible rather than towards protective T cell responses?
11. How long does the vaccine need to survive in the animal to be protective is an open question?

Key findings:

- Live vaccines remain the most effective tools being of choice for resource limited countries.
- Needs: increased safety, genetic stability, reduced virulence, ability to use in pregnant animals, and improved field practicality.
- Development should rely on well-characterized reference strains.
- Digital identification technologies (tags, records) can replace DIVA limitations.
- A good habit for monitoring the correct application of the S19 and Rev 1 vaccines in livestock farms, would be to perform serological testing control of the animals 2-3 weeks after vaccination.

Topic F – Research Priorities: Expanding Basic Knowledge

Leader: Sevil Erdenliğ Gürbilek, Harran University Faculty of Veterinary Medicine TÜRKİYE

Main question: What fundamental research is needed to improve understanding of Brucella biology and host immune responses for next-generation vaccine design?
Sub-question: Which biological and immunological mechanisms should be prioritized to guide rational vaccine development and evaluation?

Guiding points for discussion:

1. Protective immune responses: Role of humoral vs. cell-mediated immunity, relevant T-cell subsets, antibody classes, and species-specific mechanisms.
2. Influence of immunization route on protection and duration.
3. *Brucella* biology: Genetic regulation of intracellular survival, key structural components and PAMPs, metabolic adaptations enabling persistence.

Facilitator focus:

Encourage participants to highlight knowledge gaps limiting progress and propose priority research questions. Link basic research needs to potential vaccine innovation paths.

Main point of the discussion

4. If innate immunity is poor don't get a good adaptive immune response. There are few PAMPs identified for *Brucella*. Can this be overcome by adding adjuvants or trained immunity?

5. We need to evaluate which vaccine candidates give more dendritic cell activation and thus better T cell responses
6. It is still unknown what the role of interferon-gamma is in ruminants for protection against *Brucella* and this needs to be established.
7. Basic identification and biology of B cells and T cell helper and regulatory populations in ruminants needs to be done.
8. Time course of expression of particular *Brucella* genes in the host cells and outside of host cells needs to be evaluated.

Key findings:

- Lack of correlates of protection is a fundamental barrier.
- Need deeper understanding of T-cell subsets, dendritic cell activation, and innate immunity triggers.
- Characterize Brucella's genetic regulation inside host cells.
- Map infection bottlenecks and tissue tropism.

Photos from the STAR IDAZ Brucellosis Workshop, 3 November 2025

Additional Expert Input (post-workshop consultation)

Discussions during the workshop, as well as follow-up expert consultations and research presentations at the Brucellosis International Conference contributed to understanding the gaps and priorities that will help shape the Research Roadmap. These experts included the following and an abbreviated summation of important discussion points is included below:

- **Renato de Lima Santos**, Professor (Full), Universidade Federal de Minas Gerais (UFMG), Brazil,
- **Luis Samartino**, Principal researcher at *Instituto Nacional de Tecnología Agropecuaria (INTA)*, Argentina
- **Sergio Oliveira**, Professor of Immunology, University of São Paulo, Brazil
- **Dave Pascual**, Professor of Immunology (with a strong focus on Brucella research), University of Florida), USA
- **Edgardo Moreno**, Brucellosis specialist from Costa Rica
- **Brendan Wren**, UK expert linked to Brucella/zoonotic bacterial research and internationally recognized laboratories.

Standard Operating Protocols for Vaccine Trials

Further discussions outside the workshop emphasized the need for an accepted method for developing a vaccine to test for safety and efficacy such as challenge dose, tissues to evaluate, and route of immunization and challenge. Thus, the need to develop a Standard Operating Protocol (SOP) for all vaccines whether killed, subunit, etc. is needed. We need to establish the criteria for protection and determine: do we evaluate the immune responses as correlates of protection or do we simply go directly to live challenge? We need an expert international panel to come up with this SOP.

Protective antigens

There are a number of important questions to answer or think about regarding this topic:

- What makes a protective vaccine work?
- We need to establish which are smoke screen antigens vs protective antigens.
- Can a virulence factor also be a target for protective immune response?
- How are proteins modified with glycans and how does it affect their role in stimulating protective immune responses?

- How many antigens could be put in a single vector of can we vaccinate with multiple vectors containing different antigens at once – would it negate or overwhelm the immune response to one set?
- Can we use virus like particles to present brucella antigens?
- Important to keep looking at delivery systems and adjuvants as they are developed to sustain the potential for generating a non-living vaccine. DIVA

Subcellular vs live vaccines

In general, subcellular vaccines have not been found to work except in mice and thus some say to move all work out of the mouse and into livestock. There is general agreement that while S19 has some problems such as seroconverting for longer periods if not administered appropriately it has been used successfully to eradicate the disease in some countries while the rough strain RB51 has not. The important first step in eradication is to stop transmission and many feel we don't need a DIVA for this since are vaccinating the whole population. Some feel a DIVA may work for viruses but very difficult for bacteria. It is also agreed that we need to improve Rev 1, decreasing its virulence. To do this we need to identify more virulence genes. This is generally by trial and error of removing genes. In some cases, a gene knock-out may attenuate one species such as *B. ovis* but not for example *B. melitensis* but never vice versa.

Basic research

- Immunology studies in the target animals is still needed.
- Questions such as where does brucella hide in the infected animals not thoroughly answered.
- Why are some species are more pathogenic than others; similarly why does *B. melitensis* prefers goats and *B. abortus* prefers cattle.
- We need to know more about the receptors such as Fc and how they facilitate entry of the bacteria and the ligands on the bacteria.
- Why are some ruminants such as water buffalo more resistant to brucella than cattle even although they get infected (they can abort but more resistant than cattle in general).
- A policy question is how to change the policies of the regulatory agencies so we can try them out new vaccines or strategies such as asking if trained immunity can enhance the effect of the S19 vaccine. Another example is trying new adjuvants such as STING activators as is being tried in cancer patients or lipid adjuvants that activate the Caspase 11 pathway which is known to be important for protection for brucellosis (inflammatory pathway).
- Can we ascertain which small molecules can do the job of innate immunity to supplement vaccine efficacy?

B. suis and *B. canis*

Need a serological test for pigs since the current test works only 50% of the time because these are the abortus tests that are being used. Biovars 1-5 have different combinational expression of A and M antigens that needs to be considered in vaccine development. While there is no vaccine currently it may be more important to get a diagnostic test first. There are 6 million feral hogs and 50% have B. suis biovar 2 in the USA; fortunately, this biovar doesn't infect humans. *B. suis* is also a problem in China. Thus while *B. suis* is important in the US and other places it is not a priority in LMIC. It is also necessary to develop a diagnostic test as well as a vaccine for *B. canis*.

Synthesis of Overarching Scientific Themes

- Live vaccines remain the backbone of brucellosis control.
- Immunology is under-developed in ruminants; correlates of protection unknown.
- Species beyond cattle and small ruminants (camels, buffaloes, yaks) are severely underserved.
- Evaluation capacity and biosafety limitations are major global bottlenecks.
- Non-living vaccine platforms require deeper antigen discovery science.
- Diagnostics especially for pigs, buffaloes, and camels require urgent improvement.

Conclusions

The workshop produced a coherent set of priorities that align scientific feasibility with global needs. Updating the STAR IDAZ Roadmap will require integrating:

- Immediate implementation gaps (training, QC, awareness).
- Mid-term vaccine improvement strategies (safer live vaccines).
- Long-term scientific investments (correlates of protection, antigen discovery).
- Next steps include:
- Updating the Brucellosis Vaccine Research Roadmap using workshop outputs.
- Coordinating with WOAH, FAO, and donors to support infrastructure and SOP harmonisation.
- Identifying collaborative projects through the STAR IDAZ network.

Acknowledgement

We would like to express our sincere appreciation to the Scientific Committee of the Brucellosis Vaccine Research Workshop for their expertise, guidance, and invaluable contributions.

Scientific Committee Members (Authors):

- **Cynthia Baldwin** – STAR IDAZ IRC Scientific Committee
- **Ignacio Moriyón Uría** – University of Navarra, Spain
- **José María Blasco** – CITA Zaragoza, Spain
- **Raquel Conde Álvarez** – University of Navarra, Spain
- **Clara Marín Alcalá** – CITA Zaragoza, Aragón, Spain
- **Latifa Elhachimi** – STAR IDAZ IRC Secretariat

We would also like to thank all workshop participants for their active involvement, constructive discussions, and valuable perspectives shared during the sessions. Their contributions representing diverse regions and scientific backgrounds significantly enriched the outcomes of the workshop.

High level recommendation table

Priority Area	Key Recommendations	Timeframe	Stakeholders	Priority for LIMC countries
1. Improve and modernise live vaccines	- Develop safer, genetically stable derivatives of S19 and Rev1 - Remove antibiotic resistance markers - Create multivalent live vaccines (*B. abortus, B. melitensis, B. suis*)	5-10 years	Academia, industry, regulators WOAH, FAO and other International animal health organizations,	Very high
2. Evaluation frameworks & biosafety	- Develop internationally harmonized SOPs for evaluation of safety and efficacy - Establish field-trial biosafety rules - Enable LMICs to test WOAH-approved vaccines in field trials in absence of BSL-3 facilities - Establish survival duration needed for protection	1–4 years	WOAH, FAO, STAR IDAZ, national regulators	Very high
3. Address vaccines for neglected hosts & species	- Prioritise vaccine developments for camels, yacks and buffaloes - Consider multivalent vaccination platforms - Develop feasible *B. ovis* and *B. suis* vaccines	3–8 years	International animal health organizations, Research institutions, LMIC ministries	Very high High
4. Non-living vaccine innovation	- Continue research on vectors, RNA/DNA, adjuvants, nanoparticles - Focus on trained immunity inducers (BCG, glucans, lipid adjuvants) - Identify protective vs non-protective antigens	Long-term (5–15 years)	Funders, academia	Not a priority for LMIC countries
5. Strengthen DIVA strategies	- Evaluate feasibility of new DIVA vaccines under endemic conditions	2–6 years	WOAH labs, diagnostic companies	Not a priority for LMIC countries

6. Basic research priorities	- Define correlates of protection in ruminants - Map *Brucella* gene expression during infection - Improve understanding of T-cell subsets and dendritic cell activation - Identify PAMPs and innate immune triggers	1–10 years	Academia, global partners	Not a priority for LMIC countries
7. Policy & implementation gaps	- Training manuals for S19/Rev1 deployment - Strengthen veterinary services, QC, and awareness - Promote mass vaccination strategies in LMICs	Immediate–5 years	Governments, FAO, WOAH, Other international organizations	Very high

Annex 1 – Workshop participant list

Name	Affiliation / Organisation	Country
IN PERSON EXPERTS		
Jose M. Blasco Martinez	CITA, Spain	Spain
Angela Arenas	Texas A&M University	USA
Jerod Skyberg	Montana State University	USA
Phil Elzer	Louisiana State University	USA
Jacques Godfroid	Arctic University of Norway	Norway
Gabriela Hernández	SENASA	Costa Rica
Sevil Ederling	Harran University	Türkiye
Cynthia Baldwin	University of Massachusetts Amherst	USA
Clara Maria Marín Alcalá	CITA Aragón	Spain
Latifa El Hachimi	STAR IDAZ Secretariat	Belgium
Gamal Wareth	Benha University	Egypt
Edgardo Moreno	Universidad Nacional	Costa Rica
Fabrizio De Massis	IZSAM Teramo	Italy
Pr. van Heerden	University of Pretoria	South Africa
Ana Cristina Ferreira	WOAH RL CBPP / FAO RC / NRL Brucellosis	Portugal
Sue Hagius	LSU AgCenter	USA
Sam Black	University of Massachusetts Amherst	USA
Gwynneth Clay	GALVmed	Global
Sandra Cavaco	National Institute for Agrarian & Veterinary Research	Portugal
Carto Cossu	University of Pretoria	South Africa
J.J. Letesson	University of Namur	Belgium

Annex 2 – Agenda

Time	Activity	Details	Chair / Speaker / Leader
09:00 – 09:15 AM	Setting the Scene	Welcome and Opening Remarks – Overview on STAR IDAZ IRC's role, roadmap methodology, and workshop objectives	**Latifa Elhachimi** (Kreavet / STAR IDAZ IRC Secretariat)
09:15 – 10:05 AM	ssion 1 – Current ate of Brucellosis ccine Development	—	Chair: **Cynthia Baldwin** (STAR IDAZ IRC Scientific Committee)
09:15 – 09:25 AM		Innovation opportunities to improve livestock-based agriculture in LMICs	Speaker**: Sam Black** (University of Massachusetts Amherst, USA)
09:25 – 09:50 AM		Gaps and priorities for brucellosis vaccines – STAR IDAZ Roadmap (2018) and DISCONTOOLS Report (October 2024)	Speaker: **José María Blasco** (CITA Zaragoza, Spain)
09:50 – 10:05 AM		The Brucellosis Vaccine Prize!	Speaker: **Phil Elzer** (Louisiana State University) / **Gwynneth Clay** (GALVmed)
10:05 – 10:20 AM	**Coffee Break**	—	—
10:20 – 12:30 PM	Session 2 – Breakout Discussions (Round 1): Identifying and Prioritizing Needs and Gaps	Instruction for discussion topics and questions (10 min) Each topic: 30 min discussion + 10 min leader break.	**Latifa Elhachimi** (Kreavet / STAR IDAZ IRC Secretariat)
10:30 – 11:10 AM	Topic A – Countries' Needs and Vaccine Characteristics	Which countries need brucellosis vaccines, and how do local conditions influence vaccine use and desired characteristics?	Leader: **Gabriela Hernández** (SENASA, MAG, Costa Rica)
11:10 – 11:50 AM	Topic B – Priority Brucella Species and Host Targets	Which *Brucella* species and host animals should be prioritized for vaccine R&D?	Leader: **Gamal Wareth** (Benha University, Egypt)
11:50 AM – 12:30 PM	Topic C – Vaccine Evaluation	How should brucellosis vaccines be evaluated in countries lacking high-containment facilities?	Leader: **Jaques Godfroid** (Arctic Univ. of Norway)
12:30 – 01:30 PM	**Lunch Break**	—	—
01:30 – 03:30 PM	Breakout Discussions (Round 2):	Each topic: 30 min discussion + 10 min leader break.	—

	Addressing the Identified Needs and Gaps		
01:30 – 02:10 PM	Topic D – Feasibility of Non-Living Vaccines	What is the potential role and feasibility of non-living brucellosis vaccines (e.g. subunit, RNA, DNA, vectored vaccines)?	Leader: **Jean-Jacques Letesson** (U. Namur, Belgium)
02:10 – 02:50 PM	Topic E – Feasibility of Live Vaccines	What is the feasibility of developing and deploying live brucellosis vaccines in endemic regions?	Leader: **Henriette Van Heerden** (Univ. of Pretoria, South Africa)
02:50 – 03:30 PM	Topic F – Expanding Basic Knowledge	What fundamental research is needed to improve understanding of Brucella biology and host immune responses for next-generation vaccine design?	Leader: **Sevil Erdenliğ** Gürbilek (Harran Univ., Türkiye)
03:30 – 03:45 PM	**Coffee Break**	—	—
03:45 – 04:45 PM	Plenary Discussion	Presentations by leaders (6 topics × 5–10 min): Align research priorities, identify collaboration opportunities, and summarize gaps for roadmap update.	Moderators: Workshop Scientific Committee