AgResults Evaluation:
Brucellosis Vaccine Challenge Project
2019 Interim Assessment

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Acronyms

B. melitensis	*Brucella melitensis*
BSL3	Biosafety Level 3
DIVA	Differentiating Infected from Vaccinated Animals
MVP	Minimum Viable Product
PfR	Pay for results
R&D	Research and development

Preface

AgResults is a $152 million multilateral learning initiative. It promotes the development and dissemination of high-impact agricultural innovations for food security, health, and nutrition through the design and implementation of prize competitions that are a class of "pay-for-results" (PfR) project. AgResults also evaluates the effectiveness and efficiency of these prize competitions and incorporates evidence-based learning to refine the PfR approach.

By using PfR, AgResults goes beyond traditional aid measures to promote the adoption of innovative technologies with high-yield development impact. AgResults calls upon the ingenuity and drive of the private sector to identify and execute the most effective and efficient strategies to achieve development outcomes. It does so by providing incentives to private sector actors to develop and facilitate the uptake of innovative technologies and overcome market failures impeding the establishment of sustainable commercial markets for these technologies or the goods they produce. It thereby aims to achieve substantial and sustained development impacts, including improved food security and food safety, increased farmer incomes, and better health and nutrition.

AgResults is funded by the governments of Australia, Canada, the United Kingdom, and the United States, and by the Bill & Melinda Gates Foundation. The funds are managed through a Financial Intermediary Fund operated by the World Bank as its Trustee. The AgResults team comprises the Steering Committee, Secretariat, Trustee, country-specific Project Managers, and the External Evaluator. The Steering Committee oversees the implementation of AgResults and is composed of the five donors and the Trustee. The Steering Committee is responsible for strategic oversight of the initiative, including endorsement of key management decisions, approval of concepts and business plans for proposed projects, and monitoring of projects and the initiative as a whole. The Secretariat is responsible for implementing the initiative and reports to the Steering Committee. The Trustee provides financial intermediary services.

The Steering Committee appointed Abt Associates to serve as an External Evaluator for AgResults. The evaluator's role is to use rigorous scientific tools to determine to what extent the prize competitions achieve their objectives to produce private sector behaviours and social outcomes different from, and better than, what would have happened in the absence of the AgResults initiative. The evaluator defines the overall evaluation framework for the AgResults initiative and an impact analysis strategy for answering common evaluation questions for each competition. The evaluator implements and analyses field surveys, conducts qualitative market analyses, and communicates evaluation findings to the Steering Committee and wider audiences. The evaluator's role is vital to the AgResults learning agenda of understanding how donors may leverage the private sector to develop and spread agricultural innovation. As funding permits, the evaluator also assesses the sustainability of each competition's benefits once the PfR incentives are removed.

This report summarises findings from our first interim assessment, which reflects initial progress made in the Brucellosis Vaccine Challenge Project since the baseline. Abigail Conrad, PhD, headed the Abt Brucellosis team. Javier Guitian, PhD, of The Royal Veterinary College, conducted data collection, bringing expert knowledge of brucellosis, its current vaccines, and its epidemiology in low- and middle-income countries. Shawn Gilchrist, PhD, of S. Gilchrist Consulting Services Inc., conducted data collection and provided key inputs on the research design, combined with expert knowledge of commercial vaccine development. Tulika Narayan, PhD, provided overall research direction. Cris Price led the quality assurance review of the research methods.

Executive summary

AgResults Brucellosis Vaccine Challenge Project initiative background

The AgResults Brucellosis Vaccine Challenge Project aims to use a pay-for-results (PfR) mechanism to spur the development of an improved *Brucella melitensis* (*B. melitensis)* vaccine for small ruminants (i.e., sheep and goats) that is appropriate for use in low- and middle-income countries. Brucellosis (i.e., infection by *Brucella* bacteria) is one of the world's most widespread zoonoses, which are animal diseases that are communicable to humans. While vaccines exist for *B. melitensis* (one of the *Brucella* species), they are not optimal for use in low- and middle-income country contexts due in part to safety issues and limited market demand. The project will award milestones and then grand prizes to competitors for making progress towards and registering an improved *B. melitensis* vaccine. In total, the project will distribute up to $30 million to competitors.

There are 15 active competitors out of the original group of 20. These interim findings are based on information collected from 11 of the 15 active competitors. Four declined to provide an update or did not respond to our requests. The findings reflect competitors' experiences and progress in the competition from January 2018, since the baseline findings.

Key interim findings

Private sector involvement. At this early stage of the competition, the majority of competitors are satisfied with their participation. In addition, the majority of competitors reported that the competition has helped to improve or expand their organization's *B. melitensis* vaccine research and development (R&D) program, increased the priority of the B. melitensis research program in their organisation, or helped them to obtain funding. However, the majority of respondent competitors anticipate challenges completing the safety and efficacy trials needed for the 2nd milestone prize.

Technology innovation. Since entering the competition, the majority of competitors reported having completed early stages of R&D. More competitors at this stage than at baseline reported that they are engaged in pilot tests and pilot production, which are steps needed to achieve the 2nd milestone prize. The competitors continue to feel that the vaccine requirements laid out by the project are achievable within the project time period. Competitors reported resource constraints as the main barrier to achieving technological developments.

Scale of investment. On average, competitors invested a larger portion of their animal vaccine R&D budget on *B. melitensis* vaccine R&D than at baseline and there was no change in the number of staff working on the vaccine.

Next steps

The evaluation team will continue to monitor the project's implementation. We will conduct annual interim assessments until the endline. The evaluation team will conduct the endline once AgResults awards the grand prize and best-in-class prize.

1. Introduction

This report presents the interim evaluation findings for the AgResults Brucellosis Vaccine Challenge Project using data that were gathered after the competitors had been accepted into the competition in 2019. Therefore, the findings describe an assessment of participation in the project to date.

Brucellosis (i.e., infection with *Brucella* bacteria) is one of the world's most widespread zoonoses, which are animal diseases that are communicable to humans. Brucellosis causes impaired livestock productivity, which disproportionately affects impoverished, small-scale livestock producers (Dean et al. 2012; Corbel 2006; World Bank and TAFS Forum 2011). Two species of *Brucella* are responsible for most of the cases of brucellosis in humans: *B. melitensis* and *B. abortus*, which are sustained mainly in small ruminant (sheep, goats) and large ruminant (cattle) populations (Corbel 2006). For small ruminants, *B. melitensis* (one of the species of *Brucella*) infection ranked second of all diseases considered in terms of livestock units lost worldwide in an evaluation carried out by the World Bank in 2011 (World Bank and TAFS Forum 2011). *Brucella* infection in ruminants causes economic losses due to spontaneous abortion, infertility, drop in milk production, and premature culling (Singh, Dhand, and Gil 2015).

While brucellosis can infect people through multiple routes, the key to preventing human brucellosis is controlling the infection in livestock (Corbel 2006). Nevertheless, vaccination against this disease in small ruminants is uncommon among rural households in developing countries due to its limited effectiveness, concerns about safety for humans and pregnant animals, and a lack of thermostability. Despite a clear need for a better vaccine against *B. melitensis*, there is little incentive for the commercial sector to invest in this area, as the expectations for return on investment are currently unfavourable.

The project seeks to spur development of an improved vaccine for *B. melitensis* that is well suited for use in low- and middle-income countries. The project will award best 10 applications, milestone and then grand prizes to competitors for making progress towards and registering an improved *B. melitensis* vaccine. In total, the project will distribute up to $30 million to competitors.

This report is organized as follows. Section 2 presents an overview of the AgResults Brucellosis Vaccine Challenge Project and the project's theory of change. Section 3 describes the evaluation purpose, questions, and methods, followed by the data sources used in Section 4. In Sections 5-8, we present the results of the assessment for each evaluation question. Finally, in Section 9, we outline next steps for the evaluation.

2. Overview of the AgResults Brucellosis Vaccine Challenge Project

The project's objective is to provide incentives to develop and register a vaccine that is safe, efficacious, and viable for use against *B. melitensis* in small ruminants across the low- and middle-income countries. The vaccine requirements established for the project are meant to address many of the limitations of Rev-1, the existing *B. melitensis* vaccine, in reaching users in low- and middle-income countries.[1] The vaccine developers (or "competitors") are animal health companies, universities, and public animal health organisations.

The lack of incentives for the private sector to invest in this area is the main rationale for implementing this prize mechanism. The rules of the competition were designed to provide a transparent and fair incentive to stimulate innovation.

The AgResults competition is organised in three phases or "milestones". In the **first milestone (application)**, 10 applicants, called "competitors," receive a small prize of $100,000 for submitting the best ten competitive proposals. The judging panel evaluated each application based on scientific soundness and plausibility of the proposed concept, manufacturing capabilities, and availability of animal research facilities. Then, the panel recommended one of three outcomes: (1) accepted into the next phase of the competition with a payment of $100,000; (2) accepted without payment; and (3) not accepted into the competition. While the number of entities receiving the first milestone payment was limited to 10, additional accepted competitors could enter the competition without payment. All entrants, regardless of milestone 1 payment, are eligible to receive subsequent prizes.

In the **second milestone (efficacy study)**, a larger prize of $1 million will be awarded to the first four competitors that are able to demonstrate that their vaccine meets pre-established milestone 2 requirements. The first four competitors that satisfy the requirements, as determined by the judging panel, will receive a milestone 2 prize of $1 million. A competitor may be eligible to receive a separate milestone 2 prize, for a maximum of two, if they develop another vaccine that relies on sufficiently different concepts or technologies, as determined by the judging panel. No competitor has earned this prize yet.

In the **third milestone (registration)**, a single $20 million grand prize is awarded to the first competitor who registers the vaccine (milestone 3).[2] During this phase, competitors will be required to take their vaccine candidates from their milestone 2 deliverables to a registered product with a project-approved marketing authorisation. Beyond the grand prize, there is a best-in-class prize ($5 million) for a vaccine that is registered within a year of the first competitor's registration that meets at least one of the four best-in-class requirements. The best-in-class prize can be awarded to whichever competitor first meets the criteria.

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1 We note that even best-in-class product does not address all limitations of the current vaccine, such as Differentiating Infected from Vaccinated Animals (DIVA). This or other improvements may occur in the course of the AgResults competition or as a result of other research and development (R&D) efforts.

2 The vaccine must be registered in a country that is either a current member of the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products ("VICH Country")—which includes members of the European Union, Japan, and USA—or an AgResults donor country (i.e., UK, Canada, Australia, and USA).

3. Evaluation questions, methods, and data sources

The evaluation of the AgResults Brucellosis Challenge Project, like the other AgResults project evaluations, ultimately seeks to answer questions that test the key components of the project's theory of change. Our theory-based evaluation uses mixed methods to assess change in outcomes over time, between the baseline period and the endline. In this interim assessment, we assess a sub-set of the evaluation questions that are amenable to monitoring during the competition period: questions related to private sector involvement, technology innovation, and the scale of investment (Exhibit 3-1). To answer these questions, we use two evaluation methods: **qualitative assessment** and **a case comparison disease study** (see details in Abt Associates 2016). For the qualitative assessment, we gather information on competitors' experiences and progress through semi-structured questions (administered by phone interviews or in writing, depending on the respondent's preference) and a brief online, structured questionnaire (see Annex A). The case comparison disease study tracks the competitors' vaccine development progress on comparable, neglected diseases through the online questionnaire.[3]

Our data sources included semi-structured interviews with competitors and an online questionnaire. We aimed to collect data from the 15 active competitors in the competition. We collected data from 11 competitors in September 2019. We received responses to semi-structured interviews from 9 competitors and responses to the online questionnaire from 9 competitors. Online questionnaires reflect progress made through July of 2019 (to align with baseline data collect) and investments in fiscal year 2018 to capture the most recent fiscal year. The interim results are based on these data. Four competitors declined to provide data or did not respond to our interview and online survey request.

Exhibit 3-1. Evaluation questions and approaches

#	Evaluation question[4]	Method	Data sources
1	*Private sector involvement:* What evidence exists that the project was able to stimulate private sector involvement in the development of agricultural technology/ innovation?	Qualitative assessment—private competitor motivation, decision-making, and investment in developing technology from baseline to endline	• Semi-structured interviews with competitors[5] • Small sample, structured questionnaires with competitors • Public documents and media • AgResults monitoring data and documents (e.g., competition applications, competitor entry and exit, competitor investment in R&D for competition)
2	*Technology innovation:* Did the project lead to	Case comparison study of alternative disease[6] vaccine	• Semi-structured interviews with competitors and relevant experts

[3] The final set of comparison diseases are *Brucella abortus,* Q Fever, Campylobacteriosis, enzootic abortion, Salmonellosis, Toxoplasmosis, Leptospirosis, Rift Valley Fever, Bluetongue, and Nairobi sheep disease. We considered the following criteria when selecting the comparison diseases: diseases affecting small ruminants, bacteria vs. virus or parasite, zoonosis, abortion, and limited R&D activity.

[4] The evaluation questions are slightly modified from the evaluation questions in our framework to account for the project's prize competition design, which aims to only develop a technology and not scale it up.

[5] In the evaluation design, we planned to also assess non-participating entities' reasons for not participating in the project. However, due to the higher than expected participation in the competition, we found it was not feasible to collect data from non-participating entities. As competitors withdraw from the project, however, we will interview them to understand their reasons for withdrawal.

[6] The final set of comparison diseases are *Brucella abortus,* Q Fever, Campylobacteriosis, Enzootic abortion, Salmonellosis, Toxoplasmosis, Leptospirosis, Rift Valley Fever, Bluetongue, and Nairobi sheep disease. We considered the following criteria when selecting the comparison diseases: diseases affecting small ruminants, bacteria vs. virus or parasite, zoonosis, abortion, and limited R&D activity.

#	Evaluation question[4]	Method	Data sources
	development of new, useful technologies? What levels of innovation short of, or beyond, the specified requirements did the project lead to in the development of the technology?	R&D—assessment of technology development from baseline to endline comparing progress for *B. melitensis* to that of other similar diseases along key vaccine development milestones, such as creating a lab animal model, completing an efficacy study, and registering a vaccine Qualitative assessment—success and failure in meeting MVP requirements by industry and competitor organisational characteristics	• Small sample, structured questionnaires with competitors • AgResults monitoring data and documents
3	*Development impact:* What evidence exists that the project developed a technology that will have the anticipated development impact? Were the required technology specifications well suited to address the constraints expected to limit the development impact?	Qualitative assessment—actual progress and stakeholder perceptions of potential for adoption	• Semi-structured interviews with competitors and relevant experts
4	*Cost-effectiveness:* What is the evidence on the scale of any effect on private sector investment and the cost-effectiveness (relative to no intervention or traditional push mechanisms) of AgResults as a development strategy?	Cost-effectiveness simulations—calculations of the breakeven number of animal vaccinations at which the cost of the project will equal the value of saved animals and the cost of human infections averted	• Small sample, structured questionnaires with competitors • Peer-reviewed literature • AgResults monitoring and project data (e.g., governance costs, verification costs, prize amounts paid)
5	*Sustainability:* If resources and time extension to address this are provided beyond the current evaluation contract: What evidence exists that the impact of the project (e.g., private sector involvement and innovation uptake) is sustainable in the medium to long term—two years after the end of the initiative?	Qualitative assessment—actual progress and stakeholder perceptions about vaccine manufacture, sale, and adoption	• Semi-structured interviews with competitors and relevant experts
6	*Lessons learnt:* What lessons can be learnt about best practices in the design and implementation of R&D pay for results?	Synthesis of learning from other questions (integrated with learning from other technology development projects)	• Semi-structured interviews with competitors and relevant experts

4. Interim findings: Private sector involvement

Key findings

At this early stage of the competition, the majority of competitors are satisfied with their participation. In addition, the majority of competitors reported that the competition has helped to improve or expand their organization's B. melitensis vaccine research and development (R&D) program, increased the priority of the B. melitensis research program in their organisation, or helped them to obtain funding. However, the majority of respondent competitors anticipate challenges completing the safety and efficacy trials needed for the 2nd milestone prize.

To answer Evaluation Question 1 in the first interim assessment, we summarize the competitors' current perceptions about the competition and the reported influence that participation has had on their *B. melitensis* vaccine R&D. We also discuss the challenges to continued competition participation that competitors reported. These findings are based on the semi-structured responses that we received from nine competitors. Here, we discuss participation of both the private and public sector competitors to reflect how their participation may vary.

Competitors' perceptions about the competition

Competitors (six of nine respondent competitors) largely had positive perceptions about the competition, were satisfied with their experience participating so far, and found the competition rules to be clear, all of which may help to retain competitors. A few noted that they would welcome more communication and information exchange between the competitors.

Influence of competition on private sector engagement

Competitors reported varied influence that early participation in the competition has had on their organisations' involvement in *B. melitensis* vaccine R&D. Six of the nine competitors characterised how competition participation has influenced their organisations' R&D. Two of the six competitors reported that the competition has not influenced their organisations' involvement in *B. melitensis* vaccine R&D. These competitors were public and academic organisations that have had a long history of commitment to *B. melitensis* vaccine development, therefore the competition did not change their commitment. Four of the competitors—one commercial and three academic—reported that participation in the competition has facilitated or motivated an expansion or improvement of *B. melitensis* vaccine R&D. One commercial competitor reported that the competition helped them to begin or expand *B. melitensis* vaccine R&D. They reported that, "the vaccine competition has assisted the company to start the development of new animal vaccines, which without the support, it would not have been able to initiate." An academic competitor said that participating in the competition has pushed them to do things that they were not doing before the competition, such as trials in large animals. Another academic competitor stated that, "the vaccine competition helped solidify our research program in *Brucella*." One academic competitor said that the competition spurred a new collaboration to work on *B. melitensis* vaccine R&D.

Four of nine respondent competitors reported related benefits that competition participation has had. Three of the nine respondent competitors—two academic and one commercial—reported that the competition has increased the priority of the *B. melitensis* program in their organisation. Another commercial competitor noted that receiving the award from the reputable AgResults donors was a particularly valuable boost for a medium sized company like theirs.

Two other competitors—one commercial and one academic—said that the competition has helped their organisation to attract investors and obtain research funding. For example, the commercial competitor said, "our participation in the AgResults competition has been of great help to attract investors and increase their interest in our project. In addition, it has been an asset to win different grants." The academic competitor reported that the award allowed them to pursue an efficacy trial and pilot work that was not possible with their previous funding.

Challenges

Several competitors noted that they were facing or anticipated facing challenges fulfilling some requirements of the competition, which may influence their involvement in the competition or ability to achieve prizes.

Competitors primarily reported resource constraints to completing the 2nd milestone requirements. Seven out of nine competitors reported that they face challenges accessing funding—particularly the funding required for the safety and efficacy trials—given the expense of conducting animal experiments. Several competitors said that they are exploring public options for additional funding from their universities, the government, or donors. Six of nine respondent competitors also reported challenges accessing the Biosafety Level 3 (BSL3) facilities where they need to complete animal trials.[7] These challenges include the cost of using the facilities, the limited availability or capacity of the facilities, the biocontainment requirements needed, and the facility expertise required to manage *B. melitensis*. A few competitors also noted challenges identifying industry partners or did not have a clear strategy for identifying one. One academic competitor noted that they have an established commercial partnership but anticipate that additional commercial partnerships would be needed in other geographic areas. Two academic competitors raised concerns about the technical challenges of moving from a mouse model to a host, large animal model.

Beyond the 2nd milestone, five of the nine respondent competitors anticipate challenges registering the vaccine in a country specified in the competition rules, which is often not their home country. In particular, the organisations will need to complete safety and efficacy trials in large animals in the country of registration and have an international partner, which may be difficult for some competitors to accomplish.

[7] Biosafety Level 3 is the rating for pathogenic, potentially lethal agents (Level 4 is the highest biosafety rating). Facilities must meet a set of biocontainment precautions to handle Level 3 rated agents.

5. Interim findings: Technology innovation

Key findings

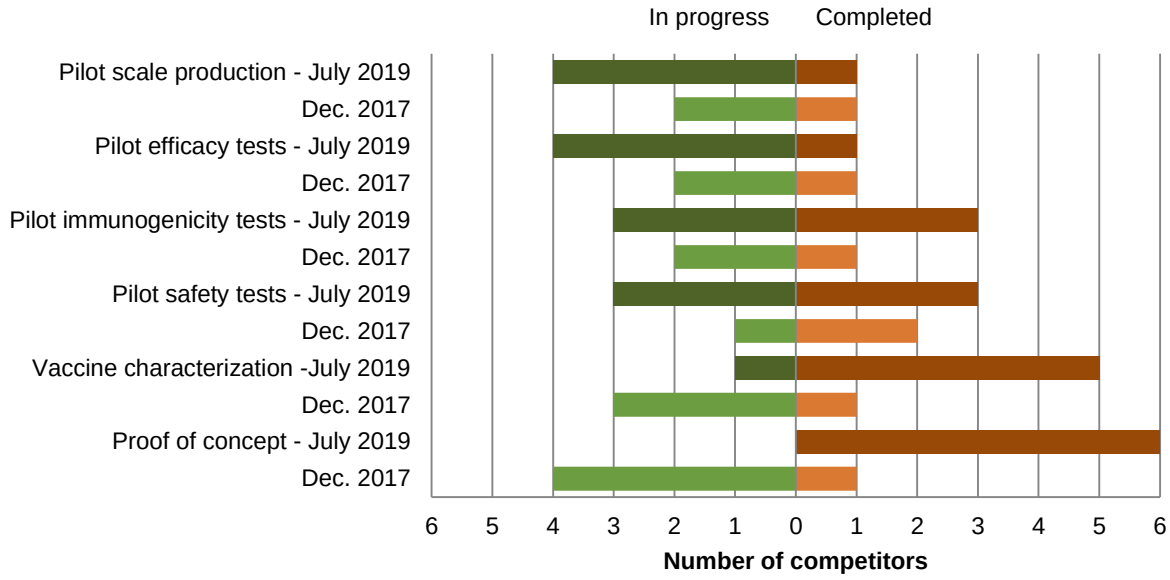
Since entering the competition, the majority of competitors reported having completed early stages of R&D. More competitors than at baseline reported that they are engaged in pilot tests and pilot production, which are steps needed to achieve the 2nd milestone prize. The competitors continue to feel that the vaccine requirements laid out by the project are achievable within the project time period.

To answer Evaluation Question 2 at the interim period, we compare progress on vaccine R&D stages between the baseline and the interim period using responses to our online survey. We also discuss R&D challenges reported by competitors based on our interviews with them. Finally, we outline the interim status of the case comparison disease exercise, which the evaluation will use to help determine whether the competition spurred innovation and development that would not have occurred without AgResults.

Developments in R&D since competition entry

Six competitors (two commercial and four academic) responded to the online questionnaire in both the baseline and the interim. Here, we will report progress made by those six competitors between the baseline period of December 2017 and July 2019. Note that several competitors reported working on several stages at once. In the online questionnaire, five of the six competitors (one commercial and four academic) reported completing the early stages of R&D—proof of concept and vaccine characterisation—compared to one at the baseline (Exhibit 5-1). In the interim period, three competitors (one commercial and two academic) reported completing the next steps of vaccine R&D—pilot safety tests and pilot immunogenicity tests—and three competitors were working on these stages (one commercial and two academic). Only one competitor completed the pilot efficacy tests and pilot scale production. This competitor is an academic organisation with an established *B. melitensis* vaccine development program and was the competitor who had completed the proof of concept at the baseline. Four competitors (two commercial and two academic) reported working on pilot efficacy tests and pilot scale production. In semi-structured responses, the majority of competitors felt that completing these steps to meet the 2nd milestone prize requirements were achievable from a scientific standpoint.

Exhibit 5-1. Competitor progress towards *B. melitensis* vaccine (2nd milestone)

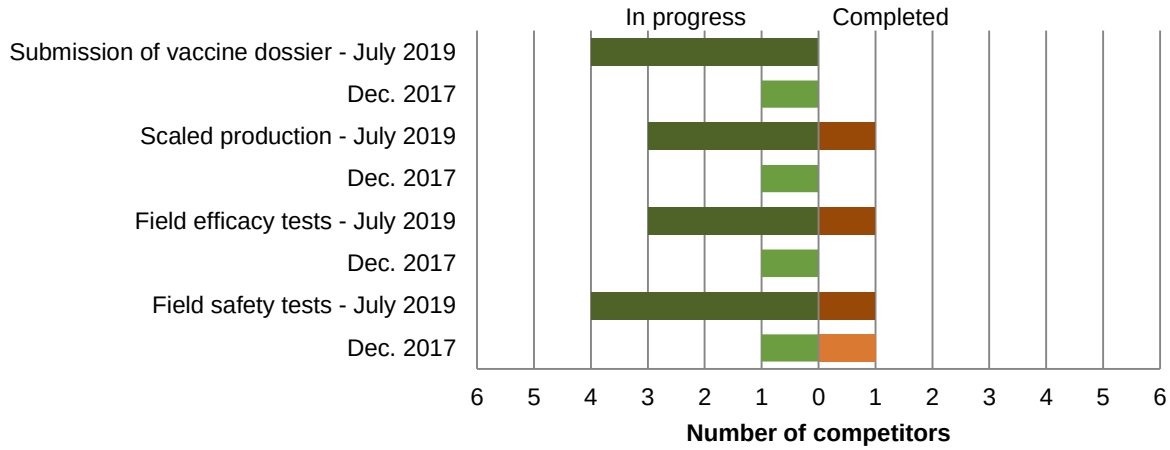


Source: Competitor online survey responses from December 2017 (n=6), July 2019 (n=6).

Competitors also reported making progress in later vaccine R&D stages, beyond those required for the 2nd milestone prize. At the interim assessment, one of the six competitors who responded to the online questionnaire at both time periods reported completing field efficacy tests and scaled production. This is the same academic competitor discussed above with an established *B. melitensis* vaccine development program. This competitor had completed steps through field safety tests at the baseline. Four of the six competitors (one commercial and three academic) reported that they were working on or had completed field safety and efficacy tests, scaled production, and vaccine dossier development, compared to only one competitor at the baseline. This shows progress beyond the reported R&D progress at baseline, although these competitors likely have significant work still required to complete these stages.

In the online questionnaire, we asked respondents to rate how confident they are that they will be able to achieve the vaccine elements during the competition timeframe. Of the nine competitors that responded to the interim questionnaire, the majority reported that they continued to feel relatively confident that the minimum viable produce (MVP) vaccine elements are feasible within the competition timeframe, although, on average, there was a reduction in confidence from baseline about achieving the MVP requirements. As at the baseline, they tend to see the best-in-class elements as more challenging to accomplish and reported a larger, though relatively small, drop in confidence about being able to achieve these versus at the baseline. In particular, competitors were less confident at the interim about the feasibility of achieving the best-in-class elements of thermo-resistant formulation, providing maximum human and animal safety, and cross-species protection.

Exhibit 5-2. Competitor progress towards *B. melitensis* vaccine (grand prize)



Source: Competitor online survey responses from December 2017 (n=6), July 2019 (n=6).

In semi-structured responses, several competitors reported that they had made R&D progress since entering the competition, even though there have not been specific advances in the field since the competition began. One academic competitor noted that the competition stimulated thinking and cross fertilization of ideas between university partners and colleagues, which has improved their understanding of the sophistication of the *Brucella* pathogen.

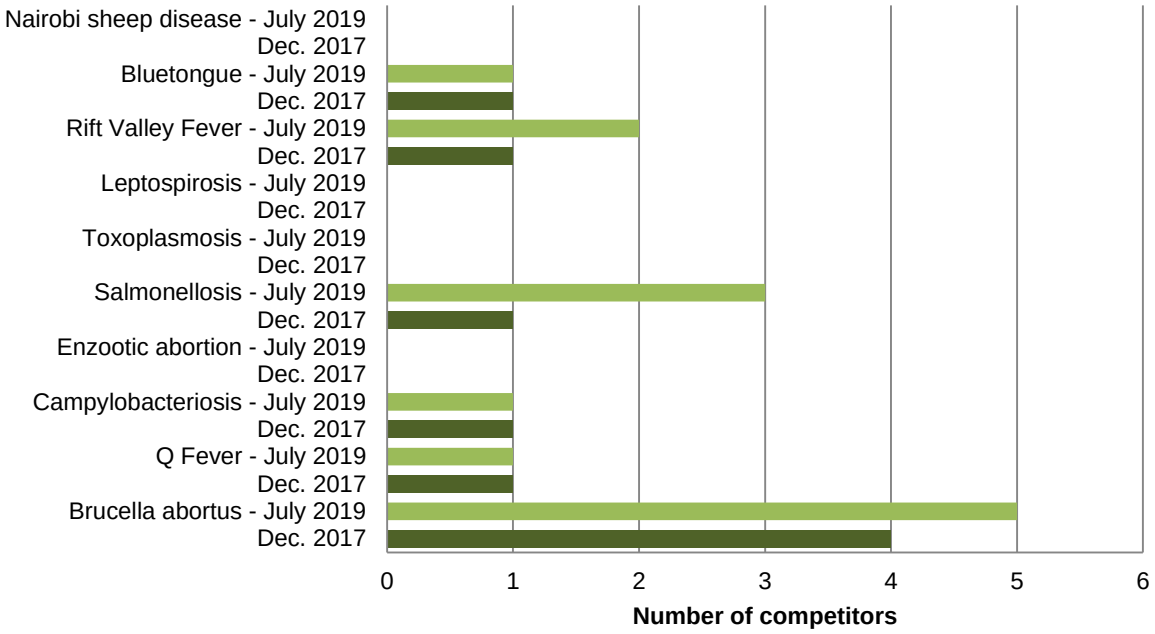
We also asked competitors whether the vaccine developments from their *B. melitensis* work have had any effect on vaccine R&D for other diseases. Six of nine competitors reported that it had not. Three competitors said that it had contributed to improvements or expansion in vaccine research for other diseases. One commercial competitor said that "the competition has assisted us to advance the use of plant-based systems for vaccine production and to add to the relatively small number of cases that demonstrate the viability of this expression system." One academic partner reported that it had helped one of the researchers expand their work on another animal disease using the same platform that they use for the *B. melitensis* vaccine candidate. Another academic competitor said that "the competition has expanded our ability to develop vaccines for zoonotic agents that require high containment."

Work on other zoonotic diseases

To help determine whether the project helps to spur the development and innovation of an improved vaccine, the evaluation compares the progress towards a *B. melitensis* vaccine with the progress that the competitors make towards similar zoonotic diseases (Exhibit 5-3). Here we present an update on the diseases that competitors were working on in the interim period.

As of July 2019, the six competitors that responded to the online questionnaire at baseline and the interim period were working on 6 of the 10 comparison diseases (Nairobi Sheep Disease, Bluetongue, Rift Valley Fever, Salmonellosis, Campylobacteriosis, Q Fever, and Brucellosis cause by *B. abortus*, Exhibit 5-3). While the list of diseases has not changed since the baseline, the number of competitors working on them has grown for Rift Valley Fever (by one competitor), Salmonellosis (by two), and Brucellosis caused by *B. abortus* (by one). These data suggest that the competition may have stimulated R&D on additional livestock diseases, although we do not have the data to establish a cause and effect relationship. This question will be further explored in interviews with competitors planned for June-July 2020.

Exhibit 5-3. Comparison diseases competitors work on



Source: Competitor online survey responses from December 2017 (n=6), July 2019 (n=6).

6. Interim findings: Scale of investment

Key findings

On average, competitors invested a larger portion of their animal vaccine R&D budget on B. melitensis vaccine R&D than at baseline and there was no change in the number of staff working on the vaccine.

Vaccine R&D budget allocation

Four competitors (one commercial and three academic) provided information on the allocation of their animal health budget in the online questionnaire in both periods. On average, these four competitors allocated 69 percent of their animal vaccine R&D budget to *B. melitensis* vaccine development during their last completed fiscal year, with a range of 4 percent to 100 percent. This is higher on average compared to the baseline in 2017, when these competitors allocated an average of 38 percent to *B. melitensis* vaccine development. Three of the four increased their budget allocation to *B. melitensis* vaccine development during this period. The largest increase was by one academic competitor, which increased their budget allocation from 50 percent to 100 percent between the baseline and interim period. One academic competitor lowered the budget allocation to *B. melitensis*, however only by one percent. Only two of these competitors reported their organisations' animal health budget at both periods.

Among the nine online questionnaire respondents at the interim period, they reported allocating 56 percent of their animal health budget on average to *B. melitensis* vaccine development in the most recent completed fiscal year, with a range of 4 percent to 100 percent. On average, the four commercial competitors and the five academic competitors allocated nearly the same portion of their animal health budgets to *B. melitensis* vaccine development. However, on average, commercial competitors had a lower average expenditure on *B. melitensis* vaccine development ($135,666) compared to academic competitors ($373,750). For the current fiscal year, the respondents on average reported a similar budget allocation to the last fiscal year for *B. melitensis* vaccine development at 53 percent. However, the commercial competitors reported a lower allocation of 47 percent on average compared to 59 percent on average for the academic competitors for the current fiscal year.

Vaccine R&D staffing

As another indicator of investment, we asked competitors how many full time R&D staff they have working on *B. melitensis* vaccine development. The number of full-time staff working on *B. melitensis* vaccine development has largely remained the same since the baseline among the five competitors that provided this information at baseline and the interim period. On average, these competitors had 4.6 full time staff working on *B. melitensis* vaccine development in the interim period. Among all nine competitors that responded at the interim period, academic competitors had a slightly higher average number of staff, with an average of 5.1 full time staff working on *B. melitensis* vaccine development, compared to 3.3 staff for commercial competitors.

7. Interim findings: Early learning

This section includes preliminary conclusions based on the information that emerged since the baseline. Additional findings related to the competition design can be found in the baseline report (Abt Associates, September 2019).

Positives

- The competition has galvanized efforts to develop an improved *B. melitensis* vaccine.
- On average, competitors increased their animal health budget allocation to *B. melitensis* research.
- More competitors are working on other zoonotic diseases.

Challenges and possible solutions

- The majority of competitors face constraints related to limited availability and access to animal facilities for testing, which cannot be easily remedied on a short-term basis.
    - Future prize designs should recognize that this is a challenge faced by solvers and delays in vaccine development due to lack of access to animal facilities should be expected. The donors could also consider providing support to entrants who lack this capacity.
- The majority of competitors, particularly the commercial organisations which have smaller budgets than the universities and public organisations, reported funding constraints.
    - Future prize designs could be tailored to fit the needs of the competitors. For example, less resourced entities could be offered partial upfront payments or larger milestone prizes. However, this approach may compromise fairness. Alternatively, all qualifying applicants can receive larger upfront payments to help sustain their participation.
- In some cases, commercial expertise is limited to a geographical area where the solver is based limiting the solver's ability to undertake global commercialization.
    - Future prize designs could include assistance with marketing or distribution to solvers at advanced stages of vaccine development.

These early learnings may evolve over the course of the project and are preliminary at this stage.

8. Evaluation next steps

The evaluation team will continually monitor the project's implementation as part of its ongoing qualitative assessment. We will conduct short, annual, semi-structured interviews and/or online surveys with competitors on their progress and activities in each year. We will also remain in regular communication with the Project Manager, the Secretariat, DFID, and the Steering Committee to keep track of any issues that arise, their importance to the project implementation, and how they are eventually resolved. This will continue up to the point of the endline.

The evaluation team will conduct the endline once AgResults awards the grand and best-in-class prizes. If the best-in-class prize is never awarded, we will complete the endline in the final year of the project. Should neither of these prizes ever be awarded, we will continue our ongoing assessment and conduct the endline in the final year of the project.

References

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Annex A

Interview guides

Competitors – Non-commercial

STATE OF *B. MELITENSIS* VACCINE R&D

1. Have there been any key advances in the last year that will help further the development of a *B. melitensis* vaccine?

***B. MELITENSIS* VACCINE R&D AT SOLVER ORGANIZATION**

2. What, if any, effect has participation in the AgResults vaccine competition had on your research group's *B. melitensis* vaccine work so far?

3. If your group works on other livestock vaccines, has the priority of *B. melitensis* vaccine research relative to other livestock R&D changed in the last year?

4. Do you currently have a dedicated team working on the *B. melitensis* vaccine development?

5. Have there been any changes in your team in last year? If yes, what has changed?

6. For the AgResults competition, how and when do you plan to find an industry partner?

    a. What role do you anticipate the industry partner playing in *B. melitensis* vaccine development?

7. What challenges are you currently facing while trying to achieve milestone 2?

    a. How are you trying to overcome these challenges?

8. Do you think the minimum viable product requirements and best in class requirements are achievable for your current team within the competition timeframe?

9. What are the major obstacles that you think your group will face in developing a *B. melitensis* vaccine that meets the minimum viable product requirements?

10. Are there additional partners, capabilities, or resources that you think your research group might need, but you do not currently have, to achieve the competition specifications?

11. What constraints, if any, might you face in registering a *B. melitensis* vaccine?

12. Has this competition affected the development of other livestock vaccines or on other components of your research program?

VACCINE PRIZE COMPETITION

13. What is your level of satisfaction with the competition so far?

    a. What has been positive about participating in the competition?

b. What has been negative about participating in the competition?

14. What is your level of satisfaction with the clarity of competition rules?

15. What would you change about the competition?

CONCLUDING

16. Is there anything else you would like to share with us that we have not discussed already?

17. Do you have any questions for us about the evaluation?

Competitors – Commercial

STATE OF *B. MELITENSIS* VACCINE R&D

1. Have there been any key advances in the last year that will help further the development of a *B. melitensis* vaccine?

***B. MELITENSIS* VACCINE R&D AT SOLVER ORGANIZATION**

2. What, if any, effect has participation in the AgResults vaccine competition had on your company's *B. melitensis* vaccine work so far?

3. If your company on other livestock vaccines, has the priority of *B. melitensis* vaccine research relative to other livestock R&D changed in the last year?

4. Do you currently have a dedicated team working on the *B. melitensis* vaccine development?

5. Have there been any changes in your team in last year? If yes, in what way?

6. What challenges are you currently facing in working to achieve milestone 2?

    a. How are you trying to overcome these challenges?

7. Do you think the minimum viable product requirements and best in class requirements are achievable for your current team within the competition timeframe?

8. What are the major obstacles that you think your group will face in developing a *B. melitensis* vaccine that meets the minimum viable product requirements?

9. Are there additional partners, capabilities, or resources that you think your research group might need, but you do not currently have, to achieve the competition specifications?

10. What constraints, if any, might you face in registering a *B.melitensis* vaccine?

11. Has this competition produced any effect on the development of other livestock vaccines or on other components of your company?

VACCINE PRIZE COMPETITION

12. What is your level of satisfaction with the competition so far?

a. What has been positive about participating in the competition?

b. What has been negative about participating in the competition?

13. What is your level of satisfaction with the clarity of competition rules?

14. What would you change about the competition?

CONCLUDING

15. Is there anything else you would like to share with us that we have not discussed already?

16. Do you have any questions for us about the evaluation?

Online questionnaire

Note, this questionnaire was programmed in SurveyGizmo, an online survey platform, so the administered questionnaire had an interactive format.

1. What is your most recent completed fiscal year?

2. What is the first month of your fiscal year?

3. What is the total expenditure in United States Dollars (USD) by your company or research group on all animal vaccine research and development in [value Q1]?

   _____ USD

4. Approximately what percentage of the total animal vaccine research and development expenditures at your company or research group was for the *Brucella melitensis* vaccine in [value Q1]?

   _____%

5. What is the total budget in United States Dollars (USD) of your company or research group for all animal vaccine research and development for the **current fiscal year**?

   _____USD

6. Approximately what percentage of the total budget in United States Dollars (USD) for animal vaccine research and development at your company or research group is allocated to the *Brucella melitensis* vaccine for the **current fiscal year**?

   _____%

7. How many full time staff currently work on *Brucella melitensis* vaccine research and development at your company or research group?

   _____

8. Please indicate all stages of *Brucella melitensis* vaccine development reached and completed by your company/research group as of July 2019. Select all that apply.

Stage	Begun	Completed
Proof of concept → A and B	❑	❑
Vaccine characterization → A and B	❑	❑
Pilot safety tests in target animal → A and B	❑	❑
Pilot immunogenicity tests in target animal → A and B	❑	❑

Pilot efficacy tests in target animal → A and B	❑	❑
Pilot scale production → A and B	❑	❑
Field safety tests → A and B	❑	❑
Field efficacy tests → A and B	❑	❑
Scaled production → A and B	❑	❑
Submission of vaccine dossier → 5	❑	❑
Vaccine registered → 5	❑	❑
Vaccine manufactured and sold → 5	❑	❑
Other. Please describe: _____	❑	❑

A. Have you started manufacturing for *B. melitensis* vaccine production? Select one.
   - ❑ Yes, through a partner
   - ❑ Yes, without a partner
   - ❑ No, but are currently developing a plan with a partner
   - ❑ No, but are currently developing a plan without a partner
   - ❑ No, not yet developed a plan

B. Do you have a plan for *B. melitensis* vaccine registration? Select one.
   - ❑ Yes
   - ❑ No, but are currently developing a plan
   - ❑ No, not yet developed a plan

9. On a scale of 1-5, where 1=not at all likely and 5=very likely, please indicate your level of confidence that your team can achieve these *B. melitensis* vaccine elements within the Competition timeframe:

Minimal Viable Product Elements

MVP elements	Enter number 1-5 1=not at all likely 5=very likely
In all stages of gestation, no more than 5% of the vaccinated animals should abort due to the vaccine strain	
Shedding levels similar or less than for Rev-1 in milk, aborted material, and vaginal and semen secretions	
Any adverse reactions are compliant with applicable regulatory criteria	
Long-term persistence of the vaccine strain for whole *Brucella* bacterium attenuated vaccines is less than 2 months	
Minimum age of vaccination 3 months	
If a live organism, demonstrates no reversion to virulence	
Administration via ocular (palpebral), other mucosal, intramuscular, subcutaneous, or other suitable innovative route	
The vaccine demonstrates 80% or higher protection compared with among unvaccinated animals in controlled trial conditions	
Single vaccination annually, or duration of protection lasts for at least two gestations with a single vaccination.	
Shelf life no less than 18 months under controlled conditions	
Affordable for smallholder farmers, including a sufficiently low cost of manufacturing.	

Best-in-class elements

Best-in-class elements	Enter number 1-5 1=not at all likely 5=very likely
A multi-species vaccine with cross protection against both *B. melitensis* in small ruminants and *B. abortus* in cattle	
An efficacious vaccine meeting the MVP requirements that would offer an enhanced level of human and animal safety	
Vaccine stays effective after being kept at a minimum of 45 degrees centigrade for 3 weeks or more	
Facilitates clearing of the infection and/or reduces abortions or clinical signs of infection in animals	

10. Does your company/research group currently work on vaccines for any of the following diseases? Select all that apply.
    - ❑ Brucellosis caused by *Brucella abortus*
    - ❑ Q Fever
    - ❑ Campylobacteriosis
    - ❑ Enzootic abortion
    - ❑ Salmonellosis
    - ❑ Toxoplasmosis
    - ❑ Leptospirosis
    - ❑ Rift Valley Fever
    - ❑ Bluetongue
    - ❑ Nairobi sheep disease
    - ❑ My organization does not work on vaccines for any of these diseases → Skip 7

11. Please indicate the stage of development for [preload disease list from 10] vaccine reached by your company/research group as of July 2019. Select all that apply.
    - ❑ Vaccine characterization
    - ❑ Pilot safety tests in target animal
    - ❑ Pilot immunogenicity tests in target animal
    - ❑ Pilot efficacy tests in target animal
    - ❑ Pilot scale production
    - ❑ Field safety tests
    - ❑ Field efficacy tests
    - ❑ Scaled production
    - ❑ Submission of vaccine dossier
    - ❑ Vaccine registered
    - ❑ Vaccine manufactured and sold

12. Please feel free to add information or make comments related to the Brucellosis vaccine competition.

    _____