What topics should be prioritised for the provision of funding by DAFM using the ERAD TB research fund in the period 2022-2024?

TB Scientific Working Group

John Griffin, Philip Breslin, Margaret Good, Stephen Gordon, Eamonn Gormley, Fraser Menzies, Simon More, Siobhán Ring and Jimmy Wiseman

14th July 2022

1 Introduction

Through the ERAD Division, DAFM funds applied research into areas relevant to the eradication of bovine tuberculosis. This research has guided and influenced the development of policy, ensuring a firm evidence base for decisions and enabling DAFM to evaluate the impact of policies and alternative strategies. This research budget has been a flexible and nimble tool enabling the relatively rapid funding of research to answer policy questions as the TB situation changes. The most recent iteration of the TB research strategy, which was published in 2018, listed eight priority areas for that call.

One of the roles of the TB Scientific Working Group (SWG), as outlined in the Bovine TB Eradication Strategy, is "Providing opinions to the Forum about themes for further scientific research which can guide and inform DAFM research funding calls for bTB issues". Under that remit, the SWG has been requested to provide an opinion on topics which should be considered priorities for funding by DAFM using the ERAD TB research fund in the period 2022-2024. Based on this opinion, DAFM will publish a renewed bTB Research Strategy for this period.

The scope of the opinion covers areas of policy-oriented scientific research relating to bovine tuberculosis eradication in Ireland. Preference is generally given to research areas more related to the TB eradication programme and related policy challenges than to fundamental biological research related to bovine TB.

2 Methodology

Setting priorities for animal health research is a complex process. To the best of the knowledge of the SWG, no formal methods have been used for this purpose in the area of animal health. In the human health field, there has been an increase in the development and use of various new methods. The Child Health and Nutrition Research Initiative (CHNRI) method is an approach commonly implemented, with over 50 published examples in the literature [1–3]. The methodology used by the SWG was guided by this method and on the implementation of the method as described by Irvine et al. [4].

The research prioritisation exercise was performed in four phases in order establish a list of priority research questions and final research themes.

Phase 1: Submission of priority research questions

Stakeholders were invited to individually draw up lists of research questions for evaluation. The stakeholders consisted of members of the TB Forum and other individuals who are knowledgeable about or participate in bovine TB research in Ireland or other countries. The list was drawn up by ERAD Division and issued by the Chair of the SWG. All individuals on the list were invited by email to submit research questions which, if answered, would assist in the eradication of bovine tuberculosis in Ireland and which should be considered as priorities for funding in the ERAD TB research fund. They were asked to frame the questions under one or more of the following thematic areas:

1. Epidemiology
2. Vaccination
3. Diagnostics
4. Economics and Social Science
5. Other

Phase 2: Thematic content analysis of priority research questions submitted

All of the submissions were examined by a subgroup of the SWG, consisting of the Chairperson and one member of the SWG. Some of the submissions were in the form of research proposals and these were converted into research questions. Recurring or overlapping questions were identified, merged and placed in the appropriate thematic group. The subgroup prepared an excel spreadsheet containing each submission and the corresponding research question and a system for evaluating each research questions as described below in Phase 3 was developed. All of the members of the SWG were consulted in relation to the overall approach for evaluating the submissions.

Phase 3: Scoring of research questions

The collated merged research questions were forwarded by email to the members of the SWG who were invited to score the research questions using predetermined criteria, as follows.

CRITERION 1: ANSWERABILITY
Can the question be answered through research?

CRITERION 2: IMPACT
If answered, could this information substantially impact the policy direction of the National Programme?

CRITERION 3: DELIVERABILITY
Is an intervention possible given political, economic and logistical considerations?

CRITERION 4: Capacity building and STAKEHOLDER engagement
Would the research contribute to capacity building in terms of collaboration, network building, stakeholder engagement and communication?

Members of the SWG were requested to answer the questions related to each criterion as “High”, “Medium” or “Low”. These were then converted to a score (“High” = 5, “Medium” = 3, and “Low” = 1). Participants were allowed to leave a response blank if they did not feel sufficiently informed to make a judgment. Blank or incomplete responses were omitted in the calculation of overall score for the question.

The rankings of the research question were based on the total Research Priority Score (RPS) according to the formula:

RPS = [(answerability + impact + deliverability + capacity building/stakeholder engagement)/4].

This provided the score of a single evaluator for a particular question. The final score for a particular research question was obtained by adding the RPS of the individual evaluators and dividing this value by the number of evaluations for that question. For example, if a single evaluator gave a score of high (5) for answerability, medium (3) for impact, medium (3) for deliverability, and high (5) for capacity building/stakeholder engagement, the RPS for that research question for that evaluator would be (5+3+3+5)/4 = 4. If there were 5 evaluators of the question and the RPS values of the individual evaluators were 4, 5, 3, 4 and 4, then the final score would be (4+5+3+4+4)/5 = 4.

Phase 4: Identification of top thematic priorities per research area

The outcome of the evaluation process was reviewed by the members of the SWG to identify the priority themes emerging from the highest ranked research questions in each thematic area (i.e., epidemiology, vaccination, diagnostics, economics and social science and other). Other factors were taken into account in this phase to identify the priority themes. In particular, consideration was given to current or recently completed research funded under the TB ERAD Research Fund with a view to ensuring continuity and consistency of bovine TB research in Ireland. The overarching principles of the DAFM TB research strategy, as outlined in Section 1 above, were also taken into account. The score attributed to a proposal may not necessarily preclude a project from being supported if it is amalgamated into a larger study or if it can be completed as a discrete project with relatively small funding or will be of short duration.

3 Results of evaluation of submissions

Submissions were received from 12 individuals or groups, with a total of 105 questions/proposals. When similar questions or proposals were merged, this left a total of 84 research questions for evaluation by the members of the Working group. The breakdown by thematic area is shown in Table 1.

Table 1 Number of questions/proposals submitted and number of research questions evaluated by members of SWG, by thematic area

Thematic area	Number of questions/proposals submitted	Number of research questions evaluated
Epidemiology	63	49
Vaccination	13	11
Diagnostics	9	8
Economics and Social Science	18	14
Other	2	2
Total	105	84

Each thematic area was further divided into thematic subgroups as shown in Tables 2 - 5 below.

a. Epidemiology thematic area

In the epidemiology thematic area, research questions were submitted on a wide range of areas, including source attribution, herd risk factors, animal risk factors, geographical risk factors, cattle breeding and genetics, *M. bovis* genetics, the role of wildlife and TB eradication strategies. Submissions were also received in relation to the development of research tools such as whole genome sequencing (WGS), mathematical modelling and big data technology.

A research question related to the directionality and extent of interspecies and intraspecies transmission of *M. bovis* received the highest score (4.9) in this thematic area. An answer to this question could provide valuable information on the relative contribution of cattle-to-cattle transmission, badger-to-cattle transmission and deer-to-cattle transmission in the epidemiology of bTB in Ireland. The objective could be achieved through the use of WGS technology. However, a lot of WGS and other data will be required from different geographical areas over an extended period of time to answer this question at a national level. Another research question was related to determining the source of an outbreak on a particular farm (Score = 3.6). WGS technology may also be of assistance in answering this question. However, resources are limited in terms of availability of WGS technology and the preparation of samples required for this process; hence, it is very unlikely that WGS sequencing will be available for all TB breakdowns in the foreseeable future. In general terms, the application of WGS technology needs to be focused and carefully managed and the use of WGS for determining the source of outbreaks at individual farm level is more of an implementation issue rather than a research issue.

There were a lot of questions relating to the role of wildlife in the epidemiology of bTB in Ireland. One question related to how badgers and deer transmit *M. bovis* to cattle. There was a general consensus among the evaluators that this is a key question and that more precise information on the specific transmission mechanisms between wildlife and cattle would be very useful in terms of implementing control strategies. However, it was also agreed that this is an extremely complex area of research and determining

precisely the transmission mechanisms would be very challenging and would require long-term research. Some work has already been carried out in this area [5,6]. These and other studies provide increasing evidence that indirect transmission, such as access by cattle to badger setts, plays a major role in the transmission of infection from wildlife to cattle. Overall, the score for this question was 3.2.

A number of submissions were related to the role of deer in TB maintenance in Ireland. The scores for these research questions were relatively low (2.1 to 3.2). One of the reasons for this is the difficulty in determining the role of deer through research. Currently, the submission of deer samples to the National Reference Laboratory are small in number and are unrepresentative of the national deer population. Using WGS on *M. bovis* isolates from cattle and deer from the Calary study, it was found that cattle and deer share highly similar *M. bovis* strains, suggesting that transmission between these species is occurring in the area [7]. Ongoing collection of more representative samples, WGS and mathematical modelling will contribute to elucidating the role of deer in the epidemiology of bTB in Ireland.

A research question related to the role of wild goats in the transmission of *M. bovis* also received a low score (1.6). This highlights the fact that the research questions were evaluated in relation to their national importance. It has been postulated that wild goats may play a role in the epidemiology of bTB in the Burren in Co. Clare. Research activities may be warranted in relation to their role in that geographical area but it is unlikely that they play a role in other parts of the country.

There were also a question relating to the key drivers of dynamic population changes in badgers that increase the probability of spillover of TB into cattle. This research question got a medium score (2.9). A detailed study has already been carried out in this area [8] and an ongoing study will contribute additional information regarding this question so a further study would be of lesser priority than research in other areas.

A number of the submissions received from stakeholders related to herd and animal risk factors, including environmental factors that may influence the epidemiology of *M. bovis*. In that context, a proposal for research on the relative contribution of cattle movement in the epidemiology of bTB using inward contact chain methodology achieved a high score (4.3). The role of cattle movement in transmitting *M. bovis* between cattle herds in Ireland is already well established (e.g., [9]) but more precise information on the contribution of this source relative to other sources would be worthwhile. Contact Chain methodology has the potential to do this. A submission was also received in relation to the potential impact of risk-based trading on the bTB prevalence The proposer of this question suggested that mathematical models could be used to model various "what if" scenarios related to risk-based trading. These would inform on the likely impact of risk-based trading in different business systems in Ireland. Such models should inform on the temporal scale of such changes, whether the outcome could be improved with additional interventions (e.g., stricter use of severe interpretation; more individual cattle restrictions based on risk etc.), how the movement structure may change and who the "winners and losers" might be. This approach has already been used in GB [10,11]. Another submission was related to risk-informed trading. Risk-informed trading policies might allow for the TB-history of herds to enter the public domain but there is no enforcement on how herds trade with each other. This obtained a score of 3.8. Basically the same approach would be used to investigate this question as for risk-based trading. However, factors such as incentives to engage in

risk-informed trading could also be investigated. Note, that most of the submissions on risk-based trading were dealt with under the social and economics theme.

Some of the research questions relating to animal, herd and geographical area risk factors received a relatively low rating. The main reason for this is the fact that many of the risk factors have already been the subject of research projects. Consequently, the role of these risk factors are already relatively well understood and it is unlikely that further knowledge would fundamentally change the national policy direction. Also, some of the studies would be complex and resource intensive to undertake. One of the proposals related to use of neck harness technology to track movements and health parameters to determine if there are any indicators of when cows are more likely to become infected. While the availability of this relatively new technology could potentially provide information on animal level risk factors for infection with *M. bovis*, this is a very complex area and there was a view among the evaluators that it was unlikely that the research would provide an evidence base for a policy that would lead to a reduction in TB incidence. Another study related to the role of farm fragmentation in the epidemiology of bTB. This would be a challenging topic to research from a scientific point of view but the question would be answerable. Given that fragmentation is an integral feature of Irish farms, it would be difficult to change this aspect of farm structure based on the findings of a TB-related study.

There was a proposal for research on the role of slurry in the transmission of *M. bovis*. The potential role of slurry in the transmission of *M. bovis* and many other pathogens is well established and there have been many studies have been carried out in this area. (See review of McCallen et al. [12] and Allen et al. [6]). Biosecurity advice to prevent transmission of *M. bovis* and other pathogens from slurry has been developed. However, important questions about the role of slurry in the epidemiology of bTB, such as its relative contribution to bTB herd breakdowns and the precise mechanism by which cattle become infected from slurry, remain outstanding. Answering these questions would be very challenging from a study design point of view. For this reason this proposal received a relatively low score (1.75). The members of the SWG are of the view that the primary focus on this area should be on the implementation of biosecurity advice rather than further research.

There was also a proposal to carry out a more general study to quantify the role of the environment in the transmission of *M. bovis*. A number of studies have been carried out in this area, including a paper by Good et al. [13] which showed that herds depopulated for bTB (by definition, at high bTB risk) were not significantly different from herds depopulated for BSE, i.e., herds with no or a low previous bTB risk. For this reason and because of the difficulty of designing a study for this type of research, this proposal received a relatively low score (1.8). Nevertheless a recent review of the environmental risk by Allen et al [6] concluded that relative importance of persistent bacilli for environmental transmission, if it occurs to any great degree, remains to be ascertained. With the new bacteriological and detection tests which are becoming available, it may be possible to shed further light on the role of the environment in the epidemiology of bTB in Ireland in future years.

The outcome of this part of the study highlighted the potential of relatively new technologies to further elucidate the epidemiology of bTB. These include whole genome sequencing, mathematical modelling, machine learning and the use of inward contact chains to elucidate the role of cattle movement in the epidemiology of bTB. In general, these achieved high scores.

The score for each question is shown in Table 2 together with its thematic subgroup.

Table 2 Questions submitted under the epidemiology theme and the score for each question, in order of descending score value

Subgroup	**Research Question arising**	
Source attribution	What is the directionality and extent of interspecies and intraspecies transmission?	4.9
Development of research tools	Can WGS be further used in badgers to determine their role in individual outbreaks? Can the integration of data from WGS and AHCS be used to provide important information on the epidemiology of bTB?	4.8
Herd risk factors	What is the relative contribution of cattle movement in the epidemiology of bTB in Ireland based on information obtained from inward contact chains?	4.3
Development of research tools	How can mathematical modelling be used to provide information on the epidemiology of bTB? In particular, how can mathematical modelling help inform our understanding of two host disease dynamics under different management scenarios? What is the idealised strategic modelling tool and tactical modelling tool for decision support in the TB programmes?	4.2
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	What is the relative contribution of badgers to the herd level of bTB in Ireland and Northern Ireland?	4.0
TB eradication strategies	Would risk-based trading reduce TB prevalence, based on mathematical/epidemiological/simulation models?	4.0
TB eradication strategies	Would risk-informed trading reduce TB prevalence, based on mathematical/epidemiological models?	3.8
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	What is the role of badgers in the epidemiology of bTB in Ireland?	3.8
Source attribution	What is the source of the outbreak on a particular farm?	3.6

Development of research tools	How can big data technology be used to elucidate the epidemiology and other matters relating to bTB?	3.3
Herd risk factors	How do relapse herds differ between dairy and sucklers factoring in badger programmes and age of animals in herds as well as the standard variables we've measured?	3.2
Wildlife population dynamics	What is the size of the national population of badgers in Ireland? Are the data provided by the programme sufficient to provide an accurate and precise estimate? How do we expect the badger population to change over time given competing effects of management and global change?	3.2
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	How do badgers and deer transmit *M. bovis* to cattle?	3.2
Wildlife population dynamics	Do we have validated, statistically robust, and independent measures of wildlife abundance in vaccination and culling areas?	3.1
Geographical area risk factors	Why does geographical clustering of bTB occur in Ireland?	3.1
Geographical area risk factors	How have material changes in the environment impacted on TB levels in cattle herds?	3.0
Herd Risk Factors	How does within-herd movement of animals affect TB spread? Which parcels are most at risk of having a neighbouring infected herd?	3.0
Herd Risk Factors	What are the herd level risk and protection factors influencing TB breakdowns in closed bovine herds based on an longitudinal analysis?	3.0
Herd Risk Factors	What are the main risk factors for new herd breakdowns?	2.9
Wildlife population dynamics	What are the key drivers of dynamic population changes in badgers that increase the probability of spillover of TB into cattle?	2.9
TB eradication strategies	How can bTB-free regions be defined and maintained in Ireland?	2.8

Development of research tools	How can host population genetic tools be harnessed to inform on effective population size, population estimation, the sustainability and viability of removals including the recently proposed "extinction vortex" in wildlife?	2.8
Herd risk factors	Herd size is the largest risk factor for bTB at herd level. Herds are also getting larger. But they also have lower animal level risk than smaller herds. What is the mechanism underlying this finding? How can herds grow within increasing their risk? What are the aspects of herd size that are modifiable risk factors? What are the husbandry differences between the highest and lowest risk ranked herds, that are of a large herd size (e.g., >300 animals)	2.8
TB eradication strategies	What is the relative impact of the following badger-related strategies on the herd levels of bTB in Ireland a) culling on its own b) vaccination on its own c) Combination of vaccination and culling	2.7
TB eradication strategies	Why is the culling of badgers effective in reducing the levels of bTB in cattle and what are the implications of this for the badger vaccination strategy?	2.7
Cattle breeding and genetics	Can genetic selection against *M. bovis* (and MAP) be used to reduce the level of transmission to cattle?	2.7
Development of research tools	Can recent advances with wildlife species distribution models predict bTB outbreaks in cattle?	2.7
Herd Risk Factors	What are the major risk factors currently driving the incidence of bTB?	2.7
Herd Risk Factors	What are the risk factors for breakdowns involving one or two standard reactors?	2.7
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	What is the prevalence of *M. bovis* in deer in Ireland, by geographical location?	2.7

M. bovis genetics	Are there phenotypic differences by *M. bovis* strain type that aid persistence?	2.7
Geographical area risk factors	What are the risk factors for herds with non-confirmed restrictions?	2.5
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	Has the background prevalence of M. bovis in badgers in areas with a low bTB incidence in cattle remained constant?	2.5
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	What is the role of deer in the epidemiology of bTB in Ireland	2.5
Herd Risk Factors	What is the role of slurry in the spread of TB infection?	2.5
Development of research tools	How can camera traps be used to improve the wildlife management approaches in the current TB scheme, and how can it hasten a reduction in infection from spillover events?	2.4
Herd Risk Factors	is there a difference in the exposure of dairy cows to badgers, related to their management, possibly around intensive grazing practices and their housed diets compared to non-dairy cows?	2.3
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB in Ireland	What is the mechanism driving an increase of bTB outbreak likelihood in farm cattle as a consequence of forestry clearfell operations? What is the mechanistic explanation for the increased risk of TB around road construction sites and forest clearfelling areas?	2.2
TB eradication strategies	Question Can a robust biosecurity assessment plan for wildlife be developed?	2.2

Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	What is the role of deer in bTB maintenance in Ireland?	2.1
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	Do wildlife hunting operations impact on the bTB levels in cattle herds. If so, what is the mechanism driving an increase of bTB outbreaks?	2.1
Herd Risk Factors	Does shed type play a role in bTB spread (Ventilation, feed railings)?	2.0
Herd Risk Factors	Should we be worried about environmental maintenance and exposure of *M bovis* to cattle? What fomite might facilitate maintenance, earthworms, amoeba, etc.?	1.8
Animal risk factors	What are the animal level risk factors influencing outbreaks?	1.8
Animal risk factors	What is the effect of metabolic stress on disease susceptibility and immune response to the TB test/	1.8
Animal risk factors	What are the risk factors and characteristics for home-reared animals that have factory lesions?	1.8
Animal risk factors	What are the animal level risk factors influencing outbreaks?	1.8
Animal risk factors	Where were factory lesion animals that were sent to the factory from a herd that did not disclose reactors subsequently and that were purchased into that herd most likely infected?	1.6
Role of wildlife (badgers, deer and feral goats) in the epidemiology of bTB	Do goats play a role in transmission of *M. bovis* to cattle as a maintenance or spillover host in certain areas of Ireland?	1.6

b. Vaccination thematic area

In the vaccination thematic area, most of the submissions were related to the effectiveness of the badger vaccination programme. The research question that received the highest score (4.4) was related to the effectiveness of badger vaccination as currently used in the field. Other submissions were related to the possibility of using badger culling in combination with vaccination as a strategy. This received a score of

3.4. The members of the evaluation group concluded that this matter could be considered as a component of the overall effectiveness of the badger vaccination programming and that simulation modelling could be used to examine different scenarios.

A submission was received in relation to the possibility of the potential of administering the vaccine through oral bait. This attracted a score of 3.4. While the proof of principle of the administration of a vaccine through an oral bait has been established [14], currently a vaccine is administered by injection to badgers in Ireland as it is likely to be more effective. Scientific studies on the delivery of a vaccine by the oral route are ongoing in a number of countries, including the UK [15], Spain [16] and France [17]. The outcome of these studies may result in an oral vaccine suitable for use in Ireland and DAFM will continue to support and collaborate with oral bait research that is being undertaken in other countries. However, the SWG is of the view that the monitoring of the parenteral vaccine should be the main focus at the moment in Ireland.

A submission was also received in relation to the possibility of vaccinating deer. This received the lowest score under the vaccination theme. The main reason for this is that members of the evaluation group were of the view that the role of deer in the epidemiology of bTB needed to be established in the first instance. Secondly vaccine efficacy would need to be demonstrated scientifically in wild deer. Most importantly, effective vaccine delivery to wild deer would be extremely challenging if not impossible from a logistical point of view.

Overall, this section of the study highlighted the need for the ongoing review of the effectiveness of the badger vaccination programme and the ongoing possibility of modification of the programme based on the review findings.

The score for each question for the vaccination theme is shown in Table 3 together with its thematic subgroup.

Table 3 Questions submitted under the vaccination theme and the score for each question, in order of descending score value

Subgroup	**Research Question arising**	
Monitoring of the badger vaccination programme	What is the effectiveness of badger vaccination as currently used int he field, in broad terms and within different badger demographic structures (age profile, survival, population turnover, local population densities, movements)?	4.4
Monitoring of the badger vaccination programme	What proportion of the badger population is being vaccinated? Is this level of population penetration [coverage] sufficient to halt TB maintenance [bring R0<1]?	4.2

Badger vaccination strategy	What would be the impact of a test and removal strategy (simultaneous removal of infected badgers and vaccination of susceptibles) in conjunction with vaccination in reducing the infection burden in cattle? What is the effect of culling badgers in vaccination areas (potentially using a simulation study?	3.4
Monitoring of the badger vaccination programme	Does the national vaccine plan provide ongoing estimates of trapping effort, population estimates, monitoring true incidence, vaccine efficacy over time, vaccine coverage, etc)?	3.4
Badger vaccination strategy	Is there still potential for administering the vaccine through oral bait?	3.4
Monitoring of the badger vaccination programme	What are (a) the densities and (b) the levels of infection in badgers among the vaccinated cohort and the unvaccinated (potentially based on a longitudinal study with captured populations)? What is the prevalence of *M. bovis* in those badger populations that are not being actively managed (potentially based on a longitudinal study)?	3.3
Badger vaccination strategy	If levels of infection in badger populations in "green field" sites are ~15%, will preventive vaccination strategies be required to achieve TB freedom in non-TB cattle hotspot areas?	2.5
Monitoring of the badger vaccination programme	What has been the impact of badger vaccination based on surveillance of badger road kill?	2.4
Badger vaccination strategy	Are there lessons we can learn from the NI TVR trial?	2.4
Monitoring of the badger vaccination programme	Could the non-inferiority trial areas be re-evaluated to see if vaccination is still performing adequately?	2.4

Vaccination of deer	Is vaccination of deer a possible strategy?	1.4

c. Diagnostics thematic area

Under the diagnostics thematic area, research questions were submitted relating to the further development of tests for diagnosis of bTB in cattle and badgers. A research question relating to PCR received the highest score (3.8). A PCR test could potentially be used in the laboratory as an alternative to bacteriology for the purposes of confirming TB infection in an animal. The use of this tests could potentially reduce the time needed to confirm infection with *M. bovis* and, consequently, this could lead to the earlier introduction of control measures in an infected herd. PCR testing could also be integrated with WGS to give a better understanding of the epidemiology of bTB in Ireland.

The second highest score (2.9) was related to ELISA blood tests. These could potentially complement intradermal testing. They are currently being used on a limited basis in the TB Eradication Programme in Ireland but do not have the required sensitivity and specificity to be used as screening tests. Such tests might be developed through further developmental work and the evaluation panel was of the view that the primary responsibility for developing these tests lie with private companies rather than government. There was also a question in relation to the development of diagnostic tests for badgers. This area of research is currently being investigated by researchers in University College Dublin.

There were also a number of submissions relating to interpretation and monitoring the implementation of the tuberculin skin test and its temporal relationship to the blood tests. Generally, these research questions received a relatively low score based on the view of the evaluators that a lot of research work has already been done in these areas. Consequently, future research work is unlikely to lead to a major impact on the TB Eradication Programme. There was also a question on whether the current cattle tuberculin potency assay is fit for its intended purpose. Currently work is being carried out in the UK and Ireland in the development of molecular defined tuberculin, a more refined tuberculin [18]. The completion of this work could make the determination of the potency of tuberculin considerably easier. This question received a relatively low score (2.4) on the basis that this question is already being addressed.

The score for each question is shown in Table 4 together within its thematic group.

Table 4 Questions submitted under the diagnostics theme and the score for each question, in order of descending score value

Subgroup	**Research Question arising**	
PCR tests	How can PCR tests be optimally utilised in the TB Eradication Programme? Can PCR be used to speed up the confirmation of *M. bovis* and be integrated directly into a pipeline for WGS?	3.8

Evaluation of blood tests	(a) Do ELISA tests have acceptable diagnostic performance (sensitivity / specificity) characteristics to suggest they could be evaluated and validated as diagnostic tests? (b) In what epidemiological scenarios would these tests be most beneficial, e.g., used in a parallel or in series with conventional tests? (c) Are there ways of adapting testing strategies to diagnose residual infection in herds with prolonged or recurrent TB outbreaks?	2.9
Diagnostic tests for wildlife	What novel tests or test platforms are available to improve the diagnosis of TB in badgers?	2.8
Interpretation of the skin test	Is there any significance difference between different readings in a test where an animal is deemed an inconclusive to the standard interpretation and the result of the subsequent inconclusive retest?	2.5
Interpretation of the skin test	What would be the impact of changing the threshold for an inconclusive animal on the sensitivity and specificity of the tuberculin test?	2.4
Monitoring the effectiveness of the tuberculin skin test	Is the current cattle tuberculin potency assay fit for its intended purpose?	2.4
Diagnostic tests to detect early infection in cattle	What are the factors that cause an animal to become infected early in a TB breakdown and what diagnostic tests can be used to detect these animals?	2.4
Relationship between blood tests and skin tests	What is the temporal relationship between blood tests and skin tests for the detection of *M. bovis* in cattle?	1.9

d. Social and economics thematic area

In the social and economics thematic area, submissions were received in relation to areas such as who benefits from the TB Eradication Programme, costs of an outbreak at farm level, farmer compensation, farmer training, economic and social drivers of

farmers' compliance with the bTB control measures, the history of the TB Eradication Programme, risk communication to farmers, including risk-based trading, stakeholder attitude to the TB eradication Programme and support to farm families during a breakdown. The highest proportion of the research questions that were submitted under this theme were related to the need for a better understanding of how risks associated with a herd breakdown are perceived by livestock owners and how information on risks can be made more accessible and relevant for individual farmers. There was a particular focus on risk-based trading. The submissions were related to different aspects of this issue, including:

- The proportion of farmers that would use risk information about herds/animals for buying decisions, if available, and the factors that would influence their level of acceptance of this approach and their willingness to adopt a risk-based approach to trading cattle
- The social, psychological, financial, technical and political impediments to risk-based trading and how these could be overcome
- The communication tools and metrics that should be used to make such information informative, openly accessible and epidemiologically relevant
- How the trading of cattle might change with the introduction of risk-based trading, who the "winners" and "losers" might be and the overall impact of the introduction of risk-based trading on the trading of cattle in Ireland

Generally, the submissions relating to a risk-based approach achieved high scores, ranging from 3.5 to 4.5.

At a more general level, one of the submissions was related to the key factors that drive various stakeholder attitudes and compliance to different TB control measures, e.g., farmers' attitude to vaccination vs. culling of badgers, biosecurity measures and TB testing standards, attitude of Private Veterinary Practitioners towards their role in the TB Eradication Programme. This obtained a score of 3.8. Understanding these factors would help to tailor messaging from DAFM to build confidence with stakeholders and maximise the benefits of different control strategies.

Another question was related to the cost (pecuniary and non-pecuniary) of a farm level outbreak. This received a score of 3.2. The evaluation group was of the view that this question could be answered through research and should be a fundamental part of any economic evaluation of the TB restriction. There was also a submission in relation to the supports that could be provided to farm families during TB herd breakdowns. This received a relatively low score of 2.3 as the evaluation group was of the view that this was more related to implementation than research.

The score for each question is shown in Table 5 together with its thematic group.

Table 5 Questions submitted under the social and economics theme and the score for each question, in order of descending score value

Subgroup	**Research Question arising**	**Overall score**

Risk communication to farmers including risk-based trading	What proportion of farmers would use risk information about herds/animals for buying decisions if available? What would need to be done to demonstrate the value of such a system to the farmer	4.0
Risk communication to farmers including risk-based trading	What needs to be done to ensure that herd risk information is openly accessible, epidemiologically relevant, informative/accepting to farmers, to facilitate risk-based decision making in terms of animal trade?	3.8
Risk communication to farmers including risk-based trading	What are the social, psychological, financial, technical and political impediments to risk-based trading? How can they be overcome?	3.8
Economic and social drivers of farmer's compliance with bTB control measures	What are the key factors that drive various stakeholder attitudes to different control measures for TB control, e.g., vaccination v culling of badgers?	3.8
Risk communication to farmers including risk-based trading	Which metrics of herd risk should be used to categorise farms into risk categories and ultimately shared with farmer/publics?	3.8
Risk communication to farmers including risk-based trading	"We all buy and sell cattle…but there are more sellers than buyers" What would the economic consequences of risk informed or risk-based trading policies? Are there any possibilities for 'gaming', creation of new suboptimal markets to develop?	3.7
Stakeholder attitudes to the TB Eradication Programme	What are the attitudes and motivations of stakeholders (farmers and PVPs) towards the TB Eradication Programme and how can these be addressed?	3.2
Cost of an outbreak	Can an economic evaluation take place of the costs (pecuniary and non-pecuniary) associated with a farm level outbreak?	3.2
Farmer compensation	Is there an issue with the levels of compensation and moral hazard in the bTB eradication scheme in Ireland? Are there possible alternatives (e.g., tiered payments, stronger QA/impact on poor testing etc.)	3.0

Farmer training	How well do farmers know the risk hotspots in their locality in terms of wildlife reservoirs of infection? What would the uptake in wildlife training/surveying be? training/surveying be?	2.7
History of bTB eradication programme	How can historical information about the TB Eradication Programme be used to improve the Programme in future?	2.3
Support to farm families during a breakdown	What further supports can be provided to farm families during TB herd breakdowns based on a study of farmer behaviour?	2.3
Impact of early culling of dairy cows on TB levels in herds	What is the impact of cow culling age on the level of bTB in cattle herds?	2.2
Benefits of the TB Eradication Programme	What are the upstream benefits of the bTB program to individuals sectors?	2.1

e. 'Other' thematic area

Two research questions were placed in "other" thematic area. These were related to the impact of policy changes on the TB Eradication programme. The score for each question is shown in Table 6 together with its thematic group. While it is recognized that it is important to determine the impact of policy changes, it is often very difficult to do this because a particular policy change is usually carried in association with, or during a similar time period, as other policy changes and the outcome is also influenced by wider environmental factors. This difficulty of answering questions of policy changes through research is the main reason why the questions in this thematic area did not achieve a score greater than 2.9.

Table 6 Questions submitted under the "Other" theme and the score for each question, in order of descending score value

Subgroup	**Research Question arising**	**Overall score**
Impact of policy changes on TB herd prevalence	What has been the impact of policy changes in the TB Eradication Programme on TB prevalence, culling of suspected reservoirs, culling of cattle, and strain prevalence?	2.9
Impact of policy changes on TB herd prevalence	How historical bTB policy changes, land use changes and changes to livestock husbandry impact on bTB prevalence?	2.9

4 Topics which should be considered priorities for funding by DAFM using the ERAD TB research fund in the period 2022-2024

The exercise described in Section 3 was useful for a number of reasons. It enabled the members of the SWG to get feedback from a variety of stakeholders on what the stakeholders considered should be the key research priorities in the TB Eradication Programme in Ireland in the coming years. A comprehensive list of potential research areas was received. The approach also facilitated the appraisal of the submissions by members of the SWG using a set of objective criteria. The methodology also contained comment boxes that facilitated a qualitative appraisal of the submissions by the evaluators.

In developing a list of research priorities for funding by DAFM, it was also envisaged that the outcome of the evaluation of the submissions would be taken into account together with other factors. Consideration was given to current or recently completed research funded under the TB ERAD Research Fund, in particular, with a view to ensuring continuity and consistency of bovine TB research in Ireland. The research themes that were identified as priorities during the previous funding period 2018-2022 were the following:

1. Evaluating the effectiveness of TB control policies in cattle, including better metrics and measurements of the impact of different types of breakdown in relation to future risk
2. Development of decision support tools to explore policy options
3. Improving diagnostic tests for TB in cattle and badgers
4. Evaluating the effectiveness of TB vaccination of badgers to protect cattle
5. Developing and obtaining marketing approval for an oral TB vaccine in badgers
6. Use of improved technology to support diagnostic testing for TB in cattle
7. Improved tools to evaluate the potency of tuberculin
8. The role of wildlife in TB epidemiology

While a great variety of proposals were received, a number of potential areas for research came to the fore. Under the epidemiology theme, it is clear that there is a need for a greater understanding of the relative contribution of the different sources of *M. bovis* for cattle in Ireland. While the potential sources of infection, namely cattle, badgers and deer are well established at this stage, their relative contribution is not well understood. The increasing availability of WGS offers considerable potential for further elucidation of this area in the coming years. This information could be used to put more focused, refined and cost-effective strategies in place to deal with the different sources. As mentioned in Section 3, the elucidation of the role of deer in the epidemiology of bTB in Ireland is very challenging. However, useful information has already been gathered in Ireland (e.g., [7,19]) and information is also available from other countries, particularly Michigan, USA [20]. Given the increasing evidence that deer do play a role as a maintenance host, there is a need for further research in this area in Ireland, including the need for more information on population dynamics throughout the country and the prevalence of *M. bovis* in the different geographical areas.

There is also a need for a greater understanding of the mechanism of transmission. In this context, the role of cattle movement is a key factor. The role of cattle movement in the transmission of *M. bovis* to new herds and to new areas is well established [21]. A risk-based trading approach has been used in various parts of the world to deal with this

[21]. While there is considerable evidence that cattle movement plays a major role in the transmission of *M. bovis* to new herds and new geographical areas in Ireland and other parts of the world, a more detailed understanding of the role of animal movements in the epidemiology of bTB could facilitate the implementation of more specific and more effective control measures.

Tools such as WGS, mathematical modelling, big data and machine learning techniques could be of considerable value in elucidating the epidemiology and other aspects of bTB. Mathematical modelling has been used for a whole variety of human and animal diseases in Ireland, including bovine viral diarrhoea. While the development of a model is more challenging for bTB because of complexity of the disease, nevertheless, it could make a major contribution to our understanding of the epidemiology of the disease and, in particular, it could be used to explore the likely impact of various policy options. Work in this area is currently ongoing at CVERA. In general, there is considerable scope for elucidating several aspects of bTB using these tools and their use should be encouraged.

In relation to the vaccination theme, the evaluation exercise highlighted the need for ongoing monitoring and evaluation of the badger vaccination programme. Badger vaccination is a key component of the bTB Eradication Programme and it is essential that the effectiveness of this programme in reducing transmission from badgers to cattle is monitored. Work is currently being done in this area at CVERA and this will need to be maintained during the period 2022 to 2024 and beyond. Other research projects relating to this should also be supported. The development of a vaccine for cattle was not included in the research proposals received. A possible reason for this is that a considerable amount of work is ongoing in the UK in this area. The objective is to have a cattle vaccine available in the UK by 2025. As part of the development of the vaccine, there will be a need for a diagnostic test that differentiates vaccinated from unvaccinated cattle. This is being developed in conjunction with the development of the cattle vaccine. It is likely that a vaccine will be useful in the control of bTB in countries not seeking to eradicate bTB – particularly developing countries. For that reason, the development of a cattle vaccine should not be considered to be a research priority in Ireland. In any event, the amending of EU legislation and international trading rules is likely to present a major challenge.

As regards the diagnostic theme, the further development of PCR tests is already underway in many countries as a potential valuable tool for confirming *M. bovis* in infected animals. In Ireland, it is being trialled at the Central Veterinary Research Laboratory. The development of new diagnostic tests for use in the field is also ongoing and should be supported.

On the social and economics theme, the evaluation exercise highlighted the need for a better understanding of the perceptions of herd owners in relation to the risks of bTB breakdowns in their herds, for example, the potential role for risk-based trading and genetically resistant sire selection. Such an understanding would be of value in determining how to create awareness among herd owners of the risks and how to encourage herd owners to take measures to deal with those risks. There is also a need for a better understanding of the factors that drive stakeholder attitudes, particularly the attitudes of farmers and private veterinary practitioners towards the TB Eradication Programme.

Taking all of the factors discussed above into account, the SWG proposes that the following activities be prioritised for research during the period 2022 – 2024. These are not necessarily in order of priority:

- Relative contribution of different wildlife reservoirs and other sources, including cattle movements, to cattle herd breakdowns, using whole genome sequencing and other methods
- Elucidation of the epidemiology of bTB and the potential impact of policy changes using mathematical/simulation models and other decision support tools
- Evaluation of the effectiveness of vaccination of badgers to protect cattle from *M. bovis*
- Enhancement of diagnostic tests for the detection of *M. bovis* in cattle and badgers
- Elucidation of the factors that drive various stakeholder attitudes and compliance to different bTB control measures, including risk-based trading

By their nature, each item on the priority list covers a broad area. A research project does not have to deal with a theme in its totality. A project that deals with a discrete component of an individual priority should be considered for funding.

The submissions received all had merit and are worthy of research. It is important to point out that the mandate received by the SWG was to set out priorities for research. By its very nature, this involved making choices in relation to the feasibility, importance and impact of the submissions received. However, it is possible that research projects not included in the priority list could have high scientific merit and that the findings from these projects could result in the implementation of measures that could have a major impact on the level of bTB in Ireland. Therefore, the SWG is of the view that research projects not on the priority list should be funded if they are of high scientific merit.

In general, there has been a proliferation of research work in many aspects of bTB in recent years. While maintaining a watching brief of research being conducted elsewhere that may be of relevance to Ireland e.g., during events such as the recent *M. bovis* 2022 conference held in Ireland and supported by DAFM/ERAD, the main focus should be on complementing this research base and expanding it in a way that will provide highly useful and highly relevant insights into bovine tuberculosis in Ireland.

References

1 Rudan I, Gibson JL, Ameratunga S, *et al.* Setting priorities in global child health research investments: Guidelines for implementation of CHNRI method. *Croatian Medical Journal* 2008;**49**:720–33. doi:10.3325/cmj.2008.49.720

2 Rudan I, Yoshida S, Chan KY, *et al.* Setting health research priorities using the CHNRI method: VII. A review of the first 50 applications of the CHNRI method. *Journal of Global Health* 2017;**7**. doi:10.7189/jogh.07.011004

3 Rudan I. Setting health research priorities using the CHNRI method: IV. Key conceptual advances. *Journal of Global Health* 2016;**6**. doi:10.7189/jogh.06.010501

4 Irvine C, Armstrong A, Nagata JM, *et al.* Setting Global Research Priorities in Pediatric and Adolescent HIV Using the Child Health and Nutrition Research Initiative (CHNRI) Methodology. 2018. www.surveymonkey.com

5 Campbell EL, Byrne AW, Menzies FD, *et al.* Interspecific visitation of cattle and badgers to fomites: A transmission risk for bovine tuberculosis? *Ecology and Evolution* 2019;**9**:8479–89. doi:10.1002/ECE3.5282

6 Allen AR, Ford T, Skuce RA. Does *Mycobacterium tuberculosis var. bovis* Survival in the Environment Confound Bovine Tuberculosis Control and Eradication? A Literature Review. *Veterinary Medicine International*. 2021;**2021**. doi:10.1155/2021/8812898

7 Crispell J, Cassidy S, Kenny K, *et al. Mycobacterium bovis* genomics reveals transmission of infection between cattle and deer in Ireland. *Microbial Genomics* 2020;**6**:1–8. doi:10.1099/mgen.0.000388

8 Gaughran A, MacWhite T, Mullen E, *et al.* Dispersal patterns in a medium-density Irish badger population: Implications for understanding the dynamics of tuberculosis transmission. *Ecology and Evolution* 2019;**9**:13142–52. doi:10.1002/ECE3.5753

9 Clegg TA, More SJ, Higgins IM, *et al.* Potential infection-control benefit for Ireland from pre-movement testing of cattle for tuberculosis. *Preventive Veterinary Medicine* 2008;**84**:94–111. doi:10.1016/j.prevetmed.2007.11.004

10 Adkin A, Brouwer A, Downs SH, *et al.* Assessing the impact of a cattle risk-based trading scheme on the movement of bovine tuberculosis infected animals in England and Wales. *Preventive Veterinary Medicine* 2016;**123**:23–31. doi:10.1016/j.prevetmed.2015.11.021

11 Adkin A, Brouwer A, Simons RRL, *et al.* Development of risk-based trading farm scoring system to assist with the control of bovine tuberculosis in cattle in England and Wales. *Preventive Veterinary Medicine* 2016;**123**:32–8. doi:10.1016/j.prevetmed.2015.11.020

12 Mccallan L, Mcnair J, Skuce R. A review of the potential role of cattle slurry in the spread of bovine tuberculosis. Agri-food and Biosciences Institute: Belfast, UK 2014.

13 Good M, Clegg TA, Duignan A, *et al.* Impact of the national full herd depopulation policy on the recurrence of bovine tuberculosis in Irish herds, 2003 to 2005. *Veterinary Record* 2011;**169**:581. doi:10.1136/vr.d4571

14 Gormley E, Ní Bhuachalla D, Murphy D, *et al.* Oral Vaccination of Free-Living Badgers (*Meles meles*) with Bacille Calmette Guérin (BCG) Vaccine Confers Protection against Tuberculosis. PLoS One 2017;12(1). doi:10.1371/journal.pone.0168851

15 Chambers MA, Aldwell F, Williams GA, *et al.* The effect of oral vaccination with *Mycobacterium bovis* BCG on the development of tuberculosis in captive European badgers (*Meles meles*). *Frontiers in Cellular and Infection Microbiology* 2017;**7**. doi:10.3389/fcimb.2017.00006

16 Balseiro A, Prieto JM, Álvarez V, *et al.* Protective Effect of Oral BCG and Inactivated *Mycobacterium bovis* Vaccines in European Badgers (Meles meles) Experimentally Infected With *M. bovis*. *Frontiers in Veterinary Science* 2020;**7**. doi:10.3389/fvets.2020.00041

17 Payne A, Ruette S, Jacquier M, *et al.* Estimation of Bait Uptake by Badgers, Using Non-invasive Methods, in the Perspective of Oral Vaccination Against Bovine Tuberculosis in a French Infected Area. *Frontiers in Veterinary Science* 2022;**9**. doi:10.3389/fvets.2022.787932

18 Middleton S, Steinbach S, Coad M, *et al.* A molecularly defined skin test reagent for the diagnosis of bovine tuberculosis compatible with vaccination against Johne's Disease. *Scientific Reports* 2021;**11**:2929. doi:10.1038/s41598-021-82434-7

19 Kelly DJ, Mullen E, Good M. Bovine Tuberculosis: The Emergence of a New Wildlife Maintenance Host in Ireland. *Frontiers in Veterinary Science* 2021;**8**. doi:10.3389/fvets.2021.632525

20 VerCauteren KC, Lavelle MJ, Campa H. Persistent spillback of bovine tuberculosis from white-tailed deer to cattle in Michigan, USA: Status, Strategies, and Needs. *Frontiers in Veterinary Science.* 2018;**5**:301. doi:10.3389/fvets.2018.00301

21 More SJ. Can bovine TB be eradicated from the Republic of Ireland? Could this be achieved by 2030? *Irish Veterinary Journal*. 2019;**72**. doi:10.1186/s13620-019-0140-x