Guidelines for the control of *Mycobacterium tuberculosis* complex in livestock

Beyond test and slaughter

World Organisation for Animal Health

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Acronyms

BCG	Bacillus Calmette–Guérin
bTB	bovine tuberculosis (disease)
CVO	Chief Veterinary Officer(s)
DIVA	test able to differentiate infected from vaccinated animals
ELISA	enzyme-linked immunosorbent assay
ESAT6 CFP10	recombinant fusion protein skin test reagent to detect *M. tb* infection
FAO	Food and Agriculture Organization of the United Nations
FGD	focus group discussion(s)
GNI	gross national income
IGRA/IFN-γ	interferon gamma release assay
LMIC	low- and middle-income country(ies)
MPB83/MPB870	*M. tb*-specific antigen proteins
M. tb	*Mycobacterium tuberculosis*
MTBC	*Mycobacterium tuberculosis* complex
Rv3615c	*M. tb*-specific antigen protein
SIT	single intradermal (tuberculin skin) test
SICTT	single intradermal comparative tuberculin (skin) test
T&S	test(ing) and slaughter(ing)
TB	tuberculosis
TST	tuberculin skin test
WHO	World Health Organization
WOAH	World Organisation for Animal Health
zTB	zoonotic tuberculosis

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1. Introduction

This set of guidelines aims to assist the World Organisation for Animal Health (WOAH) Members and stakeholders of the livestock industry in advancing the control of *Mycobacterium tuberculosis* complex (MTBC) species infection and bovine tuberculosis (bTB) disease, using strategies other than, or to complement, testing and slaughtering (T&S) of animals. It complements the framework of standards provided by the WOAH *Terrestrial Animal Health Code (Terrestrial Code)* [1] and the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*) [2].

The guidelines outline recommendations and provide guidance on key aspects of the control of MTBC species infection and bTB in livestock species that should be considered to address the specific challenges faced by countries with different epidemiologic, economic and socio-cultural characteristics. These guidelines start with an understanding of a country's epidemiologic situation and the resources and infrastructure needed to detect bTB, ending with relevant control strategies in different settings. While these guidelines focus on livestock species, they also address control strategies related to wildlife species and the zoonotic aspects of MTBC species, using the One Health approach.

The primary audience for these guidelines is bTB risk managers such as the Chief Veterinary Officers (CVO) of countries, WOAH Delegates and other relevant human or animal health authorities, but they may also be used by scientific technical service providers, such as private veterinarians involved in the implementation and maintenance of bTB control programmes. The guidelines are also expected to be useful for policy-makers, intergovernmental and non-governmental organisations (NGOs), and the private animal husbandry sector.

The use of T&S of livestock animals to control, and ultimately eliminate, bTB has been in practice for over a century [3] because it definitively removes the source of infection from the population and eliminates the opportunity for further spread of MTBC species. This strategy, accompanied by monetary compensation to affected farmers, has been successfully implemented in high-income countries. In contrast, it has never been fully implemented in most low- and middle-income countries (LMIC) where the disease is endemic, due to a combination of economic, infrastructural, cultural and religious reasons.

In September 2020, a WOAH *ad hoc* [4] Group on 'Alternative Strategies for the Control and Elimination of *Mycobacterium tuberculosis* Complex (MTBC) infection in livestock' concluded that it was necessary to elicit global expert opinion to determine potential strategies to support the control of TB in livestock in countries and regions where T&S is not currently feasible or acceptable.

These guidelines are the distillation of a comprehensive review of the scientific literature (including relevant grey literature); focus group discussions (FGDs) and interviews with key global informants; and information collected from an online survey of an expanded pool of relevant stakeholders. These included, among others, representatives of government, academia, economic organisations and donor agencies, together with farmers and community members.

The control and elimination of MTBC species and bTB disease is a long-term process, and no single control strategy is sufficient. Although, in theory, bTB in livestock species is labelled as a single disease, the epidemiology, clinical presentation, animal production and management systems, wildlife reservoir species and the potential zoonotic risk differ greatly among, and even within, countries or zones. Therefore, a 'package' of sustainable and science-based interventions is required, tailored to the specific needs, epidemiology and challenges faced by the affected countries.

These guidelines incorporate factors related to animal health, transmission of MTBC species among different livestock hosts in varying environments, as well as in wildlife and humans, and the diverse characteristics of animal populations and farming management practices. The guidelines also consider the social, cultural, political, economic, legal and religious contexts that may influence the development and sustainability of strategies to control bTB in different settings.

1.1. How the guidelines were developed

To support the Roadmap for Zoonotic Tuberculosis [5], which was jointly launched in 2017 by WOAH, the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations and the International Union Against Tuberculosis and Lung Disease, the United States Centers for Disease Control and Prevention awarded a project to WOAH for 'Strengthening animal health systems to enhance prevention, detection and response to emerging zoonotic diseases', which involved the development of guidelines for supplemental supportive strategies for bTB control in livestock.

The objective was to identify strategies other than T&S to aid in the control of MTBC infection and bTB in livestock, through a literature review and the elicitation of expert opinions via focus group discussions (FGD), interviews and an online survey. The experts were derived from different geographical backgrounds and multidisciplinary domains, such as those involved in the bovine supply chain, animal or public health policy-makers, field veterinarians, epidemiologists, meat and milk traders, and farming groups (both dairy and beef), among others.

This project was led by Dr Francisco Olea-Popelka of the Department of Epidemiology and Biostatistics, University of Western Ontario, Canada, and Dr Paula Fujiwara, former Scientific Director of the International Union Against Tuberculosis and Lung Disease, in collaboration with WOAH and its *ad hoc* Group on alternative strategies for the control and elimination of *Mycobacterium tuberculosis* complex infection (MTBC) in livestock, which comprised experts from diverse professional and geographical backgrounds. The project was implemented between May 2023 and March 2024, with three distinct but related phases (see Figure 1).

PHASE 1
Review of the literature
(May to July 2023)

A comprehensive review of peer-reviewed scientific literature was conducted, using systematic and standard approaches described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) document [6]. Relevant and current grey literature, including official reports, documents, and manuals from governments and international organisations, were also included.

PHASE 2
Expert opinion elicitation
(September to October 2023)

A multisectoral, multidisciplinary approach was adopted, involving 23 participants in FGD, interviews, and an online survey distributed to 215 individuals globally. Qualitative data from the FGD and interviews were analysed using reflexive thematic analysis (RTA), following the Braun and Clarke approach [7], to identify patterns among respondents' answers. The responses reflected diverse opinions based on the realities of each country.

The online survey achieved a completion rate of 46.5% (100/215), with responses from 37 countries across all five WOAH regions. The majority of respondents (~64%) were academics, researchers and scientists, but responses were also obtained from government officials, NGOs, community representatives, farming groups, private industry, international organisations, and private consultants. Survey data were analysed using standard descriptive statistics to evaluate and quantify participants' responses.

PHASE 3
Development of the guidelines
(November to December 2023)

Information, data and knowledge obtained from both the literature review (Phase 1) and the expert opinion elicitation (Phase 2) were used to develop the first draft of the guidelines, focusing on strategies that extend beyond T&S of animals. The first draft was shared in December 2023 with the members of the WOAH *ad hoc* Group, prior to the three-day in-person meeting in January 2024.

AD HOC GROUP MEETING AND DISCUSSION
(16–18 January, 2024)

WOAH convened an in-person meeting at its headquarters in Paris, France. The consultants presented the findings of Phases 1–2, as well as the first draft of the guidelines to experts in MTBC infection and bTB, and WOAH technical staff. Participants then shared their expertise and suggestions, and reached consensus on how the guidelines should be finalised, presented and communicated to relevant stakeholders.

1.2. How to use the guidelines

The scientific literature recognises T&S of animals as the recommended evidence-based intervention to control and eliminate MTBC infection. This approach is the basis for safe international trade as recommended by the *Terrestrial Code* Chapter 8.12., 'Infection with *Mycobacterium tuberculosis* complex'. These guidelines are written to support and improve the control of MTBC infection and bTB disease in countries where T&S of animals is not feasible or practical.

The guidelines assume that the primary responsibility for governance and action lies at the country level, typically administered by the Veterinary Authority. Despite the recognition of T&S as the only method proven to eliminate MTBC species successfully from livestock, the strategies presented in these guidelines offer alternative options to assist towards the goal of elimination, based on a country's objectives and available resources.

Issues specifically related to zoonotic TB (zTB) are discussed in Section 3.2.3. with the understanding that some of the recommendations provided in these guidelines are relevant to both animal health and public health.

The guidelines begin with advice on analysing and understanding the local epidemiology of bTB, alongside a call for government commitment and political will to provide the necessary resources and infrastructure for an effective disease control programme. A country can then develop or update its disease control programme based on the strategies recommended here, starting with *ante-mortem* and *post-mortem* surveillance, followed by disease management and targeted interventions.

As an example, country scenarios have been provided based on the epidemiology of bTB in the country, as well as the objective of the control strategy. See Annex 1.

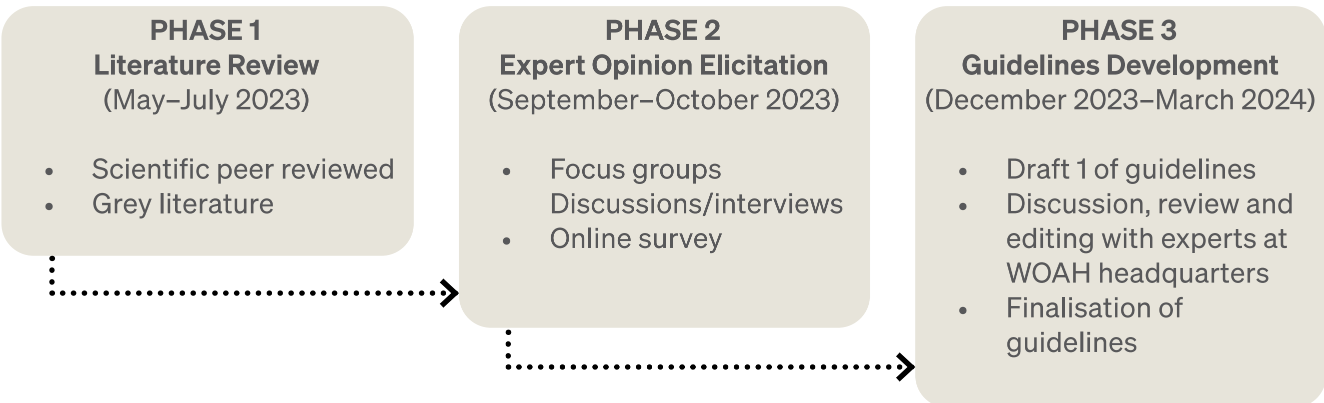

Figure 1. Flow chart for the process used to generate these guidelines

1.3. What is the expected outcome of applying the guidelines?

Applying one or more of the strategies outlined in these guidelines is expected to reduce the burden of bTB in animals, resulting in several benefits:

- Improved livestock productivity
- Mitigated public health risks
- Enhanced market accessibility
- Reduced impact on farmers' livelihoods
- Potential economic advantages by indirectly lowering the cost of intervention in affected regions

Over all, adapting these guidelines to the unique contexts of different countries will enhance the prevention, detection and control of MTBC species and bTB.

2. Where to Start

2.1. Current status of bovine tuberculosis in the country

Having robust evidence and bTB programme data, either on the animal or zoonotic health risk, is necessary to establish the 'business case' for resourcing and implementing appropriate and feasible interventions that will improve animal and human health in an evidence-based and cost-effective manner. It is also important to consider the expected evolution of the livestock sector because factors such as dairy intensification in the absence of a control strategy are known to accelerate the spread of MTBC species, which can result in substantial costs for disease elimination in the future.

BOX 1
Best practices to assess the epidemiologic burden of MTBC species and bTB in a country

- A risk assessment, or at least a description of the country's epidemiologic scenario of MTBC species and bTB in livestock as a key starting point for understanding the true disease control challenge. This can include, but is not limited to, an estimation of bTB prevalence, identification of high-risk areas or 'hot spots', assessment of the zoonotic transmission risk, information on drug resistance in humans, and assessment of animal traceability capabilities.
- A comprehensive survey or disease modelling exercise may also be needed to define the baseline and supply the basis for a strategic plan with relevant activities to decrease the burden of bTB.
- Programme data that include routine information on monitoring of activities and evaluation of outcome and progress.
- Consideration of an economic analysis of the return on investment, impact and scalability of government strategies to prevent, detect and control MTBC infection.

2.2. Resources and infrastructure

2.2.1. Regulatory frameworks and control programmes

Competent authorities at the national level should provide the needed regulatory framework at different levels, either for a standalone bTB programme or through integration with other disease control programmes, ideally leveraging existing resources and investments.

Countries may refer to *Terrestrial Code* Chapter 8.12., 'Infection with *Mycobacterium tuberculosis* complex (MTBC)', which provides guidance for countries and zones identified as free from MTBC infection in specific animal categories and species such as bovids and cervids.

Regulatory frameworks should provide an enabling environment for the implementation of bTB control strategies, linked to an associated budget for disease control. A key component of the regulatory framework is an animal identification and traceability system as per *Terrestrial Code* [1] Chapter 4.2. The system will support the assessment of disease burden and surveillance of MTBC species and bTB, thus enabling and facilitating the implementation of strategies to identify infected or diseased animals from the farm to the slaughterhouse, and assists in movement control and quarantine. Other components include quality control aspects, such as capacity building of personnel for laboratory diagnosis and testing, and regulation of the livestock supply and distribution chain to ensure that products available in the country for human consumption and use in animals are safe.

Another key enabler is to proactively educate, advocate, plan and communicate with key stakeholders (financiers, policy-makers, veterinarians, academics, businesses, communities, etc.) who can support and anticipate potential barriers to implementation (see Section 2.2.4.).

In addition, it could be useful to consider having a national accreditation scheme to recognise free or low-risk subpopulations (herds or zones) with appropriate incentives such as preferential market rates for livestock, milk or other animal products. This will also facilitate the application of movement controls and surveillance appropriate to the risk level of the herd(s)/zones concerned.

BOX 2
Guidance on developing a regulatory framework

- Conduct an internal review of government infrastructure, resources and the bTB strategic control plan.
- Assess the bTB burden in the country.
- Establish a comprehensive budget and ensure efficient fund allocation.
- Identify, educate and involve key stakeholders in the planning and implementation of the bTB programme.
- Conduct an internal assessment of the technical skills available and needed to implement strategies other than T&S of animals. It should include:
  - identification of the existing laboratory network and infrastructure;
  - identification of the availability of high-quality diagnostics and laboratory support services;
  - a means of identifying MTBC infection and bTB disease, using both *ante-mortem* and *post-mortem* methods in animals, as well as MTBC species causing zoonotic TB in humans;
  - a surveillance system to assess progress;
  - a training programme and an adequate number of staff (see Section 2.2.2.);
  - reporting, recording and evaluation of findings, including notification to WOAH.

2.2.2. Technical capacity and training

A functional bTB programme requires technically competent staff who can collectively address myriad technical issues, including bTB epidemiology, surveillance, diagnosis of MTBC infection and bTB disease in the laboratory and under field conditions, as well as the ability to respond to the needs of veterinary and industry professionals, and other stakeholders. Capacity building and training of internal stakeholders, such as orientation of new staff and in-service instruction on different aspects of the bTB programme, as well as the involvement of external stakeholders providing technical knowledge and accreditation to private veterinary and industry professionals, are important.

BOX 3
Guidance on technical capacity and training

- Conduct Knowledge, Attitude and Practices (KAP) surveys before and after implementation of control strategies other than T&S of animals, tailored to different stakeholder groups to measure their effect.
- Training on specific topics, such as how to identify MTBC infection and diagnose bTB in livestock species using the proper combinations of diagnostic tests through the use of testing algorithms, and prevention of infection in livestock, wildlife and humans.
- Training on best practices, including experiences from other countries and incorporating use of traditional knowledge, where appropriate.

...

BOX 3 (cont.)

- Implementation of accreditation or certification on bTB control training, in particular of veterinarians and meat inspectors. Properly done, this could lead to improved efficiency through the simultaneous identification of multiple diseases and reduce the need for, and cost of, testing of livestock.

2.2.3. Resource mobilisation

Leveraging resources for implementation requires a clear understanding of their availability at national and international levels, including public and private sources and development partners, including bilateral and multilateral partners and international development banks. It is important to understand that, besides financial resources, the scope of the resource environment analysis should also encompass non-monetary elements, such as policy coherence with other disease control programmes, the enabling environment for implementation, and the transfer of technology and knowledge.

The Veterinary Authority should coordinate overall resource mobilisation, ideally using national government administration funds. Other possibilities include leveraging the financial and technical capacities of the above sources with an interest in bTB, the animal husbandry industry, academic researchers and affected communities.

2.2.4. Stakeholder and partner engagement

Any effort to control MTBC infection and bTB requires that a broad coalition of advocacy and programme partners consider the science, politics, beliefs and behaviour of stakeholders, such as veterinarians, livestock owners and handlers, the livestock and food industries, and the general public.

It is important to take a One Health approach and involve the animal, human and

BOX 4
Guidance on identifying private and public stakeholders and partners

1. Potential advocacy aimed at:

- Government officials responsible for allocating funding for bTB programmes.
- Researchers and scientists who contribute to identifying new tools, improving implementation of bTB programmes, understanding stakeholder motivation (i.e. behavioural scientists) and identifying effective communication methods.
- Veterinarians and farming groups relevant to protecting the health of animals from MTBC species infection and bTB disease.
- The general community whose livelihood or lives may be dependent on cattle rearing.
- Those communities regularly engaged with stakeholders from livestock industries, such as exporters and national parks.
- Donors and development partners interested in supporting efforts to eliminate bTB.

2. Potential programme partners:

The Veterinary Authority within the Ministry of Agriculture or Livestock is usually responsible for the implementation of the bTB control programme. Other stakeholders include:

- Field veterinarians
- Farming groups and the animal husbandry industry (for dairy and beef cattle)
- Pharmaceutical companies dealing with diagnostics
- The public health department
- Academics
- Affected communities with links to zoonotic TB (abattoir workers, butchers and other food handlers, general public)

environmental sectors at the country level. For example, while Veterinary Services take the lead in managing animal health, regulating animal movement within and across borders, and developing and implementing animal disease control programmes for bTB in livestock, the human health authorities focus on the management of people with TB. Additionally, the environmental sector would address concerns related to animal habitats, land use and the impact of climate change.

At the country level, it is important that the Veterinary Authority and government officials allocate financial and technical resources for the bTB programme. Researchers, private veterinarians, farming groups, the local community, livestock exporters, national park staff and donors must be included in developing a multisectoral consortium of partners interested in supporting and contributing to the efforts to eliminate bTB.

2.2.5. Awareness and communication

Veterinary Authorities should include community awareness activities in disease control programmes that target different stakeholders, such as farming groups, the veterinary sector, animal husbandry industry, and the general community. Communication and awareness campaigns should be designed in consultation with key partners, involving local communities to enable a tailored approach to addressing local problems with feasible solutions. Materials should be adapted to the local context and language(s). MTBC infection and bTB are complex to control and, therefore, no short-term solution exists and no single strategy is perfect. Leveraging existing community awareness materials available for other diseases and combining campaigns to optimise the use of resources is recommended.

BOX 5
Guidance on awareness and communication

- Tailored awareness and communication strategies for key audiences that pinpoint the relevant information, awareness of the problem, and acceptance of the interventions needed for control of bTB should be supported, based on the findings of the bTB risk assessment.
- Tailored information should be provided to each stakeholder group affected by bTB to improve its understanding and role(s) within the country's bTB efforts, and to stress the value of controlling bTB for livestock productivity. Incentives can also be offered to farmers and producers, such as receiving a higher price for milk and meat products if herds or zones/regions are certified as bTB free.
- Behavioural science expertise is needed to address the challenges related to the acceptance, enforcement and sustainability of new strategies.

3. Control Strategies

When designing its disease control programme, each country needs to use its local epidemiologic data and its existing resources (infrastructure capacity, financial), as well as respecting its cultural factors. It should also consider its overall bTB risk and risk pathways, which may vary by: region, dairy versus beef cattle, commercial *versus* communal/pastoralist farming practices, imported *versus* indigenous cattle breeds, and cattle-exporting *versus* non-exporting regions. The disease control programme should include a combination of activities for surveillance, the biosecurity plan and disease management.

3.1. Surveillance

A surveillance programme should be implemented in accordance with *Terrestrial Code* [1] Chapter 1.4., 'Animal health surveillance'. Surveillance should aim to detect MTBC species infection and bTB disease in animals, herds and regions. It is essential for countries to measure the progress of bTB control strategies. Surveillance data are critically needed to inform different stakeholders and decision-makers of the design of strategies to be implemented in the local context to address the challenges posed by MTBC species and bTB.

Surveillance strategies comprise ***ante-mortem*** and ***post-mortem*** **screening** using diagnostic methods for live animals and during slaughter, respectively, for MTBC species infection and bTB. *Terrestrial Code* [1] Chapter 6.3. provides recommendations for the development of *ante-mortem* and *post-mortem* meat inspection programmes.

3.1.1. *Ante-mortem* surveillance

WOAH's *Terrestrial Manual* [2] Chapter 3.1.13., 'Mammalian tuberculosis', provides detailed recommendations on MTBC species and bTB screening and diagnosis. *Ante-mortem* surveillance is a key component of a bTB control programme.

Examples of tests applied include the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA) whole-blood test. It is important to note that, since 2000, numerous tests and approaches for *ante-mortem* testing for bTB have emerged. However, as of 2024, the two main tests routinely used in bTB control programmes are the TST and IGRA.

3.1.1.1. Tuberculin skin test (TST)

Terrestrial Manual Chapter 3.1.13. provides recommendations on how to perform the TST. There are various types of TST, including the single intradermal tuberculin test, injected in the cervical region (SCT) or caudal fold (CFT), and the comparative cervical test (CCT). The accuracy of the TST can vary significantly, with a sensitivity range of 52–100% and specificity of 55–99% depending on which TST is applied and its interpretation criteria (cut-off value), among other factors [8].

The TST is commonly used for estimating the prevalence of bTB. It is the cheapest available test option, especially when compared with the IGRA. However, it requires trained personnel and expertise [2, 9]. Furthermore, the TST method should only be used in unvaccinated animals because it reacts with the Bacillus Calmette-Guerin (BCG) vaccine and therefore produces false-positive results in vaccinated livestock [8, 10-12]. It requires at least two visits by a skilled veterinarian, is highly prone to variability, and repeated short-interval testing in animals may also lead to desensitisation resulting in false-negative results [8, 10, 11].

The decision to use the SCT, CFT or CCT depends on local regulations, the overall context and objectives for performing the test and the epidemiologic scenario. The CCT has higher specificity and is typically applied for surveillance purposes or at the start of a control programme in an endemic country. Once the presence of the disease is confirmed, an approach with higher sensitivity (i.e. SCT or CFT) may be preferred to avoid missing infected animals. The CCT is also useful in regions with high exposure to environmental mycobacteria (non-tuberculous mycobacteria). In contrast, the SCT and CFT, which have higher sensitivity, are frequently used to confirm freedom from infection in low-prevalence settings [2]. The testing interval (frequency) should be determined by the epidemiologic risk in the country/zone.

3.1.1.2. Interferon-gamma release assay (IGRA)

Blood tests used to diagnose bTB include the interferon-gamma release assay (IGRA), which measures cellular immune responses to tuberculin or defined antigens, and the indirect enzyme-linked immunosorbent assay (ELISA) and lateral flow assays, which are used to detect antibody responses. However, the logistics required are complex and the use of these assays in a laboratory requires specific training, which may be a constraint for laboratories in a resource-limited setting [2].

The *in vitro* IGRA is often used as an ancillary test to identify additional positive animals and may be more convenient than the TST because it does not require repeated handling of the animal or extended intervals prior to retesting. However, given that the IGRA requires time-bound stimulation of live blood cells, it may prove costly and difficult to implement, especially in remote or low-resource settings.

The IGRA is recommended to be used in conjunction with the SCT and CCT. It has been approved for use in a number of national bTB control programmes such as in Australia, the European Union, New Zealand, the United Kingdom (UK), and the United States of America (USA) [2]. In some countries, the IGRA is used for serial testing (to enhance specificity) and parallel testing (to enhance sensitivity) [2]. It is worth noting that, 'contingent on the type of assay performed, a measure of interferon (IFN-ɣ) responses is valuable both as a surrogate of infection and protection' [8].

The interferon-gamma assay (IFN-ɣ) is an ancillary assay to the tuberculin test and can be used to maximise detection of infected cattle, including bTB-freedom certification for animals or for product movement purposes and prevalence estimation [2, 13].

A comprehensive review [8] published in 2018 concluded that numerous advances have been made in the development of antigens and immune biomarkers for potential use in the diagnosis of bovine TB, such as the antigens MPB83 and MPB70, as well as DIVA antigens (ESAT-6, CFP10, Rv3615c) capable of differentiating infected from vaccinated animals.

It is recommended to combine different testing algorithms to increase the accuracy of the diagnostic results:

1. **Parallel testing:** Two (or more) screening tests are performed at the same time; the results are combined and the animal is classified as positive if any individual test result is positive. This testing method increases the sensitivity but reduces the specificity.

2. **Serial testing:** Two (or more) tests can be performed sequentially. If the result of the first test is positive, the second screening test is performed. If the second test is also positive (i.e. all tests are positive), the animal is classified as positive for bTB. This method increases the specificity, reducing the number of false-positive results [2].

BOX 6
Guidance on the use of tests and methodologies to screen for and diagnose MTBC infection and bTB disease in animals

- Staff need to be trained and accredited to conduct TST and IGRA.
- Further evaluate and expand the use of antigens (e.g. MPB83 and MPB70, and DIVA antigens such as ESAT-6, CFP10, Rv3615c) and biomarkers already developed for commercial diagnostic tests.
- Use standard and new tests in combination (testing algorithms) for the interpretation of results in parallel and/or series to increase sensitivity and specificity, respectively.

TABLE 1
Summary of tests for detection of *Mycobacterium tuberculosis* complex in livestock

Type of diagnostic test	Advantages	Drawbacks
Tuberculin skin test	• Cheapest	• Requires trained personnel • Requires at least two visits by a skilled veterinarian • Highly prone to variability • Repeated short-interval testing may lead to desensitisation of the animal, resulting in false negatives • Reacts with the BCG vaccine in vaccinated animals and produces false-positive results
Interferon gamma release assay [14]	• Reduced animal handling • Inconclusive tests can be readily repeated • Reaction of lymphocytes to various stimulants can be quantified • Stimulation controls are included • Supports early detection • Used as an ancillary test to identify additional positive animals	• Requires specific training • May be costly or difficult to implement, especially in remote or low-resource settings

3.1.2. *Post-mortem* surveillance

A common strategy to detect bTB involves the detection of macroscopic tuberculous lesions (i.e. granulomas or TB lesions) as part of meat inspection in slaughterhouses [1]. Tuberculosis lesions range from too small to be visible to the unaided eye to covering significant portions of an entire organ, and occur most commonly within the respiratory tract, particularly the lungs [1]. Identification of TB lesions in infected animals and screening for diseased animals at slaughter is an essential component to be used in combination with 'trace-back' systems to identify the source/origin (i.e. farm or other premises) of the tuberculous animal so that control strategies may be applied at the origin. *Post-mortem* surveillance data give a good independent indicator of underlying infection trends over time at population level and are useful for countries that do not have any information on the occurrence of bTB. Additionally, *post-mortem* analysis should be encouraged and used to stratify and identify high-risk areas ('hot spots') and/or affected herds, thus becoming an important source of information for resource prioritisation.

Regarding food safety, veterinary public health professionals, slaughterhouse personnel and meat handlers have a crucial role in identifying infected animals and in removing meat products containing lesions from the food chain, thus minimising the risk of zoonotic transmission to humans.

BOX 7
Guidance on slaughter surveillance

- Staff need to be trained and accredited to identify macroscopic granulomas and tuberculous-like lesions.
- Awareness needs to be raised among slaughterhouse staff regarding the importance of screening carcasses for bTB, reporting channels, and establishing a system for sample collection, testing and reporting. This includes record-keeping, in both formal and informal slaughterhouse facilities.
- Tuberculous-like lesions should be confirmed as caused by MTBC by laboratory microbiological and/or molecular methods.
- Identification of lesions need to be linked to a trace-back system to identify the potential source of MTBC-infected animals.

3.2. General biosecurity, disease management and targeted control

Biosecurity [1] involves a set of management and physical measures designed to reduce the risk of introduction, establishment and spread of animal diseases, infections or infestations to, from and within an animal population.

An effective biosecurity management system should protect the animal population within a herd and between herds from bTB, thereby reducing production losses for a business and contributing to ensuring food security at the national level. Therefore, a biosecurity management system should form an integral part of the bTB control programme.

3.2.1. Reducing intra– and inter–herd transmission of MTBC species

To minimise the risk of intra- and inter-herd transmission, early detection of infected animals through surveillance is important. It is essential to prevent transmission from infected to healthy animals, especially when the positive animal is lactating. Practices such as pasteurisation and/or boiling of dairy products, and managing animal movements within and between farms within established zones and countries, are extremely important in reducing the risk of MTBC transmission.

3.2.1.1. Pasteurisation and boiling of milk and dairy products for feeding calves

Calves should not be fed raw colostrum or milk from infected cows. Pasteurisation or boiling of milk or dairy products is known to protect nursing calves from *Mycobacterium bovis* (*M. bovis*) (the mycobacterial subspecies that causes bovine tuberculosis) in milk excreted by bTB-positive cows, thereby preventing spread within a herd [9] and significantly reducing the risk of their exposure to *M. bovis* from an infected herd. This method has been used to clear herds of infection [15].

3.2.1.2. Animal movement control

Controlling the movement of cattle herds and restricting animal mobility from infected herds is recommended to prevent and reduce the transmission of MTBC species between animals and herds. Restricting animal movements within a country, as well as between countries, is an essential strategy for preventing the importation or exportation of MTBC-infected animals, thus reducing the likelihood of introducing bTB into a bTB-free country or zone.

Terrestrial Code [1] Chapter 8.12. provides science-based recommendations for the safe international movement of animals and their products considering TB disease status. Additionally, *Terrestrial Code* [1] Chapter 5.1. provides specific information related to certification necessary for the movement of animals across country borders.

When infected animals are identified, for example during *post-mortem* surveillance, and confirmed to have MTBC infection, the herd of origin should be restricted from selling or moving animals to other premises. Testing for bTB before moving animals from farms, movement restriction of infected animals, and inspection of official bTB certificates both domestically and at international borders, are considered a highly effective control strategy for the reduction of bTB transmission. This is crucial especially in LMICs where the access to *ante-mortem* diagnostic tests is limited or there is no financial compensation provided to affected cattle owners. Whenever possible, testing and segregation to separate TST or IGRA reactors from negative animals is also recommended (see Section 3.2.1.4.).

To limit contact between animals from neighbouring farms, double fencing is recommended to prevent nose-to-nose contact.

BOX 8
Guidance to reduce transmission of MTBC species between animals and herds by controlling animal movements

- Encourage farmers to obtain bTB-free status. Better market access and/or premium milk pricing for certified bTB-free herds could be offered to farmers as an incentive to eliminate bTB from their herds.
- Capacity development of slaughterhouse personnel to identify MTBC infection and bTB disease (via laboratory tests or visible inspection, respectively).
- Animal identification and traceability systems, according to WOAH recommendations, should be in place to identify the potential source of MTBC-infected animals identified at slaughter surveillance by trained and accredited workers.
- Once infected animals are traced to the origin, movement restriction should be enforced, preventing animals from infected farms being sold to other farms, and prohibiting the movement of animals from infected farms to other zones, regions and countries.
- Limit contact between animals in the same area, for example by implementing double-fencing to prevent nose-to-nose contact between animals on neighbouring farms.

3.2.1.3. Cleaning and disinfection

Terrestrial Code [1] Chapter 4.14. recommends that Veterinary Authorities are requested to draw up regulations in their respective countries concerning the use of disinfectants on the basis of the following two principles:

1. The choice of disinfectants and of procedures for disinfection should be made taking into account the causal agents of infection and the nature of the premises, vehicles and objects that are to be treated.

2. Disinfectants should be authorised only after thorough tests have been carried out under field conditions. *Mycobacteria* are very resistant to disinfectants and a high concentration is required to destroy the organisms, as well as prolonged action [1]. Cleaning and disinfection should also be applicable to abattoirs, and proper disposal of affected organs. meat is also recommended.

BOX 9
Best practices for cleaning and disinfection of farms to control MTBC species

- Cleaning and disinfection of farm equipment and facilities, including the milking room and milking equipment, and animal feeders and drinkers.
- Use of chemical disinfectants that are effective against *Mycobacteria*.
- Periodic removal of soil from the housing.

Example 1 – The Canadian Food Inspection Agency (CFIA) recommends six basic steps for the cleaning and disinfection of premises declared infected with bTB:

1. Removal of contaminated materials and products
2. Dry cleaning
3. Wet cleaning
4. Drying (post cleaning)
5. Disinfection
6. Drying (post disinfection).

CFIA provides further guidance through its recommended protocols for cleaning and disinfection.

3.2.1.4. Testing and segregation

Testing and segregation (separation) of cattle that test positive is an important strategy in controlling and preventing the spread of bTB, especially in countries/regions where T&S of animals is impractical because of various compensation-related and socio-cultural factors.

Segregation involves separating the infected cattle from the rest of the herd to minimise transmission of *M. bovis*, which is easily spread through close proximity. This strategy has been used for over 100 years and several of the key practices and principles of testing and segregation are still relevant today.

Countries must first consider the feasibility of implementing the test and separation strategy because it is resource-intensive for individual farmers to house infected animals separately, which requires additional land, with associated financial implications. Testing and segregation is particularly pertinent in the absence of clearly defined incentives, such as monetary compensation for slaughtered bTB reactor animals, or market access or premium milk pricing for certified bTB-free herds. The progress and effectiveness of any testing and segregation strategy should be measured, such as through assessing the overall reduction in the burden of disease and the risk of spread of bTB through resale of test-positive animals. Countries should establish their own key performance indicators (KPIs) to systematically measure and evaluate the success and progression of reducing the burden of MTBC infection and bTB disease.

BOX 10
Best practices for management of reactors (test-positive) animals

Isolation and segregation of infected animals: Animals that have tested positive must be kept separated from non-infected animals for life. They are not to be sold to other farms, nor allowed to share pasture with non-infected animals. They may be moved only in the event of slaughter, and even then should be kept separated from non-infected animals.

1. **Isolation of calves from infected animals:** Calves are immediately removed from the reactor cow once born, and should not be allowed to suckle the infected animal. Such calves must be reared on pasteurised or boiled milk. These calves also need to be tested before they are placed in contact with calves from the non-reactor herd.
2. **Biosecurity:** Separate farm management practices are required for infected and healthy herds. Contact with wild animals must be prevented, **and separate grazing areas provided for healthy and infected animals.**
3. **Milk management:** Infected animals should be milked in separate areas. Their milk should be pasteurised or boiled before human or animal consumption.

Example 2 – In a study published in 1928 on the segregation method for eliminating bTB from cattle, two cattle herds, one positive and one negative for *M. bovis*, were placed in pastures 150 yards apart, without sharing any materials, and with calves removed at birth from the positive herd and tested at one year. It was found that a herd could be effectively cleared of bTB within **3 to 4 years** using this method while regularly testing cows and calves in the negative group, allowing the positive group to be eliminated naturally [16].

This technique has been implemented for over 100 years as a bTB control measure and remains highly relevant, particularly among LMICs. In this example, key animal management practices included the following:

- Two farms were used: farm A with non-reactors (TST-negative animals), and farm B with reactors (TST-positive animals), which were at 150 yards' distance from each other.
- Separate personnel were assigned to each herd; if the personnel went over to farm B to see the reactors, these personnel changed their boots before returning to farm A.
- The two herds were never allowed to be pastured in the same field or in any two fields that were side by side.
- Materials, feeding utensils and other equipment used on the two farms were kept strictly apart.
- The calves of reactor mothers (TST-positive cows) were removed at birth and raised on sterilised milk.

Example 3 – In a study in Ethiopia of a herd with 500 cattle [15], the overall herd prevalence of bTB was 48% at the time of first testing using CCT in October 2002. Based on this initial testing result, the farm was divided into a 'positive' and a 'negative' herd, and the two herds were physically separated. After the two herds were separated, three consecutive testing rounds on the negative herd and removal of the positive reactors to the positive herd were conducted. In October 2003, the first of three tests was applied to the negative herd, yielding 14% of animals positive to the CCT. In February 2004, the second test resulted in 9.5% CCT-positive animals, and the third test in May 2004 showed 1% CCT-positive animals. In this specific scenario, the percentage of positive animals **in the negative herd was reduced from 14% to 1% within 2 years.**

Key biosecurity management practices implemented in this study included the following measures:

1. The two herds were kept separated by a distance of one kilometre.
2. There was no physical contact between the two herds.
3. The negative herd was positioned at a higher geographical elevation than the positive herd.
4. Animals in both herds were fed and watered using the same management practices, but different staff were assigned to each herd.
5. The negative herd underwent three consecutive tests every four months following the initial test.
6. Positive reactors were removed from the negative herd and mixed with the positive herd.

BOX 11

Best practices for testing and segregation

Testing and segregation of MTBC-infected herds, while proven to be a relevant strategy, must consider the ability and resources of individual farmers to effectively house infected animals separately.

Best practices include:

- Establishing two physically separated herds: one with bTB-negative animals (non-reactors) and one with bTB-positive animals (reactors).
- Regularly testing all the non-reactors and monitoring their positivity over a period of time. Over time, the number of reactor animals from the non-reactor group should decrease, indicating progress.
- Transferring any test-positive animal to the reactor herd.
- Not reintroducing reactor animals to the non-reactor herd.
- Not selling reactor animals to other herds. When appropriate they need to be sent to the slaughterhouse.
- At the country level, Veterinary Authorities could monitor the number of such farms and their success in reducing reactor animals.
- Assigning different personnel to each herd.
- Using biosecurity measures to prevent cross-contamination/infection between herds by:
  - requiring personnel to change clothing and boots before entering the non-reactor farm.
  - ensuring that the two herds do not graze in the same field or adjacent fields.
  - keeping separate equipment for the infected herd and healthy herd; not using common instruments, materials or feeding utensils on the two farms.
  - if only one milking room is available, milking the non-reactor cows (negative herd) first, and the reactor cows last; cleaning and disinfecting all milking equipment and the room after milking the positive cows.

3.2.1.5. Vaccination of livestock with BCG

Vaccination of livestock against mammalian tuberculosis has long been the subject of investigation for the control of bTB in cattle and other animal species. Currently, the only available vaccine for *M. bovis* infections in cattle is the BCG vaccine [1], which contains a live attenuated strain of *M. bovis* [8]. *Terrestrial Manual* [2] Chapter 3.1.13., 'Mammalian tuberculosis', and *Terrestrial Code* [1] Chapter 4.18. 'Vaccination', provide foundational information and context regarding the use of BCG as a vaccine against mammalian tuberculosis. *Terrestrial Code* Chapter 4.18. also provides guidance to Veterinary Services on the use of vaccination in support of disease prevention and control programmes.

Current data on BCG 'vaccine efficacy' are highly variable. Reports in cattle have indicated a modest direct efficacy [10] (of approximatively 25%) for reduction in susceptibility to the disease as well as indirect effects in reducing infectiousness. A herd-level transmission dynamic model indicated that BCG vaccination may enable a substantial reduction in the future spread and overall burden of disease [10].

To optimise the use of the BCG vaccine, it is crucial to continue field testing of various animal species, environments and husbandry systems. These tests should be conducted under different levels of disease prevalence to comprehensively assess the vaccine's effectiveness. It is also essential to evaluate the practical application of tests designed to differentiate infected animals from vaccinated ones (DIVA tests) [17]. This holistic approach will ensure the vaccine's efficacy and its practical utility in diverse settings. Important factors to consider for the field evaluation of the cattle TB vaccine include, but are not limited to: 1) age at vaccination, 2) how and when to vaccinate, 3) BCG strain to use, 4) duration of vaccination, 5) vaccine application route, 6) vaccination dose, 7) differential diagnosis, 8) measurement of disease and 9) *M.bovis* challenge [12, 17, 18].

Although the BCG vaccine does not completely prevent or eliminate the risk of infection, the common consensus among researchers is that it significantly reduces the likelihood of infection, diminishes the severity of clinical signs, and subsequently lowers the transmission rate of bTB among cattle [10, 12, 17-20]. This highlights the vaccine's role in mitigating disease impact despite variations in specific measurements of 'vaccine efficacy'. Researchers have further concluded that vaccination may have a significant positive impact in high-prevalence regions, especially when implemented as a complementary strategy to ongoing bTB control efforts, as presented in the other sections in this document.

In any scenario, best practices would suggest that the use of BCG vaccination for livestock should be complemented with routine surveillance and improved general biosecurity, together with other control methods such as those measures included in Section 3.2.1. on movement control, testing and segregation, or testing and removal. Large-scale field trials to assess the efficacy and potential contribution of BCG vaccination of livestock as a component of comprehensive animal TB control plans are ongoing in several countries, including the UK and Mexico.

To assess the feasibility and effectiveness of interventions, including BCG vaccination for livestock, countries are encouraged to implement pilot projects. These projects can provide valuable data to inform a tailored approach to disease control in different contexts. Additionally, pilot projects can help countries develop a 'business case' by evaluating the lower risks and costs, as well as the direct and indirect benefits of implementing BCG vaccination or other interventions as part of a broader bTB control programme.

For countries lacking bTB control programmes but considering livestock vaccination, potential benefits include reduced public health risks, lower susceptibility to new infections amid dairy intensification, improved productivity and enhanced market access. These incentives can be pivotal in initiating TB control measures. When implementing pilot projects, countries need to monitor and evaluate the progress, outcomes and impact of the vaccination campaign. Key aspects to evaluate include the logistics of field implementation, vaccine coverage and impacts on the epidemiology of bTB.

Despite evidence of BCG vaccine-induced protection in cattle, the use of the BCG vaccine is currently prohibited in many countries [2]. This prohibition is primarily due to the vaccine's impact on the specificity of the TST, leading to false positives and the inability to differentiate between infected and vaccinated animals.

The BCG vaccine for humans has been in use for over 100 years and is one of the most widely administered vaccines globally, reaching over 80% of children in countries where it is included in the national immunisation programme. According to WHO's Essential Programme on Immunization, BCG is a critical component of childhood immunisation programmes in many countries, and authorities must ensure an uninterrupted supply of the vaccine.

If national health authorities are concerned about occasional shortages of the BCG vaccine for human use, it is important to note that veterinary vaccines operate within a separate supply chain. Veterinary vaccines must be manufactured, licensed and sold independently from human vaccines, and this distinction ensures that the production and availability of BCG vaccines for animals do not impact the supply for childhood immunisation programmes. Maintaining a clear separation between human and veterinary vaccine supply chains helps to safeguard the continuous availability of BCG vaccines for essential public health programmes.

BOX 12

Best practices for use of BCG vaccination for livestock

The use of BCG vaccination for livestock is a strategic option that could be considered under certain epidemiologic conditions, such as in high-prevalence areas. If used consistently over time in a geographical area, it has been shown to have multiple positive effects, even beyond decreased prevalence of bTB. These include reduced severity of clinical disease in livestock and wildlife species, reduced interspecies transmission (to wildlife, other domestic species, humans), improved productivity and value of livestock, and, if offered as a government service, commitment and 'buy-in' of farmers and producers.

Before BCG vaccine can be considered as a country strategy, country-specific technical issues on vaccine usage should be considered, such as:

- Specific areas of a country to deploy the vaccine.
- Vaccine coverage in herds.
- Age groups to target.
- Comparison of bTB incidence in vaccinated versus unvaccinated herds.
- Vaccine efficacy.
- Information on performance of DIVA tests.
- Scalability of vaccine usage.

Some of the drawbacks of using BCG vaccine include:

- The need to ensure a 'cold chain'.
- Lack of usefulness of BCG vaccine/vaccination in already infected animals.
- Barriers to exportation of BCG-vaccinated cattle.
- Potential for unrealistic expectations by different stakeholders on the impact vaccination would have as a strategy for TB in livestock species.
- Need (and extra cost) for a DIVA test that differentiates naturally infected animals from vaccinated animals.
- Ethical considerations in countries/regions with shortages of BCG vaccine for humans.

Further research on BCG vaccine field trials under natural conditions is needed to gather additional scientific evidence on issues such as:

- Vaccine efficacy.
- When to vaccinate cattle.
- Safety of BCG in lactating cows, calves.
- Cost-benefit analysis.

3.2.2. Wildlife–livestock interactions and risk of transmission of MTBC species

Mycobacterium bovis primarily infects cattle, but numerous other animal species can also be affected by this bacterium and other members of MTBC. These wildlife species can serve as sources of infection for cattle and other livestock. Transmission can be through direct contact between different animal species [21] or indirectly through sharing of habitats such as grazing or watering points [22]. Thus, wildlife species can act as reservoirs for *M. bovis* and other MTBC species, posing a risk to livestock through direct and indirect transmission. Examples include badgers in the UK and Ireland, wild boars in Spain, African buffalo in South Africa, brushtail possums in New Zealand and white-tailed deer in the USA [23].

In the past few decades, the most common control strategy to mitigate the risk of transmission from wildlife to livestock has been through culling of wildlife species. While culling has been a common control method, there are studies demonstrating its ineffectiveness in the bTB management strategy [24] and raising concerns about its impact on wildlife conservation.

Example 4 – In North America, a structured surveillance system exists for the at-risk wildlife population, and a selective culling strategy has been used for high-risk groups, to improve the practicality and efficacy of culling procedures [21]. A review of wildlife management strategies in Africa, spanning ten countries, found that culling did not result in the elimination of the disease among buffalo populations and was met with backlash from the community due to animal conservation concerns [25].

3.2.1.1. Vaccination of wildlife species with BCG

Despite differing opinions on the efficacy of wildlife culling practices to control bTB, it is widely acknowledged that culling involving large numbers of wildlife is costly [21] and often impractical [24], as well as being socially unacceptable. Therefore, recent studies and efforts have investigated the vaccination of wildlife as a potential contiguous control measure.

Wildlife vaccination is gaining interest as a tool for managing wildlife diseases in free-ranging wild animals. A few countries, such as the Republic of Ireland [13] and the UK [15], have approved vaccination for badgers as part of their disease control programme to control the spread of bTB.

The use of BCG vaccines in wildlife *versus* livestock represents two fundamentally distinct strategies driven by different epidemiologic, legal, regulatory and logistical considerations. In the first scenario, countries in the final stages of disease elimination without infection in livestock might consider vaccinating wildlife species, including endangered wildlife species.

However, a stated goal of disease elimination in wildlife populations may not be feasible for countries with endemic bTB. Vaccination may be used to reduce the transmission and disease burden to the point that culling becomes more feasible. Hence, while a vaccination-only programme is not recommended, vaccination of wildlife species together with a targeted removal approach may improve prospects for eventual elimination of the disease in wildlife populations.

Example 5 – A modelling study conducted on white-tailed deer in Michigan, USA, in 2024 indicated that the use of vaccination, particularly when combined with increased deer harvest (hunting or culling of deer), effectively reduces disease prevalence. In this study, researchers identified feasible integrated management strategies including vaccination and increased deer harvest that reduced disease prevalence in free-ranging deer; however, few scenarios led to disease elimination due to the chronic nature of bTB. This study concluded that, while complete elimination is challenging, sustained vaccination and research to improve vaccine effectiveness are crucial for long-term disease management [26].

Example 6 – A study that mapped the efficacy of badger vaccination in 'high-risk' areas of the UK between 2009 and 2020 used a simulated model system to map the efficacy of a badger vaccination programme. It was predicted that implementing a mass-vaccination approach post-cull would significantly reduce the number of infected badgers over time [27]. This was supported by prior studies, which reported that intra-muscular vaccination of badgers with BCG reduced the severity and risk of infection by 54% [28] and 74% [29]. Similar results were observed in field trials with possums in New Zealand [30].

Scientific data reviewed and published in 2018 [17] show that 'oral delivery of BCG vaccine to wildlife reservoirs of infection such as European badgers, brushtail possums, wild boar and deer has been shown to induce protection against TB and could prove to be a practical means to vaccinate these species at scale'.

Example 7 – In March 2023, the Irish Minister of Agriculture, Food and the Marine announced that badger vaccination would be an integral part of the Irish TB Eradication Programme [31]. For more than 15 years, research has been conducted on the use of the BCG vaccine against MTBC infections in badgers. Specifically, scientific trials that took place between 2013 and 2017 demonstrated that vaccinating badgers with the BCG vaccine is as effective as selective culling of badgers in controlling the spread of TB among badger populations. **This evidence supported the use of vaccination as an alternative to culling for managing TB in badgers [32].**

BOX 13
Best practices for minimizing risk of MTBC transmission between livestock and wildlife

Depending on parameters of cultural and societal acceptability, among options for addressing MTBC infection and disease in wildlife, best practices include:

- Interventions to limit interactions, such as fencing of areas to decrease co-mingling.
- Consideration of vaccination of wildlife species with BCG.
- Targeted wildlife culling in high-risk areas or high-risk species in line with *Terrestrial Code* Chapter 7.6.: 'Killing of animals for disease control purposes'.

3.2.3. Reducing the risk of zoonotic transmission

Zoonotic tuberculosis (zTB) is a form of TB in humans caused by transmission from animals. Historically, the available data indicate that *M. tuberculosis* is the aetiological agent for TB infection in humans, and *M. bovis* is the aetiological agent for TB in animals [33]. However, on a global level the causative MTBC is still not being differentiated to the species level for the vast majority of people with TB [4, 5, 9, 34]. While *M. bovis* is the main causal agent of bTB, other members of the MTBC (*M. tuberculosis, M. africanum, M. caprae, M. orygis,* and *M. microti*) are known to cause bTB in cattle [35] and are potentially zoonotic. WHO's End TB Strategy is targeted at reducing TB caused by *M. tuberculosis*, and in 2017, WHO recognised and included *M. bovis* as a cause of disease in humans.

Cattle are the most important animal reservoir of TB in relation to zoonotic exposure of humans. The true burden of zTB is likely underreported due to a lack of routine surveillance and diagnostic facilities in most countries. A 2022 systematic review found that surveillance data on zTB due to *M. bovis* were lacking in nearly 90% of the 119 countries analysed [36]. Furthermore, 60% of the countries were known to have *M. bovis* infections within their herds, yet fewer than 10% had implemented a zTB surveillance programme [36]. This study also concluded that zTB surveillance is highly conditioned by a country's income level, and identified a discrepancy between the level of risk of animal–human TB transmission and the extent of surveillance. In addition, fewer than 5% of the countries assessed had implemented integrated human and animal TB control programmes, which suggests low adoption of the One Health approach across the world [37].

The risk and burden of zTB in humans caused by different MTBC species varies across countries, depending on the prevalence of bTB and the level of implementation of the above-mentioned practices. A key tool to help reduce transmission of MTBC species from animals to humans is to protect the food supply directly through screening and inspection of carcasses and pasteurisation or boiling of milk and dairy products. In countries where socio-cultural and epidemiological factors facilitate the zoonotic transmission of MTBC species, data and local research on the burden, awareness and collaboration between the human and animal sectors are necessary. Disease surveillance programmes for both bTB and zTB should be implemented and priority should be given to screening communities with a high prevalence of bTB, or those with cultural practices that expose humans to MTBC species either directly from infected animals or indirectly from contaminated food products. This is essential to generate evidence on the burden of disease in humans.

To accomplish the goal of WHO's End TB Strategy, a coordinated, multisectoral One Health approach that involves animal health and public health authorities, health practitioners, veterinarians, politicians, researchers, experts in social, cultural and communication issues, economists, farming groups and local communities is necessary. It is recommended that, during the establishment of a 'business case' for bTB control in livestock, Veterinary Authorities should recognise the importance of considering

BOX 14
Best practices for zoonotic TB

To better measure and understand the challenges posed by zTB in humans, differentiating the causal agent, especially in high-risk groups, is crucial for accurate diagnosis, treatment, and prevention.

Best practices include routine surveillance of both bTB and zTB and differentiation of the causal agent (MTBC species) of TB in humans from high-risk groups potentially exposed to MTBC species of animal origin.

Zoonotic TB high-risk communities or at-risk workers include:

- Areas where socio-cultural practices increase the risk of exposure and transmission of MTBC species either directly from infected animals, or indirectly from contaminated food products.
- Areas where consumption of unpasteurised milk or untreated animal products from infected animals is common.
- Rural communities – individuals residing in areas where bTB is endemic.
- Animal health workers, livestock rearers, cattle herders, dairy workers and individuals who directly handle cattle or work in dairy production and those who come into contact with infected animals or animal products.

A One Health approach should be used, including implementing a coordinated, multisectoral programme that involves public health officials (Ministries of Health and Agriculture); health practitioners (veterinarians and physicians); politicians; basic science researchers; experts in social, cultural and communication issues; and economists, among others.

It is important to address the concerns of the community and protect them from the risk of zTB, as they depend on healthy livestock for the nutrition provided by dairy products and animal protein. The food supply should be safeguarded through meat inspection and heat treatment or pasteurisation of dairy products, with commercial producers certified and monitored for compliance with pasteurisation standards. Understanding the risk of TB transmission and 'buy-in' of rules and regulations may be facilitated by due consideration of the concerns and inputs of the community, coupled with transparent, honest, accurate and fluent communication.

not only the economic benefits derived from reducing the burden of bTB in animals, but also assessing the broader public health impacts. Controlling bTB would not only yield economic advantages, but may also contribute significantly to public health benefits by reducing the risk of MTBC zoonotic transmission, mitigating the risk of antimicrobial resistance emergence and improving the overall efficacy of health systems. This holistic perspective reinforces the interconnectedness of animal and human health in the context of TB control efforts consistent with the One Health approach.

BOX 15
Other considerations

WOAH recognises that there are limited reports on the use of antimycobacterial chemotherapy and chemoprophylaxis in livestock species, particularly with compounds such as isoniazid (INH), which is an option for first-line treatments in humans. Despite the use of antimycobacterial treatments, especially INH, in susceptible zoo and companion animals, WOAH has cautioned against using this approach for livestock. This caution is due to the potential risk that treated animals could continue to shed and transmit MTBC species to other animals and humans. Additionally, there are concerns regarding antimicrobial resistance. The position of the Quadripartite on the responsible and prudent use of antimicrobials, in alignment with the 7th edition of the WHO List of Medically Important Antimicrobials [38], and WOAH's List of Antimicrobials of Veterinary Importance [39] is that their use be discouraged for the treatment of TB in livestock.

WOAH also acknowledges the use of phytochemicals or traditional remedies for TB; however, there is currently insufficient evidence regarding their effectiveness. Therefore, this intervention is excluded from the present guidelines, while acknowledging the need for further study in this area, and the potential for emergence of new technologies and approaches.

4. Operational Research

As strategies other than T&S of animals are implemented and new tools developed, these guidelines will be reviewed and potentially updated to evaluate and incorporate progress. This will require additional research, ranging from basic science to operational and programme studies that incorporate 'learning by doing', the use of monitoring and evaluation, and behavioural and interventional studies to measure and continually improve programme performance. Thus, countries and key local stakeholders should include a learning component in their national bTB programmes that is based on knowledge gained, and allows strategies to be adapted to become more efficient. Operational and behavioural research studies should include:

- the acceptability of proposed procedures;
- how and when to discontinue or improve practice;
- how to implement findings;
- optimal communication methods.

5. Conclusion

While the T&S of livestock remains the most effective tool to control bTB disease and eventually eliminate the transmission of MTBC species, this strategy is not always feasible. These guidelines, based on a comprehensive literature review, expert opinions obtained via FGD, individual interviews, an online survey of global stakeholders, and the consensus of a panel of WOAH experts are presented in response to the difficulty that the majority of WOAH Members face in applying the T&S strategy, due to epidemiologic, religious, socio-cultural and/or economic considerations. Used in whole or in part, these strategies other than T&S of animals build a pathway towards the elimination of bTB in livestock species. Using the One Health approach, their implementation will also contribute to reducing the burden of MTBC species infection and TB in wildlife and zTB in humans. The guidelines reflect current knowledge and should be considered a 'living document'. In the future, they will require review and potential adjustments with the advent of new evidence and emerging technologies.

Annex 1

Scenarios for countries with different epidemiologic settings and resource availability

The following scenarios could inform the choice of bovine turberculosis (bTB) control strategies, based on existing epidemiologic settings, quality of Veterinary Services and economic and logistical factors. Each scenario considers resource availability, farming practices, potential interventions, benefits and challenges involved in developing context-specific bTB control plans.

Veterinary Authorities can use these scenarios to develop their own framework for developing and implementing tailored bTB control strategies.

SCENARIO 1
Bovine TB-free countries, or countries with low (2%–5%) or extremely low herd prevalence (<2%), with a fully implemented bTB national control programme, and intensive agriculture.

Country profile: officially free of bTB, or with low (i.e. 2%–5%) or extremely low herd prevalence (i.e. <2%), with an active, functioning and operational national bTB control programme, with advanced veterinary and public health infrastructure, intensive farming practices and livestock movements in accordance with WOAH standards.

Objective: to reduce bTB burden and move towards or maintain bTB-free status, adhere to international trade and welfare standards and to protect the public from zoonotic transmission of MTBC species.

What needs to be considered

- **Continuing current T&S strategy:** based on current average prevalence, as well as availability of economic resources and infrastructure to carry out T&S with economic compensation of farmers.
- **General biosecurity measures:** important to maintain using existing infrastructure.
- **Zoning**: may be used to create defined areas based on bTB risk (e.g. disease-free and control zones) to ensure safe and secure domestic and international trade.
- **Certification and traceability programmes:** using existing trade infrastructure facilitates trade from disease-free areas and ensures traceable, disease-free supply chains.
- **Vaccination of livestock using BCG:** neither recommended nor necessary for livestock in bTB-free countries, or with extremely low (<2%), or low (2%–5%) bTB herd prevalence.

How to do it: sustain economic resources to maintain advanced Veterinary Services, an active bTB national control programme, trade infrastructure and regulatory systems.

Benefits: effective bTB control, economic trade benefits, sustained export markets access, high animal health standards, public health safety.

Challenges: maintaining disease-free status (and/or low prevalence), potential MTBC species spillover from wildlife.

SCENARIO 2

Bovine TB herd prevalence greater than 5%, bTB national control programme partially implemented, good Veterinary Services, emerging economy transitioning from extensive to intensive farming.

Country profile: herd prevalence >5%, growing economy, transitioning from extensive (i.e. traditional/communal and/or pastoralist farming practices, usually with a small number of herds) to intensive farming or animal husbandry practices, growing investments in public health infrastructure.

Objective: to decrease prevalence of bTB by improving its control amid changing farming practices (extensive to intensive farming), which are known to increase bTB prevalence; improve productivity; promote and/or improve market access; reduce the risk of zoonotic MTBC species transmission.

What needs to be considered:

- **Surveillance:** measurement and assessment of the magnitude of bTB; crucial for long-term success.
- **Strategy:** updating the disease control programme along with identifying the necessary legislative and regulatory mechanisms to support activities.
- **Awareness programmes:** awareness raising among the community at high risk of disease in the animal population. This would further support the implementation of surveillance activities.
- **Zoning and compartmentalisation:** having separate areas of intensive farming to help control disease spread, support for transition to intensive farming and high-value market access; this requires fit-for-purpose surveillance, animal identification and traceability systems.
- **Animal movement controls:** requires regulatory enforcement to promote prevention of MTBC species transmission between animals, herds, countries/zones.
- **Market and policy drivers:** potential for success with specific incentives to increase market access for participating farmers (e.g. premium pricing for products from bTB-free herds); policy initiatives (e.g. mandatory testing, subsidies for BCG vaccination of livestock, compensation for slaughtered animals).
- **Testing and segregation:** in more developed regions with intensifying dairy herds, separate housing of infected animals may be precluded by lack of availability and/or cost of land.
- **BCG vaccination of livestock**: before considering roll out of BCG vaccine for livestock, it is highly recommended to continue to field test it in order to evaluate the vaccine and optimise its use in livestock (see Section 3.2.1.5.). BCG vaccination could be a cost-effective strategy, especially in countries where *ante-* or *post-mortem* surveillance is not conducted on a routine basis and where trade will not be affected by its use. The use of BCG vaccine for livestock should be considered only in countries with epidemiologic scenarios that would benefit from this strategy; for example, countries in which bTB is endemic with high bTB herd prevalence and the country is not planning to engage in trade of animals, or countries not carrying out DIVA testing.

How to do it: adapting and implementing strategies based on regional capabilities, high-risk settings; selecting interventions based on country-identified needs. These could have moderate feasibility depending on the country's Veterinary Services and infrastructure. Ensuring availability of BCG vaccines in childhood immunisation programmes.

Benefits: reduced bTB prevalence, improved animal health, economic growth in the farming and agriculture sector, improved public health and safety.

Challenges: diverse farming practices; regional disparities in bTB disease; social and economic constraints; managing bTB reactor animals; the need for DIVA testing for vaccination of cattle.

SCENARIO 3

Bovine TB herd prevalence >5%, without an active, functioning or operational bTB national control programme, low-resource setting, extensive farming.

Country profile: herd prevalence >5%, limited economic resources, *extensive* (traditional/communal, and/or pastoralist farming practices, usually with a small number of herds), weak Veterinary Services and public health infrastructure.

Objective: to manage bTB with limited resources, focusing on decreasing bTB in intensified dairy herds, and reducing the risk of zoonotic transmission of MTBC species.

What needs to be considered:

- **Surveillance:** to understand the epidemiologic situation, which rests on knowledge of susceptible animal populations and their distribution. Targeted surveillance is key in areas that are common congregation points, such as local markets and slaughterhouses, to assess the magnitude of bTB in a country.
- **Strategy:** updating or developing a disease control programme along with identifying the necessary legislative and regulatory mechanisms to support activities.
- **Awareness programmes:** awareness raising among the community at high risk of having disease in the animal population. This would further support the implementation of surveillance activities.
- **Biosecurity measures:** implementing measures could be challenging with limited feasibility. The challenges could be addressed through community training.
- **Zoning and compartmentalisation:** possible for intensive and high-risk farms towards development of disease-free, high-value herds.
- **Testing and segregation:** possible in areas with intensifying dairy herds; challenges in areas using communal farming practices.
- **BCG vaccination of livestock:** before considering roll out of BCG vaccine for livestock, it is highly recommended to continue to field test it in order to evaluate the vaccine and optimise its use in livestock (see Section 3.2.1.5.). BCG vaccine could be a cost-effective strategy, especially in countries where *ante-* or *post-mortem* surveillance is not conducted on a routine basis and where trade will not be affected by its use. Use of BCG vaccine for livestock should be considered only in countries with epidemiologic scenarios that would benefit from this strategy, for example, countries in which bTB is endemic and with high bTB herd prevalence. This strategy could be feasible for selecting high-risk areas or those areas with intensifying dairy herds, but widespread use may be limited due to logistical and resource constraints.

How to do it: use of bTB surveillance, awareness and education is key. However, due to different priorities and lack of or limited funding, infrastructure, personnel, diagnostics, and BCG vaccines, the feasibility of bTB control may be limited. Ensuring availability of BCG vaccines in childhood immunisation programmes.

Benefits: improved animal health and community livelihoods; foundation for long-term control and stability, improved public health and safety.

Challenges: to separate and house infected animals effectively requires additional land and financing; insufficient funding; the need for a DIVA test for vaccination of cattle.

SCENARIO 4

Countries with significant wildlife reservoirs of MTBC species.

Country scenario: countries with one or more wildlife species acting as reservoirs for bTB (badgers, possums, African buffalo, white-tail deer, wild boar, among others).

Objective: to prevent and/or decrease transmission of MTBC species from wildlife to livestock and to decrease MTBC infection and TB in wildlife species.

What needs to be considered:

- **Awareness programmes:** awareness raising among technical stakeholders on the risk pathways of wildlife TB, and among the local community members who are in close contact with wild animals.
- **Habitat management:** needs appropriate environmental planning, such as physical barriers to prevent contact between wildlife and cattle.
- **Testing and segregation:** can be feasible in cattle and may be useful (but controversial) where the wildlife population is significant.
- **Zoning and compartmentalisation:** can be used to establish buffer zones; compartmentalisation can be used to manage disease within specific wildlife populations or livestock herds.
- **BCG vaccination for wildlife:** logistically challenging but increasingly explored. Since 2018, Ireland has been vaccinating badgers with BCG.
- **BCG vaccination for livestock:** before considering rolling out BCG vaccine for livestock, it is highly recommended to continue to field test the vaccine in order to evaluate and optimise its use in livestock (see Section 3.2.15.). BCG vaccine could be a cost-effective strategy, especially in countries where *ante-* or *post-mortem* surveillance is not conduced on a routine basis and where trade will not be affected by the use of BCG vaccine. The use of BCG vaccine for livestock could be considered in countries in which bTB is endemic and with a high herd bTB prevalence in livestock and where significant wildlife reservoirs exist.

How to do it: using integrated wildlife-livestock disease management. This depends on the ability to manage wildlife-livestock interactions and requires an integrated multisectoral One Health approach.

Benefits: reduced wildlife-livestock disease transmission; balancing disease control with conservation, maintenance of public trust.

Challenges: transmission in livestock is driven by combined inter- and intra-specific transmission. There is a need to balance wildlife conservation with bTB disease control. Other challenges include the public perception of wildlife management, and the need for a DIVA test for vaccination of cattle, the shortage of BCG vaccine.

References

1. World Organisation for Animal Health. Terrestrial Animal Health Code. Infection with Mycobacterium tuberculosis complex. 2023 [cited 2024 Mar 14]. Available from: https://www.woah.org/fileadmin/Home/eng/Health_standards/tahc/2023/chapitre_bovine_tuberculosis.pdf
2. World Organisation for Animal Health. Terrestrial Manual. Mammalian tuberculosis (infection with Mycobacterium tuberculosis complex). 2023 [cited 2024 Mar 14]. Available from: https://www.woah.org/fileadmin/Home/eng/Health_standards/tahm/3.01.13_Mammalian_tuberculosis.pdf
3. Palmer MV, Waters WR. Bovine tuberculosis and the establishment of an eradication program in the United States: role of veterinarians. Vet Med Int; 2011: 816345 Epub 2011 May 17. PMID: 21647341; PMCID: PMC3103864. https://doi.org/10.4061/2011/816345
4. World Organisation for Animal Health. The meeting of the OIE ad hoc Group on Alternative Strategies for the Control and Elimination of Mycobacterium tuberculosis Complex Infection in Livestock. 2020 [cited 2023 Jul 28]. Available from: https://www.woah.org/app/uploads/2023/03/a-ahg-alternativestrategies-m-tuberculosis-approved-1.pdf
5. Dean A, Elldrissi A, Erlacher-Vindel E, Forcella S, Fujiwara PI, Gifford G, *et al.* Zoonotic roadmap for zoonotic tuberculosis. 2017. Available from: https://www.woah.org/app/uploads/2021/03/roadmap-zoonotic-tb.pdf
6. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D., *et al.* PRISMA extension for scoping reviews (PRISMA−ScR): checklist and explanation. Ann Intern Med. 2018 Oct 2;169 (7):467-73. Epub 2018 Sep 4. PMID: 30178033. https://doi.org/10.7326/M18-0850
7. Braun V, Clarke V. One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qual. Res. Psychol. 2021; 18: 328-52. https://doi.org/10.1080/14780887.2020.1769238
8. Waters R, Vordermeier M. Immunological diagnosis. In: Bovine tuberculosis. CABI International; 2018. https://doi.org/10.1079/9781786391520.0173
9. Livingstone P, Hancox N. Managing bovine tuberculosis: successes and issues. In: Bovine tuberculosis. CABI International; 2018. https://doi.org/10.1079/9781786391520.0225
10. Srinivasan S, Conlan AJK, Easterling LA, Herrera C, Dandapat P, Veerasami M, *et al.* A meta-analysis of the effect of Bacillus Calmette-Guérin vaccination against bovine tuberculosis: is perfect the enemy of good? Front. Vet. Sci. 2021; 8: 637580 Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7930010/
11. Vordermeier HM, Jones GJ, Buddle BM, Hewinson RG, Villarreal-Ramos B. Bovine tuberculosis in cattle: vaccines, DIVA tests, and host biomarker discovery. Annu. Rev. Anim. Biosci. 2016;4:87-109. Available from: https://pubmed.ncbi.nlm.nih.gov/26884103/
12. Bayissa B, Sirak A, Worku A, Zewude A, Zeleke Y, Chanyalew M, *et al.* Evaluation of the efficacy of BCG in protecting against contact challenge with bovine tuberculosis in Holstein-Friesian and zebu crossbred calves in Ethiopia. Front.Vet. Sci. 2021;8:702402. https://doi.org/10.3389/fvets.2021.702402
13. World Organisation for Animal Health. OIE Procedure for Registration of Diagnostic Kits. 2015 [cited 2023 Jul 28]. Available from: https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/OIE_Register_Bovigam_Abstract_v1_05.2015.pdf
14. Ghielmetti G, Landolt P, Friedel U, Morach M, Hartnack S, Stephan R, *et al.* Evaluation of. Three Commercial Interferon-γ Assays in a Bovine Tuberculosis Free Population. Front. Vet. Sci. 2021;8:682466. https://doi.org/10.3389/fvets.2021.682466
15. Ameni G, Aseffa A, Sirak A, Engers H, Young DB, Hewinson RG. Effect of skin testing and segregation on the prevalence of bovine tuberculosis, and molecular typing of Mycobacterium bovis, in Ethiopia. Vet. Rec. 2007;161(23):782-6. Available from: https://pubmed.ncbi.nlm.nih.gov/18065813/
16. Adeane CR, Gaskell JF. A segregation method for eliminating tuberculosis from cattle. J. Hyg. (Lond). 1928;27(3):248-56. Available from: https://pubmed.ncbi.nlm.nih.gov/20474965/
17. Buddle BM, Vordermeier HM, Chambers MA, de Klerk-Lorist LME. Efficacy and safety of BCG vaccine for control of tuberculosis in domestic livestock and wildlife. Front .Vet. Sci. 2018;5:259. https://doi.org/10.3389/fvets.2018.00259
18. Milián-Suazo F, González-Ruiz S, Contreras-Magallanes YG, Sosa-Gallegos SL, Bárcenas-Reyes I, Cantó-Alarcón GJ, *et al.* Vaccination strategies in a potential use of the vaccine against bovine tuberculosis in infected herds. Animals (Basel). 2022;12(23):3377. https://doi.org/10.3390/ani12233377
19. Retamal P, Ábalos P, Alegría-Morán R, Valdivieso N, Vordermeier M, Jones G, *et al.* Vaccination of Holstein Heifers with Mycobacterium bovis BCG strain induces protection against bovine tuberculosis and higher milk production yields in a natural transmission setting. Transbound. Emerg. Dis. 2022;69(3):1419-25. https://doi.org/10.1111/tbed.14108
20. Ábalos P, Valdivieso N, Pérez de Val B, Vordermeier M, Benavides MB, Alegría-Morán R, *et al.* Vaccination of calves with the Mycobacterium bovis BCG strain induces protection against bovine tuberculosis in dairy herds under a natural transmission setting. Animals (Basel).12(9), 1083. 2022. https://doi.org/10.3390/ani12091083
21. Miller RS, Sweeney SJ. Mycobacterium bovis (bovine tuberculosis) infection in North American wildlife: current status and opportunities for mitigation of risks of further infection in wildlife populations. Epidemiol. Infect. 2013;141(7):1357-70. https://doi.org/10.1017/S0950268813000976

22. Sichewo PR, Vander Kelen C, Thys S, Michel AL. Risk practices for bovine tuberculosis transmission to cattle and livestock farming communities living at wildlife-livestock-human interface in northern KwaZulu Natal, South Africa. PLoS Negl.Trop. Dis. 2020;14(3). https://doi.org/10.1371/journal.pntd.0007618
23. Palmer MV. Mycobacterium bovis: characteristics of wildlife reservoir hosts. Transbound. Emerg. Dis. 2013;60 Suppl 1:1-13. https://doi.org/10.1111/tbed.12115
24. Donnelly CA, Woodroffe R, Cox DR, Bourne FJ, Cheeseman CL, Clifton-Hadley RS, *et al.* Positive and negative effects of widespread badger culling on tuberculosis in cattle. Nature. 2006;439(7078):843-6. https://doi.org/10.1038/nature04454
25. de Garine-Wichatitsky M, Caron A, Kock R, Tschopp R, Munyeme M, Hofmeyr M, Michel A. A review of bovine tuberculosis at the wildlife-livestock-human interface in sub-Saharan Africa. Epidemiol. Infect. 2013;141(7):1342-56. https://doi.org/10.1017/S0950268813000708
26. Pandey A, Feuka AB, Cosgrove M, Moriarty M, Duffiney A, VerCauteren KC. Wildlife vaccination strategies for eliminating bovine tuberculosis in white-tailed deer populations. PLoS Comput. Biol. 2024 Jan 4;20(1). https://doi.org/10.1371/journal.pcbi.1011287
27. Langton TES, Jones MW, McGill I. Analysis of the impact of badger culling on bovine tuberculosis in cattle in the high-risk area of England, 2009-2020. Vet. Rec. 2022;190(6). https://doi.org/10.1002/vetr.1384
28. Carter SP, Chambers MA, Rushton SP, Shirley MD, Schuchert P, Pietravalle S, *et al.* BCG vaccination reduces risk of tuberculosis infection in vaccinated badgers and unvaccinated badger cubs. PLoS One. 2012;7(12). https://doi.org/10.1371/journal.pone.0049833
29. Chambers MA, Rogers F, Delahay RJ, Lesellier S, Ashford R, Dalley D, *et al.* Bacillus Calmette-Guérin vaccination reduces the severity and progression of tuberculosis in badgers. Proc. Biol. Sci. 2011;278(1713):1913-20. https://doi.org/10.1098/rspb.2010.1953
30. Nugent G, Yockney IJ, Whitford EJ, Cross ML, Aldwell FE, Buddle BM. Field Trial of an Aerially-Distributed Tuberculosis Vaccine in a Low-Density Wildlife Population of Brushtail Possums (Trichosurus vulpecula). PLoS One. 2016;11(11). https://doi.org/10.1371/journal.pone.0167144
31. McConalogue C. Animal Diseases. Minister for Agriculture, Food and the Marine, Ireland. 2023 [cited 2023 Jul 28]. https://www.oireachtas.ie/en/debates/question/2023-03-09/23/#pq-answers-23
32. Martin SW, O'Keeffe J, Byrne AW, Rosen LE, White PW, McGrath G. Is moving from targeted culling to BCG-vaccination of badgers (Meles meles) associated with an unacceptable increased incidence of cattle herd tuberculosis in the Republic of Ireland? A practical non-inferiority wildlife intervention study in the Republic of Ireland (2011-2017). Prev. Vet. Med. 2020;179:105004. Available from: https://pubmed.ncbi.nlm.nih.gov/32361147/
33. Ramanujam H, Palaniyandi K. Bovine tuberculosis in India: The need for One Health approach and the way forward. One Health. 2023;16:100495. https://doi.org/10.1016/j.onehlt.2023.100495
34. Olea-Popelka FJ, Muwonge A, Perera A, Dean AS, Mumford E, Erlacher-Vindel E, *et al.* Zoonotic tuberculosis in human beings caused by Mycobacterium bovis - a call for action. Lancet Infect Dis. 2017. https://doi.org/10.1016/S1473-3099(16)30139-6
35. Harini Ramanujam, Kannan Palaniyandi. Bovine tuberculosis in India: The need for One Health approach and the way forward. One Health, (16). 2023. https://doi.org/10.1016/j.onehlt.2023.100495
36. de Macedo Couto R, Santana GO, Ranzani OT, Waldman EA. One Health and surveillance of zoonotic tuberculosis in selected low-income, middle-income and high-income countries: A systematic review. PLoS Negl. Trop. Dis. 2022;16(6). https://doi.org/10.1371/journal.pntd.0010428
37. One Health High-Level Expert Panel (OHHLEP), Adisasmito WB, Almuhairi S, Behravesh CB, Bilivogui P, Bukachi SA, *et al.* One Health: A new definition for a sustainable and healthy future. PLoS Pathog. 2022;18(6). https://doi.org/10.1371/journal.ppat.1010537
38. World Health Organization. List of Medically Important Antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use. Geneva: World Health Organization; 2024. [cited 2024 Mar 14]. Available from: https://cdn.who.int/media/docs/default-source/gcp/who-mia-list-2024-lv.pdf?sfvrsn=3320dd3d_2
39. World Organisation for Animal Health. List of Antimicrobials Agents of Veterinary Importance. 2021 [cited 2024 Mar 14]. Available from: https://www.woah.org/app/uploads/2021/06/a-oie-list-antimicrobials-june2021.pdf

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