

OIE Reference Laboratory Reports Activities

Activities in 2021

This report has been submitted : 2022-01-19 16:25:42

Name of disease (or topic) for which you are a designated OIE Reference Laboratory:	Bovine tuberculosis
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Website:	https://www.gov.uk/government/organisations/animal-and-plant-health-agency
Name (including Title) of Head of Laboratory (Responsible Official):	Ian Hewett, CEO
Name (including Title and Position) of OIE Reference Expert:	Dr Jason Sawyer Head of Immunology & Vaccines Workgroup, Department of Bacteriology, APHA Weybridge
Which of the following defines your laboratory? Check all that apply:	Governmental

ToR 1: To use, promote and disseminate diagnostic methods validated according to OIE Standards

1. Did your laboratory perform diagnostic tests for the specified disease/topic for purposes such as disease diagnosis, screening of animals for export, surveillance, etc.? (Not for quality control, proficiency testing or staff training)

Yes

Diagnostic Test	Indicated in OIE Manual (Yes/No)	Total number of test performed last year	
		Nationally	Internationally
Indirect diagnostic tests			
Gamma interferon micro (2 antigen) assay	Yes	286254	0
Gamma interferon extended micro (3 antigen) assay	Yes	7586	8
IDEXX ELISA serology test - bovine	Yes	10254	0
IDEXX ELISA serology test - camelid	No	1516	0
EnferPlex serology ELISA - camelid	No	1487	0
Chembio DPP VetTB lateral flow rapid antibody test (non-bovine)	No	1100	0
Direct diagnostic tests			
Culture (bovine)	Yes	8088	0
Culture (non bovine)	Yes	365	0
Mycobacterium tuberculosis molecular typing (spoligotyping, VNTR and WGS)	Yes	3698	0
DNA testing of cattle to confirm identity	Yes	132	0

**ToR 2: To develop reference material in accordance with OIE requirements, and implement and promote the application of OIE Standards.
To store and distribute to national laboratories biological reference products and any other reagents used in the diagnosis and control of the designated pathogens**

or disease.

2. Did your laboratory produce or supply imported standard reference reagents officially recognised by the OIE?

No

3. Did your laboratory supply standard reference reagents (non OIE-approved) and/or other diagnostic reagents to OIE Member Countries?

Yes

Type of reagent available	Related diagnostic test	Produced/ provide	Amount supplied nationally (ml, mg)	Amount supplied internationally (ml, mg)	No. of recipient OIE Member Countries	Region of recipients
Cattle DIVA skin test antigens	Cattle TB testing & research	Provide	0	3 mg	1	<input type="checkbox"/> Africa <input type="checkbox"/> Americas <input type="checkbox"/> Asia and Pacific <input checked="" type="checkbox"/> Europe <input type="checkbox"/> Middle East
Cattle blood test reagents	Cattle TB testing & research	Provide	99 mL	0	1	<input type="checkbox"/> Africa <input type="checkbox"/> Americas <input type="checkbox"/> Asia and Pacific <input checked="" type="checkbox"/> Europe <input type="checkbox"/> Middle East
Cattle IGRA controls	Bovigam test	Provide	100 mL	600 mL	14	<input type="checkbox"/> Africa <input type="checkbox"/> Americas <input type="checkbox"/> Asia and Pacific <input checked="" type="checkbox"/> Europe <input type="checkbox"/> Middle East

4. Did your laboratory produce vaccines?

No

5. Did your laboratory supply vaccines to OIE Member Countries?

No

ToR 3: To develop, standardise and validate, according to OIE Standards, new

procedures for diagnosis and control of the designated pathogens or diseases

6. Did your laboratory develop new diagnostic methods validated according to OIE Standards for the designated pathogen or disease?

Yes

7. Did your laboratory develop new vaccines according to OIE Standards for the designated pathogen or disease?

No

Name of the new test or diagnostic method or vaccine developed	Description and References (Publication, website, etc.)
APHA has introduced the routine use of whole genome sequencing (WGS) for genotyping of <i>M. bovis</i> . This will replace the use of spoligotyping and VNTR.	The test has been accredited to ISO17025 by UKAS

ToR 4: To provide diagnostic testing facilities, and, where appropriate, scientific and technical advice on disease control measures to OIE Member Countries

8. Did your laboratory carry out diagnostic testing for other OIE Member Countries?

No

9. Did your laboratory provide expert advice in technical consultancies on the request of an OIE Member Country?

No

ToR 5: To carry out and/or coordinate scientific and technical studies in collaboration with other laboratories, centres or organisations

10. Did your laboratory participate in international scientific studies in collaboration with OIE Member Countries other than the own?

Yes

Title of the study	Duration	Purpose of the study	Partners (Institutions)	OIE Member Countries involved other than your country
Field evaluation of BCG vaccination in cattle	on-going	To evaluate the efficacy of BCG in cattle in field situations in Ethiopia	Armauer Hansen Research Institute and Addis Ababa University	ETHIOPIA
Evaluation of inactivated vaccine efficacy in badgers	on-going	Assess efficacy of inactivated TB vaccine in badgers	Neiker Institute & SERIDA	SPAIN
Badger bait deployment studies	on-going	Investigate uptake of baits in badger population	ANSES & ONCFS	FRANCE
Accelerating Bovine tuberculosis Control in Developing Countries - India	on-going	TB control in India	Penn State University, Multiple Indian partners, Cambridge University, Universidad Complutense de Madrid, Douwe Bakker	INDIA SPAIN THE NETHERLANDS UNITED STATES OF AMERICA
Improvements in blood based TB test for cattle	on-going	Improvements in blood based TB test for cattle	University College Dublin	IRELAND
Replacement of the International Standard Bovine Tuberculin	on-going	To produce a replacement International Standard Bovine Tuberculin	This is an international study led by the OIE	
Cattle vaccine and DIVA development	on-going	Cattle vaccine and DIVA development	AgResearch	NEW ZEALAND
Improved TB skin test delivery systems	on-going	Improved TB skin test delivery systems	MIT	UNITED STATES OF AMERICA
Discovery of novel antigens for TB serology	on-going	Discovery of novel antigens for TB serology	Antigen Discovery Inc	UNITED STATES OF AMERICA
Investigation of M.bovis levels in cattle faeces	on-going	Investigation of M.bovis levels in cattle faeces	Department of Agriculture, Food and the Marine (DAFM)	IRELAND

ToR 6: To collect, process, analyse, publish and disseminate epizootiological data relevant to the designated pathogens or diseases

11. Did your Laboratory collect epizootiological data relevant to international disease control?

Yes

If the answer is yes, please provide details of the data collected:
APHA is involved in the collection of data relevant to the bovine TB disease situation in Great Britain.

12. Did your laboratory disseminate epizootiological data that had been processed and analysed?

Yes

If the answer is yes, please provide details of the data collected:
Statistics and analysis of bovine TB disease situation in Great Britain are available at the following website: https://www.gov.uk/government/collections/bovine-tb

**13. What method of dissemination of information is most often used by your laboratory?
(Indicate in the appropriate box the number by category)**

a) Articles published in peer-reviewed journals: 36

1. Arrieta-Villegas C; Vidal E; Martin M; Verdes J; Moll X; Espada Y; Singh M; VILLARREAL-RAMOS B; Domingo M; Perez de Val B (2020) Immunogenicity and protection against *Mycobacterium caprae* challenge in goats vaccinated with BCG and revaccinated after one year. *Vaccines* 8 (4) 751.
<https://doi.org/10.3390/vaccines8040751>

2. McDonald J; DELAHAY R; McDonald R (2019) Bovine tuberculosis in badgers: Sociality, infection and demography in a social mammal. In: *Wildlife Disease Ecology: Linking Theory to Data and Application*; Wilson K (ed); Fenton A (ed); Tompkins D (ed); 342-367.

3. ARNOLD ME; Courcier EA; Stringer LA; McCormick CM; PASCUAL-LINAZA AV; Collins SF; Trimble NA; Ford T; Thompson S; Corbett D; Menzies FD (2021) A bayesian analysis of a test and vaccinate or remove study to control bovine tuberculosis in badgers (meles meles). *PLoS ONE* 16 (1) e0246141.
<https://doi.org/10.1371/journal.pone.0246141>

4. Mekonnen GA; Gumi B; BERG S; Conlan AJK; Ameni G; Wood JLN (2021) A case of early neonate bovine tuberculosis in Ethiopia. *Clinical Case Reports* 9 (1) 487-490. <https://doi.org/10.1002/ccr3.3563>

5. MIDDLETON S; STEINBACH S; COAD M; McGill K; Brady C; Duignan A; Wiseman J; Gormley E; JONES GJ; VORDERMEIER HM (2021) A molecularly defined skin test reagent for the diagnosis of bovine tuberculosis compatible with vaccination against John's disease. *Scientific Reports* 11, Article number: 2929.
<https://doi.org/10.1038/s41598-021-82434-7>

6. ROMERO MP; Chang Y-M; Brunton LA; PROSSER A; UPTON P; REES E; TEARNE O; ARNOLD M; Stevens K; Drewe JA (2021) A comparison of the value of two machine learning predictive models to support bovine tuberculosis disease control in England. *Preventive Veterinary Medicine* 188, 105264.
<https://doi.org/10.1016/j.prevetmed.2021.105264>

7. Ayalew S; Wegayehu T; Taye H; Wassie L; Girma S; BERG S; Mihret A (2021) Drug resistance conferring mutation and genetic diversity of *Mycobacterium tuberculosis* isolates in tuberculosis lymphadenitis patients; Ethiopia. *Infection and Drug Resistance* 14, 575-584. <https://doi.org/10.2147/IDR.S298683>

8. BIRCH CPD; CHAMBERS MA; LESELLIER S (2021) A combined measure of tuberculous lesions for assessing the efficacy of vaccination against tuberculosis (*Mycobacterium bovis*) in European badgers (*Meles meles*) supports the 3Rs principle of reduction. *Vaccine* 39 (11) 1661-1666. <https://doi.org/10.1016/j.vaccine.2019.10.079>

9. SMITH GC; BUDGEY R (2021) Simulating the next steps in badger control for bovine tuberculosis in England. *PLoS ONE* 16 (3) e0248426. <https://doi.org/10.1371/journal.pone.0248426>

10. Srinivasan S; Conlan AJK; Easterling LA; Herrera C; Dandapat P; Veerasami M; Ameni G; Jindal N; Raj GD; Wood J; Juleff N; Bakker D; VORDERMEIER M; Kapur V (2021) A meta-analysis of the effect of Bacillus Calmette-Guerin vaccination against bovine tuberculosis: Is perfect the enemy of good? *Frontiers in Veterinary Science* 8, Article 637580. <https://doi.org/10.3389/fvets.2021.637580>
11. Yang-Turner F; Volk D; Peto T; ROBERTS T; HERREROS J; ELLIS R (2020) ViewBovine: A microservices-powered web application to support interactive investigation of bovine tuberculosis infection pathways. 2020 IEEE World Congress on Services (SERVICES), Beijing, China, 2020, 4-6.
12. Edmans MD; Connelley TK; Jayaraman S; Vrettou C; VORDERMEIER M; Mak JYW; Liu L; Fairlie DP; Maze EA; Chrun T; Klenerman P; Eckle SBG; Tchilian E; Benedictus L (2021) Identification and phenotype of mait cells in cattle and their response to bacterial infections. *Frontiers in Immunology* 12, Article 627173. <https://dx.doi.org/10.3389/fimmu.2021.627173>
13. Fielding HR; McKinley TJ; DELAHAY RJ; Silk MJ; McDonald RA (2021) Characterization of potential superspreader farms for bovine tuberculosis: A review. *Veterinary Medicine and Science* 7 (2) 310-321. <https://doi.org/10.1002/vms3.358>
14. Kohler H; Liebler-Tenorio E; Hughes V; Stevenson K; Bakker D; Willemsen P; Bay S; Ganneau C; Biet F; VORDERMEIER HM (2021) Interferon- γ response of Mycobacterium avium subsp. paratuberculosis infected goats to recombinant and synthetic mycobacterial antigens. *Frontiers in Veterinary Science* 8, Article No. 645251. <https://doi.org/10.3389/fvets.2021.645251>
15. Marjamaki PH; Dugdale HL; DELAHAY R; McDonald RA; Wilson AJ (2021) Genetic, social and maternal contributions to Mycobacterium bovis infection status in European badgers (Meles meles). *Journal of Evolutionary Biology* 34 (4) 695-709. <https://doi.org/10.1111/jeb.13775>
16. Queval CJ; Fearn A; Botella L; Mitermite M; WOUFF E; VILLARREAL-RAMOS B; Garcia-Jimenez W; Heunis T; Trost M; Werling D; Salguero FJ; Gordon SV; Gutierrez MG (2021) Macrophage-specific responses to human- and animal-adapted tubercle bacilli reveal pathogen and host factors driving multinucleated cell formation. *PLoS Pathogens* 17(3): e1009410. <https://doi.org/10.1371/journal.ppat.1009410>
17. STEINBACH S; Jalili-Firoozinezhad S; Srinivasan S; Melo MB; MIDDLETON S; KONOLD T; COAD M; Hammond PT; Irvine DJ; VORDERMEIER M; Kapur V (2021) Temporal dynamics of intradermal cytokine response to tuberculin in Mycobacterium bovis BCG-vaccinated cattle using sampling microneedles. *Scientific Reports* 11, Article number: 7074. <https://doi.org/10.1038/s41598-021-86398-6>
18. Taye H; Alemu K; Mihret A; Wood JLN; Shkedy Z; BERG S; Aseffa A; The ETHICOBOTS consortium (2021) Factors associated with localization of tuberculosis disease among patients in a high burden country: A health facility-based comparative study in Ethiopia. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases* 23, 100231. <https://dx.doi.org/10.1016/j.jctube.2021.100231>
19. Almaw G; Mekonnen GA; Mihret A; Aseffa A; Taye H; Conlan AJK; Gumi B; Zewude A; Aliy A; Tamiru M; Olani A; Lakew M; Sombo M; Gebre S; Diguimbaye C; Hilty M; Fane A; Muller B; Hewinson RG; ELLIS RJ; NUNEZ-GARCIA J; PALKOPOULOU E; Abebe T; Ameni G; Parkhill J; Wood JLN; The ETHICOBOTS consortium; BERG S; van Tonder AJ (2021) Population structure and transmission of Mycobacterium bovis in Ethiopia. *Microbial Genomics* 7 (5). <https://doi.org/10.1099/mgen.0.000539>
20. Belay M; Tulu B; Younis S; Jolliffe DA; Tayachew D; Manwandu H; Abozen T; Tirfie EA; Tegegn M; Zewude A; Forrest S; Mayito J; Huggett JF; Jones GM; O'Sullivan DM; Martineau HM; Noursadeghi M; Chandran A; Harris KA; Nikolayevskyy V; Demaret J; BERG S; VORDERMEIER M; Balcha TT; Aseffa A; Ameni G; Abebe M; Reece ST; Martineau AR (2021) Detection of Mycobacterium tuberculosis complex DNA in CD34-positive peripheral blood mononuclear cells of asymptomatic tuberculosis contacts: an observational study. *Lancet Microbe* 2 (6) e267-e275. [https://doi.org/10.1016/S2666-5247\(21\)00043-4](https://doi.org/10.1016/S2666-5247(21)00043-4)
21. BIANCO C; SANCHEZ-CORDON P; SPIROPOULOS J; SCHOCK A; VIDANA B (2021) Never forget the pulmonary pathology of Mycobacterium bovis in the alpaca (Vicugna pacos)! *Vet Record Case Reports* 9 (1) e31. <https://doi.org/10.1002/vrc2.31> R11600 2 TB Impact factor: 0.220
22. McLoughlin KE; Correia CN; Browne JA; Magee DA; Nalpas NC; Rue-Albrecht K; WHELAN AO; VILLARREAL-RAMOS B; VORDERMEIER HM; Gormley E; Gordon SV; MacHugh DE (2021) RNA-SEQ transcriptome analysis of peripheral blood from cattle infected with Mycobacterium bovis across an experimental time course. *Frontiers in*

Veterinary Science 8, Article No. 662002. <https://doi.org/10.3389/fvets.2021.662002>

23. Almwaw G; Conlan AJK; Ameni G; Gumi B; Alemu A; Guta S; Gebre S; Olani A; Garoma A; Shegu D; Yimesgen L; Nigusie D; Wood JLN; Abebe T; Mihret A; BERG S; The ETHICOBOTS consortium (2021) The variable prevalence of bovine tuberculosis among dairy herds in Central Ethiopia provides opportunities for targeted intervention. *PLoS ONE* 16 (7) e0254091. <https://doi.org/10.1371/journal.pone.0254091>

24. RIMDAP E; DUNCAN D; HARRIS KA; BROUWER A; AVIGAD R; UPTON P; DALE J (2021) Bovine TB infection status in cattle in Great Britain in 2019. *Veterinary Record* 189 (2) e750. <https://doi.org/10.1002/vetr.750>

25. van Tonder AJ; Thornton M; Conlan AJK; Jolley KA; Goolding L; MITCHELL AP; DALE J; PALKOPOULOU E; HOGARTH P; Hewinson RG; Wood JLN; Parkhill J (2021) Inferring *Mycobacterium bovis* transmission between cattle and badgers using isolates from the Randomised Badger Culling Trial. *bioRxiv preprint N/A*. <https://doi.org/10.1101/2021.05.27.445931>

26. Bayissa B; Sirak A; Worku A; Zewude A; Zeleke Y; Chanyalew M; Gumi B; BERG S; Conlan A; Hewinson RG; The ETHICOBOTS consortium; Wood JLN; VORDERMEIER HM; Ameni G (2021) Evaluation of the efficacy of BCG in protecting against contact challenge with Bovine tuberculosis in Holstein-Friesian and Zebu crossbred calves in Ethiopia. *Frontiers in Veterinary Science* 8, Article 702402. <https://doi.org/10.3389/fvets.2021.702402>

27. Lyashchenko KP; Sikar-Gang A; Sridhara AA; Johnathan-Lee A; Elahi R; Lambotte P; Esfandiari J; Duthie M; Reed SG; JONES G; VORDERMEIER HM; Thacker TC; Palmer MV; Waters WR (2021) Novel polyprotein antigens designed for improved serodiagnosis of bovine tuberculosis. *Veterinary Immunology and Immunopathology* 240, 110320. <https://doi.org/10.1016/j.vetimm.2021.110320>

28. SMITH F; ROGERS F; TOMLINSON A; ARNOLD L; BENTON C; SPYVEE P; BOXALL S; Whiteside J; DELAHAY R (2021) A novel approach for trap-side restraint and blood sampling in European badgers. *European Journal of Wildlife Research* 67 (5) Article number: 86. <https://doi.org/10.1007/s10344-021-01520-3>

29. Sirak A; Tulu B; Bayissa B; Gumi B; BERG S; Salguero FJ; Ameni G; The ETHICOBOTS Consortium (2021) Cellular and cytokine responses in lymph node granulomas of *Bacillus Calmette Guerin* (BCG)-vaccinated and non-vaccinated cross-breed calves naturally infected with *Mycobacterium bovis*. *Frontiers in Veterinary Science* 8, Article number: 698800. <https://doi.org/10.3389/fvets.2021.698800>

30. Taye H; Alemu K; Mihret A; Wood JLN; Shkedy Z; BERG S; Aseffa A (2021) Global prevalence of *Mycobacterium bovis* infections among human tuberculosis cases: Systematic review and meta-analysis. *Zoonoses and Public Health* 68 (7) 704-718. <https://doi.org/10.1111/zph.12868>

31. Alcaraz-Lopez OA; Flores-Villalva S; Cortez-Hernandez O; Viguera-Meneses G; Carrisoza-Urbina J; Benitez-Guzman A; Esquivel-Solis H; Werling D; Bodes FJS; VORDERMEIER M; VILLARREAL-RAMOS B; Gutierrez-Pabello JA (2021) Association of immune responses of Zebu and Holstein-Friesian cattle and resistance to mycobacteria in a BCG challenge model. *Transboundary and Emerging Diseases* 68 (6) 3360-3365. <https://doi.org/10.1111/tbed.13939>

32. Swift BMC; Barron ES; Christley R; Corbetta D; Grau-Roma L; Jewell C; O'Cathail C; MITCHELL A; Phoenix J; PROSSER A; Rees C; Sorley M; Verin R; Bennett M (2021) Tuberculosis in badgers where the bovine tuberculosis epidemic is expanding in cattle in England. *Scientific Reports* 11, Article number: 20995. <https://doi.org/10.1038/s41598-021-00473-6>

33. Taylor EN; Beckmann M; VILLARREAL-RAMOS B; VORDERMEIER HM; Hewinson G; Rooke D; Mur LAJ; Koets AP (2021) Metabolomic changes in naturally map-infected Holstein-Friesian heifers indicate immunologically related biochemical reprogramming. *Metabolites* 11 (11) 727. <https://doi.org/10.3390/metabo11110727>

34. Khatri B; Keeble J; Dagg B; KAVEH DA; HOGARTH PJ; Ho MM (2021) Efficacy and immunogenicity of different BCG doses in BALB/c and CB6F1 mice when challenged with H37Rv or Beijing HN878. *Scientific Reports* 1, Article number: 23308. <https://doi.org/10.1038/s41598-021-02442-5>

35. Mazorra-Carrillo JL; Alcaraz-Lopez OA; Lopez-Rincon G; VILLARREAL-RAMOS B; Gutierrez-Pabello JA; Esquivel-Solis H (2021) Host serum proteins as potential biomarkers of bovine tuberculosis resistance phenotype. *Frontiers in Veterinary Science* 8, Article: 734087. <https://doi.org/10.3389/fvets.2021.734087>

36. van Tonder AJ; Thornton MJ; Conlan AJK; Jolley KA; Goolding L; MITCHELL AP; DALE J; PALKOPOULOU E;

HOGARTH P J; Hewinson RG; Wood JLN; Parkhill J (2021) Inferring Mycobacterium bovis transmission between cattle and badgers using isolates from the Randomised Badger Culling Trial PLoS Pathogens 17(11) e1010075. <https://doi.org/10.1371/journal.ppat.1010075>

b) International conferences: 0

c) National conferences: 0

d) Other:

(Provide website address or link to appropriate information) 0

**ToR 7: To provide scientific and technical training for personnel from OIE Member Countries
To recommend the prescribed and alternative tests or vaccines as OIE Standards**

14. Did your laboratory provide scientific and technical training to laboratory personnel from other OIE Member Countries?

No

ToR 8: To maintain a system of quality assurance, biosafety and biosecurity relevant for the pathogen and the disease concerned

15. Does your laboratory have a Quality Management System?

Yes

Quality management system adopted	Certificate scan (PDF, JPG, PNG format)
ISO17025	ISO17025 2021 Cert.jpg
ISO9001	ISO9001 certificate 2020-2023.pdf

16. Is your quality management system accredited?

Yes

Test for which your laboratory is accredited	Accreditation body
Culture (bovine and non-bovine)	UKAS
Gamma interferon ELISA	UKAS

17. Does your laboratory maintain a “biorisk management system” for the pathogen and the disease concerned?

Yes

(See Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, Chapter 1.1.4)

ToR 9: To organise and participate in scientific meetings on behalf of the OIE

18. Did your laboratory organise scientific meetings on behalf of the OIE?

No

19. Did your laboratory participate in scientific meetings on behalf of the OIE?

No

ToR 10: To establish and maintain a network with other OIE Reference Laboratories designated for the same pathogen or disease and organise regular inter-laboratory proficiency testing to ensure comparability of results

20. Did your laboratory exchange information with other OIE Reference Laboratories designated for the same pathogen or disease?

No

21. Was your laboratory involved in maintaining a network with OIE Reference Laboratories designated for the same pathogen or disease by organising or participating in proficiency tests?

No

22. Did your laboratory collaborate with other OIE Reference Laboratories for the same disease on scientific research projects for the diagnosis or control of the pathogen of interest?

No

ToR 11: To organise inter-laboratory proficiency testing with laboratories other than OIE Reference Laboratories for the same pathogens and diseases to ensure equivalence of results

23. Did your laboratory organise or participate in inter-laboratory proficiency tests with laboratories other than OIE Reference Laboratories for the same disease?

No

Note: See Interlaboratory test comparisons in: Laboratory Proficiency Testing at:
<http://www.oie.int/en/our-scientific-expertise/reference-laboratories/proficiency-testing> see point 1.3

ToR 12: To place expert consultants at the disposal of the OIE

24. Did your laboratory place expert consultants at the disposal of the OIE?

No

25. Additional comments regarding your report: