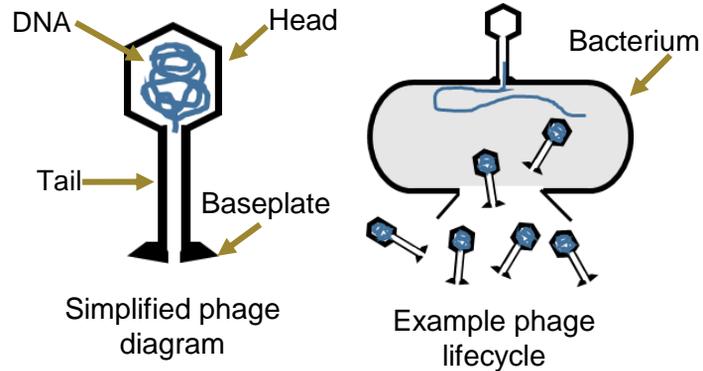


Development of the Actiphage[®] test for bovine TB

What is a phage?

A bacteriophage - more commonly known as a phage - is a virus which infects bacteria. Phage infect their bacterial hosts by injecting their DNA into the bacterial cell, which is then forced to make new phage particles. Once the new phage are made, the viruses then rupture the bacterial cell. This releases the new phage into the environment, which in turn can infect more bacteria.

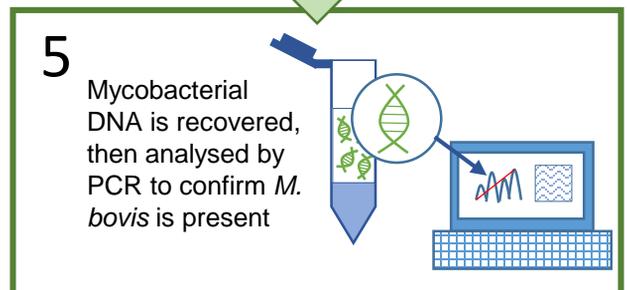
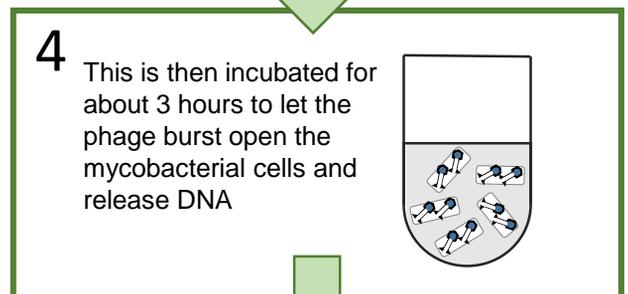
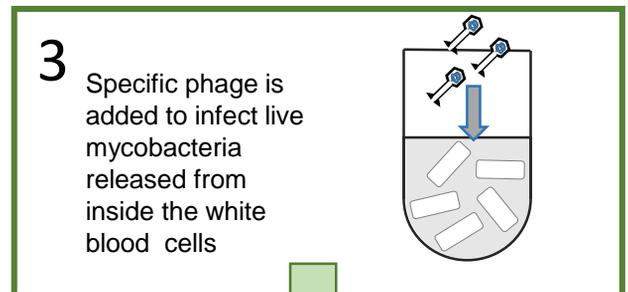
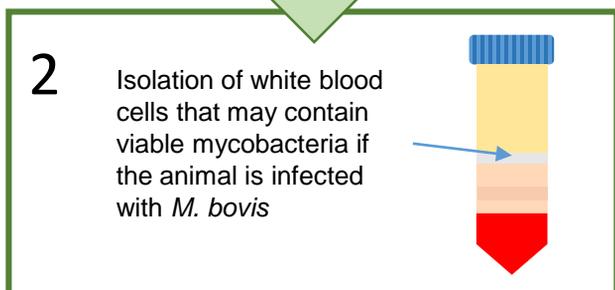


How can phage testing identify TB-infected animals?

Phage-based methods of detection use a specific phage capable of infecting bacteria responsible for a disease. The activity of the phage is then used as an indicator that bacteria are present in a sample taken from an animal [1]. This is different to other diagnostic tests for TB, which typically measure the immune response of an animal (e.g. the skin test), or grow the bacteria in the lab (e.g. culture). Phage testing methods have been developed to experimentally detect *Mycobacterium avium* subspecies *paratuberculosis* (which causes Johne's disease) in blood and milk [2,3]. Recent research has also developed a phage test from *Mycobacterium bovis* (which causes bovine TB) in blood cells from cattle [4,5] and other species.

How does the Actiphage TB test work?

Phage testing for bovine TB uses a phage that specifically infects mycobacteria. A process called PCR (polymerase chain reaction) then analyses the DNA released from the bacteria to confirm the presence of *M. bovis*. Below is an outline of the current process for the Actiphage test by PBD Biotech. The whole testing process takes 6-8 hours from when the sample is received in the lab



The Actiphage test is in development and not yet validated

The current Actiphage® blood test for TB in cattle is not a validated test and as yet there are no definitive values for the test's sensitivity, specificity, positive predictive value or negative predictive value. Nor is there any evidence showing that the test can help reduce TB breakdown duration.



A recent study published by the tests manufacturer [5] carried out Actiphage testing on 41 cattle which had already tested positive to the tuberculin skin test (SICCT). All 13 of these cattle with visible lesions tested positive to the Actiphage test, while 26/28 (93%) of non-visible lesioned animals (NVL) tested positive. The study also tested 45 uninfected cattle (from an area with no TB), all of which tested negative on the Actiphage test. This study estimates that *relative to the skin test*, the Actiphage ® has a sensitivity of 95% and a specificity of 100%. However, further trials are needed to confirm test accuracy and validate the Actiphage test.



Use of phage testing

Actiphage from PBD Biotech can be used on a private basis in England and Wales, with prior permission from APHA or Welsh Government [6] in herds with chronic or persistent TB breakdowns. Cattle keepers should first speak with their private vet to discuss use of non-validated tests, and check whether their herd is eligible to apply. Animals that test positive to Actiphage or any other non-validated test will not be compulsorily slaughtered, and no compensation is paid. Test-positive animals must either be voluntarily slaughtered, or restricted to the holding for life. Testing with non-validated tests does not affect the statutory testing regime or lifting of movement restrictions in TB breakdown herds.



Where can I find more info?

For more information on a range of TB topics visit www.tbhub.co.uk. This sheet was produced as a part of a Knowledge Exchange project funded by NERC. For more info and to download the full list of TB factsheets visit www.tbknowledgeexchange.co.uk.

Studies referenced

1. Van der Merwe et al. (2014) Analyst
2. Stanley et al. (2007) Applied and Environmental Microbiology
3. Swift et al. (2013) Journal of Microbiological Methods
4. Swift et al. (2016) Virulence
5. Swift et al. (2019) Microbial Biotechnology
6. In England and Wales, cattle keepers and vets can find more details about exceptional private use of the Actiphage test at <http://apha.defra.gov.uk/vet-gateway/non-valid-tb-testing/> and <https://gov.wales/use-non-validated-tests-cattle-herds>