



Animal health and welfare

Bovine TB: Gamma interferon

Wider roll-out of the gamma interferon (g-IFN) blood test across Great Britain

On 23 October 2006, the Government introduced a new policy designed to improve the testing of cattle for bovine TB (bTB), by extending the use of the gamma interferon (g-IFN) diagnostic blood test in Great Britain. The g-IFN test is now used more widely, alongside the tuberculin skin test, to improve the sensitivity of the testing regime and identify more infected animals more quickly (see below for details). Using both tests in this way can help to speed up the resolution of confirmed TB breakdowns by identifying as many infected cattle as possible at the earliest opportunity.

Under this policy the g-IFN test is now applied mainly in 3 and 4 yearly testing parishes in an attempt to ensure that infection in such areas does not become established in cattle or wildlife. The test continues to be available to use as a disease control tool in areas of high bTB incidence.

Circumstances under which the gamma interferon test is used

The use of g-IFN test is now mandatory, to enhance sensitivity and detection of infected cattle, in the following prescribed circumstances:

- ▶ All confirmed new bTB incidents (CNIs) in 3 or 4 yearly tested herds, including those that fail to resolve through repeated skin tests or where complete or partial de-population is contemplated;
- ▶ CNIs that have failed to resolve through repeated skin testing in 1 and 2 yearly tested herds, including those herds where a complete or partial de-population is contemplated;
- ▶ At the first inconclusive reactor (IR) retest in unresolved IRs in herds in 1 and 2 yearly tested herds.

Additionally, the test is used occasionally to enhance specificity in the following limited circumstances:

- ▶ Non-specific reactor procedure for unconfirmed breakdowns in 2, 3, or 4 yearly tested herds
- ▶ Suspected fraudulent reactors

Under the new policy up to an estimated 45,000 tests will be completed each year, thus trebling recent usage rates. Monitoring the usage of the g-IFN test is ongoing and key statistics are updated monthly.

A news release was issued to announce the new policy. An information leaflet (37 KB) will be provided to all affected farmers. A Welsh version (39 KB) is also available.

More information is available on these prescribed circumstances for the g-IFN test.

Testing cattle for bovine TB

As set out in the Government strategic framework for the sustainable control of bovine tuberculosis (bTB) in Great Britain, the Government will continue to develop a sound scientific evidence base by supporting research to improve our understanding of the disease and generate new tools, particularly in relation to diagnostics and vaccines.

Tuberculin skin test

One of the key challenges in controlling bTB lies in detecting infection in individual live animals. The onset of signs of TB in cattle is usually slow, and infected animals may be infectious for months or years before a diagnosis based on clinical signs can be reached. As a result, diagnosis of bTB must rely on detecting **infection** with the causative bacterium, rather than **disease** by the use of immunological tests.

Routine screening for bTB relies on one of the variants of the intradermal tuberculin test, also known as the skin test, which has been in use in Great Britain since 1942. The technique and interpretation of the tuberculin tests is tightly prescribed in Council Directive 64/432/EEC (as amended).

Gamma interferon blood test

In the late 1980s, a new laboratory-based blood test, the gamma interferon (g-IFN) test, was developed in Australia for the diagnosis of bTB. Evidence from field trials overseas is that the g-IFN test is less specific than the comparative tuberculin skin test - the primary test for bTB in the British Isles. Therefore, it cannot be used in place of the skin test for mass bTB screening of cattle in a situation where the disease is rare, as this would result in too many false test-positive animals.



However, the g-IFN test has good sensitivity, appears to detect infected animals earlier than the skin test and can be repeated as often as necessary without the need to wait 60 days between tests. Additionally, the two tests detect marginally different groups of animal with some animals only disclosing to one or other diagnostic test. Therefore, this test is used in many countries in combination with the skin test, to improve the detection of infected cattle in herds with persistent bTB problems or with a high prevalence of disease and so hasten the resolution of confirmed bTB breakdowns.

The g-IFN test is not a replacement for the tuberculin skin test. The skin test is the best screening test for bTB. European legislation stipulates that the two variants of the skin test are the primary ante-mortem tests for TB in cattle in the EU. This includes routine, targeted, pre-export certification and repeat bTB testing of infected herds. The g-IFN test is only approved as an ancillary diagnostic tool.

The gamma interferon field trial (and other ad hoc usage)

Between November 2002 and October 2005, Animal Health (formerly SVS) and the Veterinary Laboratories Agency (VLA) conducted a field trial to assess the potential benefits of using the g-IFN test in tandem with the tuberculin skin test in herds with confirmed bTB breakdowns.

The trial aimed to find out whether the use of this test alongside the skin test would significantly shorten the time period that cattle herds with confirmed bTB remain under restriction.

It was projected that 600 herds would need to be enrolled into the trial to meet this aim but due to very slow recruitment because of a range of factors, the results from only 195 herds were available for analysis when the trial was stopped in October 2005. This was an inadequate number to give statistically reliable results regarding impact of g-IFN usage on the length of a breakdown.

However around 9,000 g-IFN tests were performed as part of the trial up to its closure in 2005 with a further 14,000 samples taken from chronically infected herds under Animal Health ad hoc usage protocols over the same period.

This level of sampling provided invaluable field experience in using the test, identifying the value and performance of the test under GB conditions and establishing the basis for protocols required for its wider use in the TB control policy.

The results of the trial [PDF](#) (857 KB), published on 10 August 2006, showed that in problem TB herds about 12% of animals passing the skin test are testing positive to the blood test and of the blood test positives about 18% are shown to be grossly infected or culture positive in almost half of the herds blood tested.

Combined use of skin testing and blood testing resulted in more infected animals being detected than using skin testing alone. Broadly similar results were obtained in the ad hoc usage of the test with 15%-20% of skin tests negative, g-IFN positive animals confirmed at slaughter.

Trial to test the specificity of the gamma interferon test

Because of concerns regarding the specificity (accuracy of a test to correctly identify negative animals) of the g-IFN blood test, a trial was set up to establish this aspect of its performance under GB conditions. The results of this trial [PDF](#) (335 KB) were also published on 10 August 2006.

By sampling over 1,000 animals in 24 herds considered free of TB in 4 year testing parishes, a specificity value of around 96% was achieved when running the test with the tuberculins as used for skin testing or when using more specific antigenic proteins. When both types of antigens are combined to maximise specificity the test was around 99% specific. When samples from herds who had bought in animals from herds with a recent history of TB were removed from the trial results the specificity figures marginally improved. These results are in agreement with previously published data from other countries around the world.

Following the experiences gained from the g-IFN pilot trial, ad hoc usage of the g-IFN test over the last 3 years and the obvious benefits of the test in identifying infected cattle missed by skin testing, the Government has announced wider mandatory use of the g-IFN test under prescribed circumstances. This projects that up to an estimated 45,000 g-IFN tests will be carried out each year, thus trebling recent usage of the test.

Significance of unconfirmed disease (via post mortem / culture) in animals testing positive to the gamma interferon test

It is a common misconception that, as 4 out of 5 animals testing positive to the g-IFN test are not confirmed in the slaughterhouse or laboratory, they are false positives. **This is not necessarily the case.** In *M. bovis*-infected cattle, responses to immunological tests for TB can be detected soon after infection, i.e. before the development of TB lesions visible in a cursory post-mortem examination of g-IFN test reactors. Isolation of the causative organism in the laboratory is not straight-forward. This is even more difficult in cases where no visible lesions are available for culture in the laboratory and culture has to be attempted from a pool of grossly normal lymph nodes in which the bacterial load may be too low for successful identification of the organism.

Because it is impossible to find out in a living animal whether the reaction to the g-IFN test is due to infection with *M. bovis* or another micro-organism, all test reactors are slaughtered on a precautionary principle. The g-IFN test is being deployed in herds with confirmed TB or in animals in high-risk areas with two consecutive inconclusive results to a tuberculin skin test, all of which increase the predictive value of a positive g-IFN test result (i.e. the probability that a g-IFN test reactor is truly infected).

It is clear that in infected herds animals testing positive to the g-IFN test should be removed as the immunological response demonstrates they have been exposed to infection and represent a potential risk to other animals. In addition, work in the Republic of Ireland shows that these animals are 7 to 9 times more likely than a g-IFN test negative animal to disclose as a skin test reactor at subsequent skin tests if not removed from the herd.

Page last modified: 04 December, 2007