To: Heads of Environmental Health Services (England)

Copies: Directors of Trading Standards (England),
LACORS, TSI, CIEH

15th July 2008

Reference: ENF/E/08/047

Dear Colleagues,

REGULATION (EC) 853/2004 - TB TESTING USING THE GAMMA INTERFERON BLOOD TEST

The Agency has become aware that some Authorities may be unclear about the implications of positive reactions to TB tests carried out on dairy cattle using the Gamma Interferon blood test. This letter is intended to provide information about the use of the test and to clarify that, as with tuberculin skin test reactors, milk from gamma interferon test reactors is prohibited from entering the food chain.

EC Regulation 853/2004 (Annex III, Section IX, Chapter I, Paragraph 1.2(b)) requires that raw cows’ milk must come from animals belonging to a herd which is Officially Tuberculosis Free (OTF). Milk which does not satisfy this condition may only be sold for human consumption after it has been heat-treated (Annex III, Section IX, Chapter I, Paragraph 3). Similarly, milk from herds which have lost their OTF status cannot be used to make unpasteurised milk-based products. Furthermore, the milk from individual cows that have reacted to an official TB test must not enter the food chain.

Under Defra’s TB Control Programme, regular TB testing of cattle herds is carried out with a frequency dependent upon the local incidence of TB. This ensures that most cases of TB in cattle are detected in the early stages of infection, before the development of clinical signs and the shedding of bacteria in milk. The tuberculin skin test has been in use for many years to detect TB in live cattle and continues to be the primary screening test for bovine TB. Additionally, since 2002 the gamma interferon blood test has been approved in GB as an ancillary parallel test that supplements the skin test in a limited range of scenarios, generally in situations where the OTF status of a dairy herd has already been lost following identification of reactors to a skin test. The combined use of the two tests improves the sensitivity of the TB testing regime compared to using either test alone, thus speeding up the identification of infected cattle and helping resolve TB breakdowns more quickly.

Animals reacting to either or both tests are regarded as TB ‘reactors’ and are compulsorily slaughtered by Animal Health as soon as possible after their identification. As in the case of skin test reactors awaiting removal from a farm, milk from cows reacting to a gamma interferon test is also prohibited from being sold for human consumption.
When a dairy herd is placed under TB movement restrictions, for whatever reason, the Divisional Veterinary Manager at Animal Health will notify the relevant Chief Environmental Health Officer. Service of the TB restriction notice (TB2) effectively suspends the OTF status of that herd.

I am enclosing, as an Annex to this letter, a Q and A prepared by Defra which explains what the Gamma Interferon test is and sets out the background to its use in Great Britain. Any queries related to the content of the Q and A should be referred to your local Animal Health Divisional Office. Further details on the gamma interferon test (and policy) can be found on the Defra website through the following link: http://www.defra.gov.uk/animalh/tb/control/gamma.htm

If you have any questions in relation to this letter, please contact:

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Yours faithfully,

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Gamma Interferon test Q&A

Background/ general

1. What is the gamma interferon test?
The gamma interferon (γ-IFN) test is a laboratory-based blood test developed in Australia, in the late 1980s, for the diagnosis of bovine TB in cattle.

Gamma interferon is a cytokine (immunomodulator protein) produced by certain cells of the immune system (memory T cells) in animals infected with certain pathogens (such as M. bovis). The gamma interferon test measures the amount of γ-IFN released by T-cells in 24-hour whole blood cultures stimulated with bovine tuberculin, avian tuberculin, a mitogen (positive control), and no antigen (negative control).

2. How long has the gamma interferon test been used in Great Britain?
As a research tool, it has been used in GB since the mid-1990s. Since 2002 the gamma interferon test has been used alongside the skin test, in certain circumstances (generally within herds with severe or persistent confirmed M. bovis infection). Up until the end of 2006, this took place both within the context of a randomised field trial of selected herds in parts of England and Wales, and in other herds outside that trial.

3. How did the GB gamma interferon test policy change in 2006?
On 23 October 2006 a revised set of criteria for the deployment of the gamma interferon test in the field was rolled out across Great Britain. The new policy was supported by industry organisations and the veterinary profession and endorsed by the Independent Scientific Group reporting to Defra. Under this policy, greater use is made of the test than previously (as an ancillary test in conjunction with the primary (skin) test) – and in certain specified scenarios its use is now mandatory (see Q5 for full details of scenarios in which gamma interferon test is used).

4. Why do we use the test?
The gamma interferon test is mainly used, alongside the tuberculin skin test, to improve the sensitivity of the testing regime by identifying more infected animals more quickly (‘to enable detection of the maximum number of infected animals’ as provided for in Annex B of Council Directive 64/432/EEC). This is known as ‘parallel testing’ – animals reacting to either or both tests are regarded as infected and removed.

Using both tests in this way offers better sensitivity than using either test alone, thus speeding up the identification of infected cattle and helping resolve confirmed TB breakdowns more quickly. The gamma interferon test is used in the circumstances prescribed below. The main focus is in confirmed breakdown herds in 3 and 4 year testing parishes, to reduce the risk of the disease becoming established in low prevalence areas.
5. When is the gamma interferon test used?
The gamma interferon test is used:

- On tuberculin test-negative animals in all confirmed new TB incidents in 3 or 4 year testing parishes;
- On tuberculin test-negative animals in severe TB incidents, to inform decisions around whole or partial herd slaughter;
- On tuberculin test-negative animals in herds in high risk areas with persistent, confirmed infection that fail to resolve through repeated short-interval tuberculin tests and have taken basic herd bio-security precautions; and
- On inconclusive reactors that fail to resolve at their first tuberculin retest in herds in 1 and 2 yearly testing parishes.

- Additionally, Animal Health may also use the blood test as a serial test (where animals need to test positive to both tests) to improve specificity and reduce the probability of a false positive result:
- In chronic, unconfirmed TB incidents in 2, 3 or 4-yearly testing areas, where non-specific cross reactions to tuberculin are suspected; and
- For re-testing of tuberculin test reactors with abnormal skin responses or where interference with the skin test is otherwise suspected.

nb The test is used only on animals aged over 6 months.

nb. For serial testing purposes only, a slight modification of the normal test protocol is applied to enhance the specificity of the assay.

6. How is the gamma interferon test carried out?
An Animal Health (AH) vet or Animal Health Officer takes blood sample from each animal under test. This sample is sent in temperature controlled packaging to a VLA laboratory where it is cultured in the presence of the antigens described above (Q1).

If, in response to antigen stimulation, the blood cells produce $\gamma$-IFN above the pre-determined threshold, the animal is deemed to have been infected with bovine TB. The test results are sent to the relevant AH Divisional Office, who will notify the cattle owner and arrange removal and slaughter of any test positive animals (or re-sampling of individual animals where required). Reactors to the gamma interferon test have the same legal status as reactors to the tuberculin skin test, which means that they must be compulsorily removed and slaughtered with compensation.

7. How many gamma interferon tests are carried out each year? And how many give a positive result?
Regularly updated statistics on the application/results of gamma interferon tests are published on Defra’s website.

Between October 2006 (i.e. when the current policy was launched) and end March 2008 42,825 tests were carried out, 4,535 of which produced a positive result.

8. How do we know that the gamma interferon test works?
All scientific evidence (e.g. from extensive published research and widespread field use both in Britain and across the world) demonstrates that the gamma interferon test is effective at disclosing infected animals that are missed by the skin test. It has been fully validated, and has been tested extensively in GB conditions.

The gamma interferon test procedures at VLA are UKAS accredited and each sample must pass stringent quality control checks before results are released to AHDOs. These include measures to demonstrate that the blood was taken appropriately, that it was transported to the laboratory in the correct way, and that the blood quality is sufficient to be confident of an accurate result. Only once all these criteria are satisfied will results be released.

Furthermore, the gamma interferon test has been listed in the World Organisation for Animal Health(OIE) manual, and approved in EU legislation as an ancillary test (to the skin test) for bovine TB.

9. Why use it alongside the skin test? Why do the two tests reveal different numbers of infected animals?
European legislation only permits member states to use the gamma interferon test as an ancillary test i.e. alongside the skin test. The gamma interferon test has better sensitivity than the skin test, and may well detect infected animals that have been missed by the skin test. In short, research shows that the skin and gamma interferon tests identify different populations of infected animals - maximum testing sensitivity is achieved when they are used together (parallel testing).

It should be noted that whilst most skin-test reactors (but not all) might be expected to also provide gamma interferon positive responses the converse is not always true. Since the blood test is the more sensitive of the two diagnostic methods, and may detect animals earlier after infection, there is likely to be a larger number of infected cattle that are gamma interferon positive than skin-test positive alone, especially in herds where a TB breakdown has been identified at an early stage. Research in Ireland shows that in infected herds, gamma interferon test reactors are 7-9 times more likely to become reactors at a subsequent skin test than gamma interferon test negative animals in the same herd.

Legal issues

10. What is the legal basis for the use of the test and removal of reactors?
Section 32 of the Animal Health Act 1981 provides the Secretary of State with the power to slaughter bovine animals that are affected with disease, those that are suspected of being affected, or those which have been exposed to infection, in this case, bovine TB. The Tuberculosis (England) Order 2006, made under the Animal Health Act, provides the relevant powers for the Secretary of State to require bovine animals to be tested with the skin test or the gamma interferon test.

11. What is the legal status of animals reacting to the gamma interferon test?
Animals showing a positive reaction to the gamma interferon test in Great Britain are deemed to be “reactors” within the meaning of the TB (England) Order 2007 and
therefore have the same legal status as an animal showing a reaction to the skin test. They should be isolated, pending removal and slaughter, and not subjected to any further TB testing. As with skin test reactors, milk from gamma interferon test reactors is prohibited from being sold for human consumption.

12. Is compensation provided for gamma interferon reactors?
Yes, compensation is provided in the same way as it is for skin test reactors. The relevant date for assessing the appropriate level of payment is the date of blood sampling.

DEFRA/VLA/AH
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