Animal & Plant Health Agency

APHA Briefing Note 33/19

Change to the Inconclusive Reactors (IR) Policy in Persistent TB Breakdowns in Wales

Date issued: 20 December 2019

Purpose

1. To inform vets in Wales of a change in policy for Inconclusive Reactors (IRs) in persistent herd TB breakdowns.

Background

2. Persistent herd breakdowns, of 18 months duration or longer, are herds in which the policies on cattle testing and removal in TB breakdowns have not fully eliminated bovine TB infection from the cattle population.

3. The Welsh Government considers all IRs identified under severe interpretation in these herds as being at a significantly higher future risk of being removed for TB control purposes than clear testing cattle.

4. Bovine TB is an infectious disease and not removing all of the infected cattle from a herd can have future adverse consequences for the herd and its TB status.

5. No single test, or combination of tests for bovine TB provides 100% test specificity and 100% test sensitivity. As sensitivity is increased, specificity inevitably is lowered. The Welsh Government aims to continually review whether the balance between specificity and sensitivity is the best one available for any given circumstance in our continued efforts to control the disease. The IDEXX Antibody test has recently become a relevant test in Wales. This has provided the opportunity to review the existing policy of slaughtering all IRs in persistent TB breakdowns, as there are now additional options for the testing of higher risk animals. This review has resulted in a policy change.

When will this change come into effect?

6. The change in policy will come into effect from the 01/01/2020.

Who will it affect?

7. This policy will affect keepers of herds which have undergone TB breakdowns with a duration of over 17 months.

Summary of the new policy

8. Standard IRs (see definition below) will be slaughtered with compensation. Severe IRs (see definition below) will be tested with both a parallel Interferon-gamma test (the “gamma test”) and an IDEXX Antibody test (the “antibody test”). Any test positive animals will be slaughtered with compensation.

9. The policy will be in place fully by February 2020. For most herds during January 2020, severe IRs will only be tested using the gamma test, unless there are large numbers of severe IRs identified at a single Short Interval Test (SIT), when an antibody test of those animals may also be scheduled by the APHA case vet.

The new policy in detail

10.

- All skin tests in a herd with a TB breakdown exceeding 17 months in duration will be read at severe interpretation.
- OVs should confirm readings for all severe IRs also at standard interpretation, as standard IRs will be slaughtered
- From and including the first Short Interval Test (SIT) after the TB breakdown has been 17 months in duration, all standard IRs will be slaughtered and all severe IRs will usually be sampled for both a gamma test and an antibody test from 10-30 days after TT1 of the skin test, until an exit position is reached.
- The existing policy on animals, which are severe IRs at consecutive tests on 2 or 3 occasions, will remain the same as in non-persistent herd breakdowns. APHA case vets may consider removing some of these animals as Dangerous Contacts (DCs), but it is expected that the previous policy of removing all standard and severe IRs will not be adopted for any individual herd.
- *Exit position* - the exit position is reached at an SIT, when there is a clear testing result, or only severe IRs are identified (no change to existing policy).
- *Action at the exit position* – APHA will subject the severe IRs to a gamma test only (no change to existing policy).
- *Consequences of gamma testing in the exit position*:

- If all of the IRs at the final clearing test (2nd clear test) have a negative gamma test result, then the test interpretation will revert to standard and movement restrictions will be revoked (no change to existing policy).
- If any of the severe IRs out of a group of severe IRs are positive to the gamma test, then antibody tests will be carried out on stored serum samples collected at the time of gamma sampling from all severe IRs in the group (10-30 days post TT1).
- Following a gamma, or antibody test positive result, two clear SITs at severe interpretation are needed, before movement restrictions can be withdrawn (no change to existing policy).

An FAQ which covers managing IRs in persistent TB breakdowns can be found on the Welsh Government's website: https://gov.wales/bovine-tb-eradication-programme-frequently-asked-questions.

For the specific attention of OVs

11. DNA reactor tags will need to be used in all reactors and standard IRs. Do not apply DNA tags to severe IRs.

12. Keepers should be informed that all severe IRs must be kept in isolation from the rest of the herd until their status is resolved. IRs should be kept isolated from reactors awaiting slaughter.

Definitions and further information:

Persistent herd breakdown – herds in which the duration of the breakdown has been 18 months or longer.

Standard IR (in this document) – Animals showing a positive bovine reaction where the bovine reaction is 1 or 2mm more than the avian reaction. (N.b.- animals showing a positive bovine reaction and a negative avian reaction are reactors at severe interpretation).

Severe IR (in this document) – Animals showing a positive bovine reaction and where the bovine reaction is either 1 or 2mm less than, or equal to, the positive avian reaction.

Exit position – an SIT at which changes are made to the policy, as the herd gets closer to clear testing.

Specificity - the probability that the test will be negative in animals that DO NOT have the infection. It can be considered as a measure of the false-positivity rate e.g. a specificity of 99.98% means 1 in 5000 animals are likely to be false positives.

Sensitivity - the probability that the test is positive when used in an INFECTED animal. It can be considered as a measure of the proportion of infected animals identified e.g. a sensitivity of 80% means that 8 out of 10 infected animals are likely to be correctly identified and 2 out of 10 are likely to remain undetected from a single test.

Relevant test - a skin test, or any other diagnostic test approved by the Welsh Ministers for the diagnosis of bovine TB in cattle, or other bovidae. APHA can require a relevant test to be undertaken on a cattle farm by the service of a Test Notice. Any animal positive to a relevant test will be slaughtered and compensation will be paid to the keeper for the loss of that animal. Only those tests, which have been validated and have been performed at least 1000 times on cattle in Wales, with satisfactory results are considered for approval as a relevant test. All relevant blood tests in Wales can only be performed by APHA.

Antibody test – must be carried out 10-30 days post TT1 of the skin test, because the skin test boosts the antibody responses to a detectable level in those animals exhibiting a response to M.bovis infection. The gamma test on severe IRs should usually be arranged for the same day as the antibody test, unless a targeted herd gamma test has been carried out at TT1 or TT2 of the skin test.

Samples for antibody testing from severe IR animals – APHA will communicate with the keeper directly to arrange for the testing and collection of blood samples by APHA staff.

Test specificities/sensitivities and positivity rates:

	Sensitivity	Specificity
Skin test at standard	81 (77.3 – 84.7)	99.98 (99.9 – 100)
Skin test at severe	85	99.91
Gamma test	90.0 [87.2-92.8]	96.5 (95.3 – 97.7)
IDEXX Antibody test	64.6 (59.7 – 69.5)	98 (97.5 – 98.4)

Inconclusive reactors in persistent herd breakdowns FAQ

What happens to Inconclusive reactors (IRs) in persistent herd breakdowns?

- All cattle testing inconclusive at standard interpretation of the skin test are removed as reactors.
- Cattle testing inconclusive at severe interpretation of the skin test will be subject to both a gamma interferon blood test and an antibody test (IDEXX).
- This policy will be fully in place by February 2020. For most herds during January 2020, severe IRs will only be tested using the gamma test, unless there are large numbers of severe IRs identified at a single Short Interval Test (SIT), when an antibody test of those animals may also be scheduled by the case vet.

When is the exit position reached?

- The exit position is reached when there is a clear test or there are only cattle testing inconclusive at severe interpretation remaining, at which point:

    - severe interpretation IRs will be gamma interferon tested only.
    - If all of the severe interpretation IRs test clear at the final clearing test, the testing regime will return to standard interpretation and the herd will be released from restrictions.
    - If any of the group of severe testing IRs test positive at the gamma interferon test, the remaining severe testing IRs in the group, which are negative to the gamma interferon test will need to be tested with an IDEXX antibody test and have a negative result.
    - Two clear Short Interval Tests at severe interpretation are needed following the removal of any skin test reactor, IR, Direct Contacts, gamma test positive, or antibody test positive animal, before movement restrictions can be withdrawn.

What is the evidence for the revised policy?

Analysis has been performed on TB testing data from the 10 most persistent TB breakdowns in Wales between 2010 and 2015. This analysis showed that a high number of standard and severe interpretation Inconclusive Reactors became reactors at further testing.

Why has the policy changed?

We are continuously learning from the situation on the ground and our TB Eradication Programme is designed to react flexibly to such changes.

Now that the IDEXX Antibody test has become a 'relevant' test in Wales, meaning that it has been fully approved under the legislation for official testing, this has provided additional options for testing higher risk animals and to review the existing policy of slaughtering all IRs in persistent TB breakdowns. This review has resulted in the new policy going forwards.

What is the IDEXX Antibody test and how will this new test enhance the existing regime?

The **IDEXX** Antibody test is fully validated with the World Organisation for Animal Health (the OIE). It has now been used over a thousand times in Wales in higher risk animals with satisfactory results.

Our current understanding is that once an animal is infected with TB and has generated an immune response to the organism (M.bovis), it is then considered to be infected for the rest of its life. The animal's immune response to the presence of this organism may at different times be either a cell-mediated immune response, or an antibody mediated response, or both. The aim of the skin and gamma interferon tests is to detect a cell mediated response, whereas the aim of the IDEXX Antibody test is to detect an antibody response.

The quoted specificities and sensitivities of this test compared with the other official tests for bovine TB are:

	Sensitivity	Specificity
Skin test at standard	81 (77.3 – 84.7)	99.98 (99.9 – 100)
Skin test at severe	85	99.91
Gamma test	90.0 (87.2 – 92.8)	96.5 (95.3 – 97.7)
IDEXX Antibody test	64.6 (59.7 – 69.5)	98 (97.5 – 98.4)

The results of deploying the IDEXX Antibody test in higher risk animals in persistent TB breakdowns in Wales over a 20 month period compared with the gamma interferon test are:

Testing by APHA in Wales between Jan 18 – Aug 19	Numbers tested	No. of positives	% positivity
Gamma test in persistent breakdowns	45902	2240	4.9%
IDEXX Antibody test *	3614	260	7.2%

The IDEXX Antibody test must be carried out 10-30 days post TT1 (date of the tuberculin injection) of the skin test, because the skin test boosts the antibody responses to a detectable level in those animals exhibiting a response to M.bovis infection.

Specificity means the probability that the test will be negative in animals that DO NOT have the infection. It can be considered as a measure of the false-positivity rate e.g. a specificity of 99.98% means 1 in 5000 animals are likely to be false positives.

Sensitivity means the probability that the test is positive when used in INFECTED animals. It can be considered as a measure of the proportion of infected animals identified e.g. a sensitivity of 80% means that 8 out of 10 infected animals are likely to be correctly identified and 2 out of 10 are likely to remain undetected.

What if the severe IRs become gamma positive or antibody positive?

All severe Inconclusive Reactors (IRs) (when the exit strategy is **not** reached) are tested using a parallel gamma test and an antibody test. Any gamma positive or antibody test positive animal is removed for TB controls.

Is it possible for severe IRs to be removed when they have passed a gamma test and an IDEXX Antibody test?

The default position is that cattle, which are severe IRs on two consecutive (or non-consecutive) skin tests will receive a gamma test and an antibody test, after each skin test result.
APHA case vets do have the discretion to remove these animals as Direct Contacts (DCs), without applying additional blood testing. However, if an animal becomes a severe IR at a third consecutive test, then it will be automatically removed with compensation. DC removal will be considered by the APHA case vet on individual merit and not by default.

What is the gamma and the antibody test results do not agree?

Animals with a positive result to any of the official tests are removed for TB control. The gamma test and antibody test identify animals showing different immunological responses to M.bovis, as the animal's response to the infection changes over time. We would expect few animals to be both positive to the gamma test and positive to the antibody test.

What if a persistent herd breakdown becomes Officially TB Free (OTF)

TB restrictions would be lifted and the releasing Short Interval Test (SIT) cannot be used as a pre-movement test. Any pre-movement test requires at least a 60 day interval from the latest skin test. This is not a change from the existing policy.

Does it mean that I could not sell cattle?

You could not sell cattle that require a clear pre-movement test, before movement, but there are exemptions to the requirement to pre-movement test, for example, movements direct to slaughter, or a dedicated slaughter market, or animals which are under 42 days old.