Animal &
Plant Health
Agency

APHA Briefing Note 13/21

Introduction of the Operational Use of Whole Genome Sequencing (WGS) for bTB Purposes

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Purpose

To inform Official Veterinarians (OVs) that from 19th April 2021, the Animal and Plant Health Agency (APHA) has replaced genotyping with whole genome sequencing (WGS) as the genetic typing method used to determine the different strains of *Mycobacterium bovis (M. bovis)* isolates in GB.

Background

1. Until now, APHA has been using genotyping as the method of genetic typing to characterise the specific strain of *M. bovis* for TB breakdowns in GB.

2. Genotyping involves a combination of spoligotyping and variable number tandem repeat (VNTR), both targeting specific regions of the *M. bovis* DNA sequence in order to characterise it and assign a genotype.

3. ‘Home ranges’ are areas where particular genotypes are common and are used to compare isolates from new TB incidents with the previous known distribution of the particular genotype identified.

4. Home range maps are an attempt to capture the geographical localisation (endemic regions) of the various genotypes of *M. bovis* found in GB. They have proved extremely useful for identifying the expected genotype at a given location and support epidemiological investigations at national, regional and individual incident level.

5. In recent years, APHA has been developing WGS to replace genotyping. WGS involves analysis of the entire *M. bovis* DNA sequence to characterise different strains. This allows a greater degree of differentiation (‘granularity’) between *M. bovis* isolates than genotyping.

6. WGS results have been considered alongside standard genotyping information and have helped APHA to better understand how bTB infection is spreading, and sources of infection at local, regional and national level.

What's Changing?

1. APHA has rolled out the routine operational use of WGS from 19th April 2021.

2. This is a phased roll out, with Phase 1 replacing genotyping and introducing new nomenclature and home ranges, and therefore new home range maps.

3. Based on their genome sequence, *M. bovis* isolates are now assigned to WGS clades. These are defined as groups of phylogenetically related isolates based on similarities across their whole genome sequences.

4. Details of WGS clade results will be included in the Farm Level Data Reports produced by APHA for keepers of new TB breakdown herds.

5. Although the majority of genotypes are assigned to a single WGS clade, 1:1 correlation between the two systems does not occur in all cases. This is due to differences in the mutation processes that generate variation in the molecular markers that are used by each method (whole genome vs specific parts of the genome).

- A number of genotypes are split into multiple WGS clades (e.g. genotype 9:d is split into twelve distinct WGS clades). This means that isolates with genotype 9:d can in fact be quite different across their genomes. Hence, in this case the WGS clade information is more useful than the genotype information since it allows for further differentiation within this particular genotype.
- Equally, a few genotypes are assigned to the same WGS clade (e.g. some of the genotypes within spoligotype 9 and spoligotype 17, as well as spoligotype 22 are assigned to WGS clade B6-83). This means that isolates with these genotypes are in fact quite similar across their genomes and therefore more closely related than suggested by their genotype.

4. APHA is already working towards Phase 2, where phylogenetic analysis of WGS data will be refined to routinely assist epidemiological investigations by APHA.

Further Information

- You can find more information about WGS on the TB Hub website at https://tbhub.co.uk/whole-genome-sequencing-of-m-bovis-isolates-in-great-britain/