ANNEX A

TOOLS & PROCESSES

DAERA has developed and continues to develop a programme of TB intervention seeking to identify infection in cattle and then act to remove infected animals promptly (Abernethy et al., 2006). The main means of identification is the testing programme. It also has a number of existing powers enabling it to limit cattle movement for the purpose of disease control. TBSPG have reviewed the existing programme and processes and sought to add and enhance these either through expansion or addition.

On 20 January 2016, the European Commission's Food and Veterinary Office (FVO) published its Final Report on the audit conducted 1-5 June 2015 to evaluate the effectiveness and the progress of Northern Ireland's TB eradication Programme (FVO, 2015). The TBSPG (the group) has been consulted on, and has been involved in devising and/or implementing actions in response to each of the 10 recommendations. Many of these actions require enhancement of existing processes.

TBSPG is recommending a suite of measures that can be used as appropriate.

The proposed cattle measures can be grouped into five overarching key strategies:

1. **Improved Surveillance**

    1.1.   A new contract for the provision of TB Testing services

    1.2.   Routine Post Mortem Examination

2. **Improved Management of bTB Infected Herds**

    2.1.   The severe interpretation of the skin test

    2.2.   Increased usage of Interferon Gamma (IFNG) testing

    2.3.   Full and partial depopulations

    2.4.   Chronic herds

    2.5.   Requiring a herd test prior to restocking after a TB breakdown

    2.6.   Reducing the number of NVL reactor animals required for a herd to be considered OTW

    2.7.   Fattening Herds operating under alternative conditions

    2.8.   Introducing an additional 6 month test for derestricted herds

3. **Additional Control Strategies**

    3.1.   Genetic Susceptibility of bovines

4. **bTB Programme Integrity**

    4.1.   DNA tagging

    4.2.   TB Reactor – Quality Assurance Checks

5. **Additional Decision Making Support**

    5.1.   Genotyping of *Mycobacterium bovis*

    5.2.   Geographic Information System (GIS)

ANNEX A

TOOLS & PROCESSES

1.   IMPROVED SURVEILLANCE

1.1.   A new contract for the provision of TB Testing Services

1.1.1. Issue

The provision of TB testing and associated services has been considered by both the TBSPG and DAERA. DAERA has developed a new contract for provision of TB testing services which came into effect from 11 April 2016. This was taken forward ahead of the TBSPG's final report as part of normal business and delivery improvements; however, in developing the contract DAERA has liaised closely with TBSPG to ensure that current and future needs can be accommodated. Therefore while the new arrangements are focused on the current provision of testing services, DAERA is also sighted on a range of possible future changes that may be necessary to deliver relevant TBSPG recommendations. A second phase of PVP services procurement may therefore be necessary.

In the new bTB testing contract there is an emphasis on testing quality and it is expected that this will improve test sensitivity and detection rates. In addition associated TB testing services (such as insertion of DNA tags in reactors by the disclosing PVP, provision of biosecurity advice, training and involvement in bTB control on a farm) will lead to a more inclusive role for the AVS in the bTB programme.

Looking forward, there may be potential to further develop contractual arrangements with PVPs to implement some of the recommendations in the TBSPG strategy.   The services that may in future are likely to centre on the use of PVP knowledge and skills to provide support and bespoke advice to farmers. These are described further in the Detail section below.

1.1.2. Recommendation

The TBSPG has been involved in discussion and agreed that the nature of the new contract ties in with their direction of travel and it is content with the introduction of the arrangements in the new PVP contract. TBSPG recommends that DAERA ensures the optimum levels of test sensitivity are achieved through robust training, management and monitoring of all testing vets.

It is also recommended that DAERA continue to work closely with TBSPG/TBEP to **ensure that any future contractual arrangements with PVPs reflect the agreed recommendations** in this report.

1.1.3. Rationale for change

A new contract was required to bring TB testing services into a legal framework, supported by a public service contract which must be adhered to by both PVPs and DAERA; to review DAREA's position to ensure that the contract provides a value for money service following the procurement in England and Wales; and to implement the Public Accounts Committee (PAC), EU Commission Food and Veterinary Office (FVO) and the NI Assembly Agriculture and Rural Development (ARD) Committee report recommendations regarding quality of testing, communication and provision of bio-security advice, which would require contract changes. Also the additional training and provision of bio-security advice will begin to fulfill the TBSPG's objective of improved awareness and

ANNEX A

TOOLS & PROCESSES

communications. In addition, the emphasis on the quality of testing should lead to earlier detection of infection, reducing the opportunity for spread.

Looking forward, in order to implement any TBSPG recommendations on the provision of advice and support to farmers. In addition, the audit/review reports mentioned above also include recommendations relating to the involvement of PVPs in bTB control and providing biosecurity advice.

1.1.4. Evidence

The 2009 NI Audit Office (NIAO)/PAC report and annual bTB detection rate comparisons plus the 2015 FVO audits, ARD committee review, the approach to improving testing quality taken by other authorities and the new contractual arrangements in England and Wales (particularly Wales) indicated the need to upgrade contractual arrangements whilst also seeking to preserve the environment for a future, more collaborative relationship between the Department and PVPs (Anon., 2012; NIAO, 2009; VEU, 2015b).

1.1.5. Detail

Under the new contract, the farmer will continue to nominate their preferred practice to carry out their bTB testing. DAERA sets the price, based on benchmarking of fees paid in the rest of the British Isles. Practices that wish to test under the new contract had to agree to meet all contractual requirements. There is an emphasis on training, communication, involvement in the resolution of TB breakdowns, local bTB controls, and provision of advice, testing quality and contract management.

The new contract can be viewed at: https://www.daera-ni.gov.uk/publications/tb-testing-services.

Some of the elements of the new contract, intended to improve overall quality include;

(a)   All PVPs will attend one mandatory bTB Programme CPD update seminar each year

(b)   At least one Senior PVP per testing practice will meet the DVO at least once per year to discuss overall practice performance and individual PVP tester performance data;

(c)   The Practices and local DVO will be informed of audit and supervision results; any penalties that have applied in-year; performance against Key Performance Indicators (KPIs); and individual tester performance data reports. The practice is responsible for supervising each PVP once a year;

(d)   DAERA will audit at an increased level using a strengthened supervision protocol. To increase the efficiency of the process there will be penalties for failure to provide accurate itineraries.

Any additional contracts would provide the framework to implement some of the recommendations of this strategy, allowing PVPs to be more directly involved in the programme and, in particular to provide bespoke advice and support their clients.

ANNEX A

TOOLS & PROCESSES

1.1.6. Impact

The new contract should reduce TB testing unit costs (testing volumes may rise and fall in parallel to fluctuations in animal bTB levels). An associated improvement in the quality of TB testing will lead to an increase in test sensitivity and therefore in the number of reactors detected. However, in time, the earlier detection of infection will lead to reduced infection levels and therefore a reduction in compensation and testing payments.

1.1.7. Costs

It is still anticipated that this leaves the Department with a substantial budgetary deficit in relation to TB compensation in 2016-17 with early forecasts suggesting this could be in the order of £4m. Any additional PVP services will add costs, in 1-3 years time, to pay for greater PVP involvement in provision of advice and support to clients as well as involvement in farm and area based bTB control. However these activities should improve PVP knowledge and morale and should lead to improved bTB control at a local level.

1.1.8. Timeline

The new TB testing contract commenced on 11 April 2016 and a system has been developed to feed back testing performance to PVPs similar to that described by Duignan et al. (2012). It is anticipated that additional contractual arrangements could be introduced within 1 year of the TBSPG strategy being agreed, subject to DAERA identifying project resource.

1.2. Routine Post Mortem Examination

1.2.1. Issue

Every bovine animal slaughtered in Northern Ireland is subject to post mortem inspection by DAERA employed Meat Inspectors (MIs) who work in the Veterinary Public Health Programme (VPHP), under the direction of the Official Veterinarian (OV). The primary purpose of the inspection is public health but it also forms an important part of TB surveillance. In 2015 the DAERA Veterinary Epidemiology Unit (VEU) completed a report that compared the rate at which the different slaughterhouses in Northern Ireland detected suspect bTB lesioned animals at routine slaughter (VEU, 2015d). The report concluded that there was a range of LRS submission, and bTB confirmation rates, across the abattoirs and that the differences are likely to be due to factors within the slaughterhouses. The TBSPG and auditors from the FVO have considered and discussed these findings. The FVO made a recommendation in their audit report (FVO, 2015) and DAERA has taken immediate steps to implement the recommendation.

1.2.2. Recommendation

The TBSPG agrees that this important aspect of disease surveillance must be as rigorous as possible, and uniformly applied, across all Northern Ireland slaughterhouses. The group agrees with the approach being taken by DAERA and recommend that it continues to monitor surveillance outcomes.

ANNEX A

TOOLS & PROCESSES

1.2.3. <u>Rationale for change</u>

The VEU report, referred to above, highlighted an apparent variation in LRS submission and confirmation rates that are likely to be due to factors within the slaughterhouses (VEU, 2015d). The FVO report recommended that DAERA ensures that submission rates of suspected bTB lesions and detection rates of animals with tuberculosis lesions are adequate to increase the sensitivity of surveillance for bTB in cattle slaughterhouses and detect potentially infected animals (FVO, 2015).

1.2.4. <u>Evidence</u>

VEU report as detailed above (VEU, 2015d). Such variations between slaughterhouses have been observed in both Ireland (Frankena et al., 2007) and England (Shittu et al., 2013) with improvements being observed once the issue had been highlighted in Ireland (Olea-Popelka et al., 2012). The improvement in submission rates (risk) was also associated with a slight fall in confirmation rates (risk) (Olea-Popelka et al., 2012). Granuloma submission rates in Ireland averaged 25 per 10,000 cattle slaughtered (range 11-58 per 10,000; (Olea-Popelka et al., 2012) while the National Granuloma Submission Program (NGSP) in Australia suggests a background incidence of granulomata of 1 per 1,000 cattle slaughtered; the NGSP was considered a critical component of the Australian eradication plan (More et al., 2015). Within the USA, a minimum granuloma submission rate of 1 per 2,000 cattle slaughtered is the target for each slaughterhouse (USDA, 2009).

1.2.5. <u>Detail</u>

In response to the VEU report, TBSPG discussion and FVO recommendations DAERA has taken immediate steps to implement a plan to resolve the issue. This includes:

(a)   The VPHP have held meetings to consider how to maximise submissions and organized TB sampling and awareness training for MIs.

(b)   Performance monitoring and supervision forms have been revised to enhance verification procedures and records.

(c)   The deployment of inspectors on line was the subject of a Food Standards Agency (FSA) review. Furthermore the line management of inspectors formed part of a separate internal review of VPHP management and bTB surveillance will be prioritised.

(d)   VPHP management evaluate submission rates, for all abattoirs each quarter.

(e)   Feedback on the laboratory results of submitted samples is provided to each MI team every quarter.

(f)   A new management information report has been produced by DAERA's Veterinary Epidemiology Unit (VEU). It makes it easier to gather the information required to assess post mortem examination outcomes, bTB indicators and provide feedback to MI teams. Early indications, based on data extracted during the development process, are that submission rates have already increased.

(g)   The VEU conducts a statistical analysis of the submission rates.

ANNEX A

TOOLS & PROCESSES

(h)   The Food Standards Agency in Northern Ireland (FSANI) has included post mortem verification key performance indicators as part of the revised 2016-2017 Service Level Agreement between FSANI and DAERA.

(i)   A slaughterhouse minimum submission target of 1 per 1,000 animals routinely slaughtered should initially be set and regularly reviewed.

1.2.6. Impact

The impact of the implementation of these measures is expected to be an increase the number of suspect lesions reported at routine slaughter. This will increase the sensitivity of our surveillance, resulting in earlier detection of infection and therefore a reduction in spread. At farm level, it will result in an increase in the number of herds that will be restricted, additional skin testing, additional laboratory tests and additional risk testing. An estimate of the number of herds restricted pending laboratory results, is 500, from these there will be an estimated 250 new breakdowns in previously OTF herds, of which 141 will be confirmed breakdowns.

An estimate of the number, based on a 50% increase in suspect cases is 522 additional LRS each requiring histopathology and 473 requiring mycobacterial culture. Of these an estimated 287 culture positive samples will be submitted for *M. bovis* genotyping. An estimated 235 new breakdowns in previously OTF herds will be generated. Of these, 141 will be confirmed breakdowns each requiring cleansing and disinfection of the premises, generating an estimated 1006 additional herd tests, 429 additional individual animal tests including 784 individual animals, 685 additional exported animals requiring notification of competent authorities, requiring an additional 1287 Veterinary Officer hours and 1553 Administrative Officer hours. It is estimated that TB will neither be confirmed nor ruled out in a further 75 herds requiring each to complete a herd test, cleansing and disinfection of the premises, and requiring an estimated 225 hours of Veterinary Officer time and 150 hours of Administrative Officer time. There will be an estimated additional 19 herds which will have TB infection definitively ruled out, requiring no additional herd testing or bTB control measures other than issue and removal of BT25 notices, and discussions with the herd keeper (by telephone or in office). Staff time for these herds is likely to be *deminimis*. There would also be an average of 5 LCT tests per TB herd breakdown.

1.2.7. Timeline

Ongoing implementation, with subsequent regular monitoring and follow up analysis.

ANNEX A

TOOLS & PROCESSES

2. IMPROVED MANAGEMENT OF bTB INFECTED HERDS

2.1. The severe interpretation of skin test

2.1.1. Issue

The sensitivity of the skin test (ability to detect infected animals) can be increased by applying a more stringent interpretation of test results (severe interpretation).There is clear evidence that animals that are positive on severe interpretation in a TB breakdown herd but not removed are at increased risk of becoming reactors. Earlier removal would reduce the risk of further spread of infection.

2.1.2. Recommendation

DAERA's current policy is that one of the first two herd tests in an OTW breakdown must be fully interpreted on severe interpretation and there is discretionary removal of severe reactors at other tests during the course of an OTW breakdown. The group recommends that DAERA should expand their use of severe interpretation during a TB breakdown to, as a minimum, compulsory removal of all animals that are inconclusive on standard interpretation during the course of an OTW breakdown.

In the medium term, it is recommended that **further epidemiological analysis** should be carried out to assess the case to further increase the use of severe interpretation. This would involve assessing the relative risk posed by animals that are positive on severe interpretation in OTS/singleton breakdowns or in risk tests.

2.1.3. Rationale for change

Increased severe interpretation of the skin test to increase test sensitivity will facilitate the removal of more infected animals from the herd at the earliest opportunity. This would reduce the risk of further spread of infection within the herd and to other herds and wildlife. This is in line with TBSPG's strategic aim which is to identify the infection as early as possible, act and remove.

2.1.4. Evidence

There is clear evidence that animals that are positive on severe interpretation in a TB breakdown herd, but not removed, are at significantly increased risk of becoming reactors (VEU, 2015a). A VEU report (January 2015) concluded:

(a)   During a TB breakdown, animals that are positive under severe interpretation, but are left in the herd because standard interpretation was applied, are 8 times more likely to subsequently become reactors than animals that tested negative at the same herd tests.

(b)   The number of additional subsequent TB breakdowns that would have been avoided if all animals positive on severe interpretation had been removed during breakdowns in 2007/2008 was 135.

ANNEX A

TOOLS & PROCESSES

(c)   The high rate of future reactors in animals positive on severe interpretation, the high TB confirmation rate (47%) and the high relative risk compared to herd-mates demonstrates a strong case for removing these animals.

(d)   Epidemiological advice is that, during a TB breakdown, animals that are positive on severe interpretation should be removed as reactors.

(e)   The report did not differentiate between OTW and OTS/single reactor breakdowns. This is of particular relevance if a decision is made for breakdowns with 2 or more NVL reactor breakdowns to be made OTW, as it would mean that only tests in breakdown herds with a single unconfirmed reactor would be interpreted on standard interpretation.

VEU figures show that in the 12 months to the end of February 2016 there were 267 animals that were positive on severe interpretation, in restricted herd tests, and not interpreted as reactors.

There is also evidence that animals that are inconclusive (on standard interpretation) and have then had a clear retest are at higher risk of subsequently becoming reactors or having TB lesions detected at routine slaughter. Researchers in the Republic of Ireland have shown that animals with a previous inconclusive history were 8 times more likely to have a confirmed TB lesion detected at routine slaughter; that an inconclusive animal that has passed a subsequent retest is significantly (almost 4 times) more likely to be diagnosed with TB at a later date than control animals; and that previously inconclusive animals that moved out of the disclosing herd within 6 months of their retest were 12 times more likely to be bTB positive at the next test/slaughter compared to all animals in the national herd (Clegg et al., 2011a, 2011b). Therefore animals that are inconclusive on standard interpretation in an infected herd are likely to represent an increased future risk, even if they test clear at retest. VEU figures indicate that in 2015 there were 330 such animals.

2.1.5. Detail

There is a clear indication that an intensification of the use of severe interpretation is justified to control infection more effectively and the Group is aware that DAERA Veterinary Officers have been reminded of the merit of applying severe interpretation.

DAERA produces a management report, listing all animals in TB breakdowns (both OTS and OTW) that are positive on severe interpretation but not removed, is run every two weeks for each S/DVO's attention.

Current DAERA staff instructions are that one of the first two whole herd tests in an OTW breakdown must be fully interpreted or reinterpreted under severe interpretation. Severe and "super severe" interpretation can also be applied to any other test during the breakdown, and may be applied fully or partially. Decisions will depend on the individual herd.

2.1.6. Impact

Removal of animals that are positive on severe interpretation

ANNEX A

TOOLS & PROCESSES

The annual number of such animals is likely to be 200-300 in 150 to 200 herds. Removal of these animals would lengthen the period of restriction for some herds and result in additional testing.

The figures are based on data covering the 12 months to the end of August 2015 for which the actual number of animals was 245 and the number of herds was 171.

Of the 171 herds, 48 involved leaving severe positive animals in RH2 tests (de-restriction tests in OTW herds) of which approximately 40 had no other reactors, and 95 at RH1 (first short interval test in an OTW breakdown or de-restriction test in an OTS breakdown) of which approximately 75 had no other reactors.

Therefore the maximum number of herds that would have had their restrictions lengthened would have been 115. The number may be lower because all the animals were made inconclusive and would have been retested so a proportion would have become reactors anyway.

Removal of Animals that are inconclusive on standard interpretation

Based on 2015 figures, there would have been 330 additional animals removed as reactors and approximately 130 herds would have required additional testing as these would have been the only positive animals at the relevant tests.

2.1.7. Timeline

Changes to the interpretation of OTW tests could be implemented immediately following approval of the new TB Eradication Strategy and Implementation Action Plan. Further epidemiological analysis would be carried out in the medium term and should be completed within 1-2 years of the implementation of the new strategy.

2.2. Increased usage of Gamma Interferon Testing

2.2.1. Issue

Gamma Interferon testing increases the sensitivity of live animal TB surveillance but the number of samples that can be tested in Northern Ireland is currently restricted by financial and practical constraints (i.e. laboratory capacity, cost and logistics).

Separate studies by AFBI and CVERA have shown that animals that are Gamma Interferon positive are at higher risk of becoming TB skin test reactors (SCITT - Single Comparative Intradermal Tuberculin Test) in the future.

There is also substantial experimental evidence that the gamma interferon test will detect infected animals prior to detection by the SCITT, or that otherwise may not have been detected. It is therefore concluded on first principles that there is a disease control benefit however this benefit at herd level has not yet been quantified.

2.2.2. Recommendations

The Group recommends that the **use of Gamma Interferon testing is expanded** to remove as many infected animals as early as possible.

ANNEX A

TOOLS & PROCESSES

It is recommended that the use of gamma interferon testing **is significantly increased** so that a larger number of herds and more animals could be tested with this more sensitive test. Large herds and pedigree herds which are currently not eligible for testing should be included.

It is recommended that if it is determined that a Gamma Interferon test is required it should be made **compulsory for the herd-keeper to comply**. The removal of Gamma Interferon test positive animals should also be compulsory. The constraints that limit the number of samples and the selection of herds must be resolved to achieve this e.g. DAERA policy would have to be changed to allow testing of pedigree herds and laboratory capacity would have to increase.

It is recommended that the **wider use of the gamma interferon test** on the basis of local epidemiological assessment is deployed on an area basis, and that it is used to resolve high risk herds/groups or whenever depopulation is considered, provided other measures are in place to reduce the risk of the introduction of further infection.

It is also possible that a REP or DRT may recommend **additional compulsory use of Gamma Interferon testing** in a particular breakdown situation

The above application of the Gamma Interferon test would increase the likelihood that infected animals are detected within TB affected herds. The Gamma Interferon test may also be utilized to provide assurance that SCITT (skin test) TB reactors are the result of a genuine response to the test. This counter-fraud measure is discussed later (under TB reactor Quality Assurance Checks).

The implementation of these recommendations would require a phased approach as outlined below.

2.2.3. Rationale for change

The reason for change is to achieve a more widespread increase in test sensitivity at the earliest opportunity in the herds which evidence suggests would most benefit from the gamma interferon test. This would be achieved through resolution of the logistical and technical constraints that currently result in herd selection being significantly influenced by non - disease criteria which decreases the overall benefits of using the test. Resolution of these barriers should bring significant benefits and improvements to enable effective targeting for bTB eradication and improved delivery of the programme.

2.2.4. Evidence

Other countries such as the Republic of Ireland, England, Wales and Spain have been increasing their use of Gamma Interferon and reported benefits in its use in bTB infected herds. The evidence for the specific recommended changes is based on AFBI papers (Lahuerta-Marin et al., 2015, 2016), manufacturers data sheets, analysis of data by VSAHG TB section.

In addition the report of the FVO Audit of the DAERA TB Programme in June 2015 recommended that all available evidence supporting a more extensive use of Gamma Interferon testing in herds where bTB has been confirmed is fully taken into account, and that all necessary arrangements are made to facilitate that use in order to accelerate detection and elimination of infected animals from those herds (FVO, 2015).

ANNEX A

TOOLS & PROCESSES

The European Commission working document on Eradication of Bovine Tuberculosis in the EU (SANCO/10067/2013) says that parallel testing using the Gamma Interferon test increases the sensitivity of the diagnostic regime. This allows earlier removal of a considerable number of infected animals that would have given a false negative reaction to the skin test and would otherwise have remained undetected for an undetermined period potentially facilitating spread of infection. The document recognises that this slightly reduces test specificity but is likely to accelerate the eradication of infection from the herd.

Sensitivity is the proportion of infected animals that test positive, while specificity is the proportion of non-infected animals that test negative. There is an inverse relationship between them. Standard interpretation of the SCITT is described as having low sensitivity (50-60%), but very high specificity (~ 99.9%). Severe interpretation of the SCITT is described as having moderate sensitivity (66-77%), and high specificity (98.9- 99.7%) (de la Rua Domenech et al., 2006). The Gamma Interferon test, at current interpretation cut off values, is described as having high sensitivity (~ 75-80%), but moderate specificity (~ 96%) (Alvarez et al., 2012; de la Rua Domenech et al., 2006). Parallel testing using severe interpretation of the SCITT and the current Gamma Interferon test, is described as having very high sensitivity (~ 85%), but low specificity (~ 90%). The low specificity limits the use of the Gamma Interferon test in low prevalence areas/herds (Gormley et al., 2013).

2.2.5. **Detail**

In February 2016, with the agreement of TBSPG, DAERA made changes to the way that Gamma Interferon testing is used. These changes included:

(a)   Use of the ESAT6 antigen was stopped;

(b)   Test positive cut off was increased from 0.05 to 0.1 (the manufacturer's recommended cut off);

(c)   High turnover fattening herds were excluded; and,

(d)   The use of the test was changed from whole herd to only the cohorts of previous reactors or animals with confirmed lesions at slaughter.

The use of only one test well per sample with a repeat test if the reading is between 0.09 and 0.1 has also been introduced.

These changes have led to a slight increase in the number of samples that could be tested but significant logistical changes would be needed to deliver a sufficient increase to allow compulsory testing and removal to be introduced.

Implementation of actions to sufficiently increase the sampling capacity should be phased in leading to an increased sample capacity of around 50,000 samples per year. This would require changes to laboratory capacity in AFBI and the resolution of practical constraints, namely:

(a)   Allow delivery of diagnostic samples outside 8 hours of sampling (a research requirement)

(b)   Sampling after a skin test has been completed (a research requirement)

(c)   Increasing laboratory capacity and reducing cost.

ANNEX A

TOOLS & PROCESSES

Resolution of constraints a. and b. will be dependent on research projects that have been commissioned from AFBI and are due to complete in 2017. In the meantime, DAERA and AFBI should work together to increase laboratory capacity.

Resolution of these issues will enable DAERA to:

(a)   Facilitate Gamma Interferon testing of all herds regardless of size (as long as it is feasible);

(b)   Include pedigree herds in testing;

(c)   Achieve more uniform Gamma Interferon test coverage across Northern Ireland;

(d)   Compulsorily remove all Gamma Interferon test positive animals;

(e)   Gamma Interferon testing of herds days after a skin test has been completed to allow early use of the test in infected herds;

(f)   Use the Gamma Interferon test for scrutiny of testing results e.g. where there are a large number of skin test positive animals.

2.2.6. Impact

There would be an impact in terms of additional samples, additional animals removed and compensation. There is no published evidence upon which to quantify actual disease control benefits at this time.

It should be noted that any reduction in compensation will affect costings and uptake while Gamma Interferon testing remains voluntary.

2.2.7. Timeline

It is envisaged that it would be possible to make the changes needed to introduce compulsory Gamma Interferon testing and removal of Gamma Interferon positive/skin test non-positive animals within 2 years of agreement of the Strategy. Increases in the test capacity will be phased in as financial resources and laboratory facilities become available and potentially in advance of compulsory testing.

2.3.   Full and Partial Depopulations

2.3.1. Issue

Herd depopulation is a well-used tool for the control and eradication of infectious diseases in livestock. The aim of this policy is to eliminate infection in the herd by removing of all infected/high risk animals. Its application is not particularly widespread in Northern Ireland, often because of the risk of re-infection from wildlife or other sources. Removal of negative contact animals is covered in current DAERA staff instructions.

The VEU produced a paper (VEU, 2015c) ahead of the FVO Audit in June 2015.

The FVO report included a recommendation on herd depopulation and DAERA has responded in its action plan. The FVO also suggested using Gamma Interferon testing in place of herd depopulations where the benefit of depopulation is in doubt.

ANNEX A

TOOLS & PROCESSES

DAERA intends to improve its guidelines on depopulation in the TB staff instructions, informed by the VEU report.

2.3.2. Recommendation

TBSPG recommends that in addition to application of more severe levels of SCITT interpretation and use of Gamma Interferon testing, the benefits of **depopulation as a control measure should be positively considered in herds with multiple reactors**, and partial depopulation should be particularly considered in herds where those reactors represent a significant proportion of a particular group. The existing infection levels in the locality, and likelihood of recurrence should play a major part in these considerations. It is also essential to identify how resource is best utilised.

2.3.3. Rationale for change

The VEU report and the FVO have indicated that depopulation can be beneficial in certain circumstances. However, both point out deficiencies in the DAERA approach. Reviewing and enhancing the DAERA approach should lead to bTB control benefits. It also ties in with the use of severe/supersevere interpretation of the SCITT and Gamma Interferon testing.

2.3.4. Evidence

Depopulation of TB affected herds has been shown to be an effective strategy in Ireland (Good et al., 2011). The VEU paper indicated that that any depopulation policy needs to be combined with biosecurity measures to prevent reintroduction (for example, as experienced in GB following restocking after the FMD epidemic; Carrique-Maes et al., 2008). Given the rare use of depopulation, ongoing monitoring of its effectiveness, including assessment of the future bTB risk following repopulation of these herds is required. Also, depopulation is likely to be most cost effective in herds where it is possible to prevent external reintroduction and in cases where depopulation prevents spread to neighbouring OTF herds and into a previously infection-free wildlife reservoir. In addition, the success of partial depopulations relies on the correct identification of the at risk epidemiological unit so within herd transmission can be disrupted. Therefore the correct implementation of depopulation is important to the success of the policy.

2.3.5. Detail

Procedures would be strengthened. A review would be conducted, informed by the FVO and VEU reports, with a view to improving the decision making around herd and partial depopulations (FVO, 2015; VEU, 2015c).

2.3.6. Impact

This may result in more animals being removed as Negative In-Contacts but, if applied correctly, this should result in a reduction in the number of subsequent reactors and an increase in the interval to the next TB breakdown.

2.3.7. Timeline

ANNEX A

TOOLS & PROCESSES

Implementation should be within 12 months of the strategy being agreed.

2.4. Chronic Herds

2.4.1. Issue

It is recognised that certain herds have a much greater tendency to develop prolonged and recurrent TB breakdown incidents. These have become termed chronic herds. Chronic herds are an issue for farmers and DAERA because of the length of time they are restricted, the frequency of recurrence and the number of animals removed. Therefore the resultant disruption to business, costs and impact on other herds are disproportionate when compared to average breakdowns. In their Review of Bovine TB in Northern Ireland (2012) the ARD Committee made two specific recommendations on chronic herds (Anon., 2012). Details of the current position in relation to these recommendations were outlined in DAERA's report to the PAC.

The FVO, in their report of the 2015 audit, listed the ineffective policies to clear up chronically infected herds (residual infection) as one of the main factors holding back progress in the eradication of the infection (FVO, 2015).

There is no single solution; however, the implementation of many of the individual measures being considered by TBSPG should result in a significant reduction in the number and the impact of these herds.

2.4.2. Recommendation

The Group recognises chronic herds as an entity, recommends implementation of measures that will be relevant to resolving or minimising their impact and recommends that the findings of **ongoing research into chronic herds** is used to develop the approach to dealing with them.

2.4.3. Rationale for change

VEU papers investigating chronic herds have shown that during the period from 2001 to 2003, 27% of herds contributed 56% of the total number of bTB reactor animals (VEU, 2013a). During the period 2005 to 2010, almost 40% of reactors were found in chronic herds. The identification of risk factors associated with chronic bTB incidents allows for better understanding of why some herds continually fall into this chronic category and for the implementation of more effective control measures.

2.4.4. Evidence

The evidence is provided by VEU papers and the references within them. England, Wales and the Republic of Ireland have introduced or are piloting measures to reduce the number of chronic herds. In Wales an initiative to tackle persistent TB breakdowns is currently being implemented and is reported to be leading to a reduction. Investigators work from a list and investigate 4 per month. Enhanced management of persistent breakdowns includes; a VO visit if the herd has been a breakdown for more than 18 months and requires 2 tests to clear; repeat visit; internal case meeting; use additional measures; and an external meeting with PVP (paid) and farmer. They seek to work out the driver(s) for the problem and implement counter measures. The measures include biosecurity advice,

TOOLS & PROCESSES

compliance checks, testing regularity, Gamma Interferon testing, severe interpretation, test histories especially previously inconclusive reactor animals. At the time of writing, Wales had seen a 40% reduction in the number of persistent breakdowns since the start of the initiative.

In the most recent VEU study, the case definition for long duration incidents (679, over 5 years) was any confirmed bTB breakdown of greater than one year. The case definition for recurrent incidents (657, over 5 years) was confirmed bTB breakdown of less than one year followed by two or more bTB incidents within 2 years of the end of the initial bTB incident (Doyle et al., 2016).

The duration of a breakdown was associated with local TB herd prevalence, the number of associated cattle herds, the total years restricted in the previous five years, the total number of TB reactors during the incident and the presence of a bTB lesion at routine slaughter (LRS). The number of TB reactors at the disclosing test was also significant but associated with a reduced odds of a long duration incident (Doyle et al., 2016).

Recurrence was associated with high local TB herd prevalence, movement intensity into the herd, total years restricted in the previous five years, herd size, total number of TB reactors during the restricted incident and presence of a LRS (Doyle et al., 2016).

The paper points out that the present control strategies implement protocols of contiguous testing around bTB confirmed incidents. However, this approach in heavily infected localities may not be enough to prevent herds in these areas developing chronic bTB characteristics. Given that the case definitions used in the study encompass almost 40% of the total number of reactors returned in the study period, prioritising resources towards such herds could be potentially very beneficial. The implication of the negative association between number of reactors at disclosure and the odds of the incident attaining a long duration is that more severe initial interventions would lead to more favourable long term outcomes. Along similar lines, the odds of a recurrent incident were increased with total reactor numbers found during a bTB incident of less than one year. This may indicate that certain types of bTB incidents were not tested strictly enough to ensure freedom from infection.

2.4.5. Detail

The approach to dealing with chronic herds would involve using relevant measures and processes, already identified by TBSPG, in a package targeted at herds that fall within the definition of chronic herds. The definition and the approach can be adjusted to ensure the feasibility of delivery. The research projects into chronic herds should continue and findings used to develop the approach.

The solution would include a combination of existing and new measures aimed at resolution, prevention of recurrence and reducing the risk posed to other herds, including:

a. **Communication** with farmers explaining why and how investigation work is to be carried out on their herd.

b. **Detailed veterinary investigation** – to identify risks and recommend the measures to be applied. Note this may conclude that nothing can be done until the farmer changes their farming practices e.g. purchasing policy.

ANNEX A

TOOLS & PROCESSES

c.   **Involvement of PVP** – testing, advice, input to investigation, meeting/discussion with Veterinary Officer and farmer.

d.   **Provision of specific biosecurity advice**

e.   **Enforce legally required biosecurity measures** such as isolation, restricting high risk groups to specific fields and stopping moves to farm fragments.

f.   **Early robust intervention**, removal of risk animals at an early stage in a new breakdown herd.

g.   **Maximise sensitivity of surveillance in the herd** – ensure quality testing of the herd, severe and super severe interpretation, review readings of previous tests and remove suspect animals, use of Gamma Interferon testing, removal of negative in contact animals.

h.   **Consider fraud** – use DAERA tester, revisit to check reactors (re-measure and Gamma Interferon testing), and laboratory examination of skin flaps.

i.   **Dealing with infection in the locality** – wildlife intervention, area testing, area group meetings and actions e.g. agreements between farmers re grazing, training

j.   **Reduce future risk (to other herds)** – additional 6 month test,

k.   **Future policies** e.g. compensation, fragmentation, biosecurity improvement notices, wildlife intervention.

2.4.6. Impact

In the 5 years to the end of 2010, there were 679 long duration incidents and 657 recurrent incidents. These incidents involved 1,088 unique herds. During the same period, there were 7,045 new TB breakdowns. Given that the chronic TB incidents encompassed almost 40% of the total number of reactors returned in the study period, prioritising resources towards such herds could be potentially very beneficial from a financial and bTB control perspective.

2.4.7. Timeline

Not all the measures that may be implemented to strengthen how chronic herds are dealt would be available straight away. Therefore a phased approach would be necessary, starting with the tools that are available and expanding as others become available.

2.5.   Require a herd test prior to restocking after a bTB breakdown

2.5.1. Issue

DAERA currently allows keepers to move replacement stock into breakdown herds before they have re-tested any of the remaining cattle in the herd which had negative results at the test at which reactors were disclosed. This is in breach of EU legislation and was highlighted by the FVO in their June 2015 audit visit (FVO, 2015). The EU legislation requires a <u>negative</u> full herd test, before allowing movement onto a farm <u>following any</u>

ANNEX A

TOOLS & PROCESSES

disclosure episode (OTS and OTW) and further prevent restocking of herds subject to epidemiological assessment.

The implications for non-compliance must be weighed against the current uncertainties regarding the relationship with the EU following the outcome of the June 2016 referendum on exiting the European Union.

Great Britain and the Republic of Ireland have changed their TB policy to address this issue. Great Britain is still not fully compliant but the Republic of Ireland is, although it has caused issues with producers. Northern Ireland is therefore out of step with both Great Britain and the Republic of Ireland.

Full compliance is unlikely to provide benefit in terms of infection reduction, but it is suggested that there is a benefit in preventing moves into a TB breakdown herd until one full herd test has been completed, regardless of the test outcome.

2.5.2. Recommendation

TBSPG recommend that DAERA adopts a phased approach and moves immediately to prevent restocking of all TB breakdown herds until after the first herd test (and subsequent removal of any reactors). In the medium term the Group recommends preventing restocking of herds that do not test clear at the first retest (subject to epidemiological assessment). Licensed moves in exceptional circumstances would be allowed e.g. for welfare reasons.

In the longer term, the TBEP should consider whether it would be beneficial to move towards full compliance i.e. require a negative full herd test, before allowing movement onto a farm following any disclosure episode (OTS and OTW) and further prevent restocking of herds subject to epidemiological assessment, with licensed moves into breakdown herds allowed in exceptional circumstances, after epidemiological assessment.

TBSPG recognise that the Department would have to consider if legislative changes are necessary.

2.5.3. Rationale for change

While there may only be relatively small benefits in moving towards full compliance with current EU legislation, there is the potential for any non-compliance to impact either through infraction proceeding or as a barrier to trade. On this basis, TBSPG recommend moving towards compliance with EU legislation. The outcomes of the EU Referendum on 23 June 2016 would have to be taken into consideration.

2.5.4. Evidence

Epidemiological evidence presented by DAERA's VEU, plus the EU Commission and FVO officials' comments.

Evidence of the impact is provided in a CVERA study (Clegg et al., 2013) which found that only a small proportion of subsequent TB breakdowns (1.8%), or extended TB breakdowns (2.7%), could be directly attributed to the animals moved in (i.e. only the introduced animals became reactors). It also found that the timing of introduction of animals is important regardless of the result of the first herd test. Only herds into which animals were

ANNEX A

TOOLS & PROCESSES

introduced <u>before</u> the first test had an increased risk of subsequent breakdown (the risk was 1.5 times higher). Herds into which animals were introduced <u>after</u> the first retest, even if the test was not clear, had no greater risk of a subsequent breakdown compared with herds that did not introduce any animals.

This study has two significant implications. First it shows that a move towards full compliance may have some bTB control benefits, i.e. prevention of restocking until a test, even with no regard to result, would bring benefits. Equally, however, it also clearly indicates that "full" movement control provides a relatively small benefit in terms of infection, particularly in regard to the outcome of the herd test.

DAERA data indicates that the proportion of animals that were moved into breakdown herds in 2014 and became reactors during the course of the breakdown was 0.31% (135/43,120). The animal incidence for all cattle in Northern Ireland in 2014 was 0.55%.

England and Wales amended their cattle movement controls so that one test (not necessarily a clear test) and a veterinary risk assessment are required before they allow restocking.

In England where the OTF status has been suspended or withdrawn as a result of a reactor in any type of test, licences authorising cattle movements on to a holding must not be considered until: the first short interval test (SI) following suspension or withdrawal of the OTF status has been completed (a check test (CT) does not qualify as the first post breakdown test in reactor-triggered breakdowns); all reactors from that test have been removed; and a veterinary risk assessment has been carried out. The risk assessment is carried out in accordance with TR55 "Guidance notes for Veterinary Risk Assessment".

In England, where OTF status has been suspended as a result of an LRS: movements on can be considered after a clear CT (whole herd); if reactors are disclosed at the CT then no moves on must be considered until after the first SI; if a positive culture result is received for the LRS case then no further moves on must be allowed until after the first SI.

Exceptions may be considered for movements to be authorised by a specific licence for: replacement of suckler calves on welfare grounds; and purchased bulls in exceptional circumstances only and where Artificial Insemination (AI) cannot be used as an interim measure.

The intention of these measures is to limit the group of cattle which may potentially become infected, if a substantial reservoir of undisclosed cattle infection remains on the premises.

In Wales, after the first short interval test following a breakdown and the subsequent removal of any reactors, a veterinary risk assessment (in accordance with TR55) will be carried out. Depending on the outcome, movements under licence into the restricted herd may be considered. The first short interval test does not need to be clear before any moves take place. Exceptions may be considered and movements authorised by a specific licence for replacement suckler calves on welfare grounds and purchased bulls in exceptional circumstances only and where AI cannot be used as an interim measure.

In the event of subsequent reactors being identified, the ban on inward movement is re-imposed pending removal and slaughter outcome of the reactors. It may be lifted then based on veterinary risk assessment.

ANNEX A

TOOLS & PROCESSES

In early 2014, the Republic of Ireland enforced the rule that there had to be at least one clear herd test after a breakdown before any animals can be moved into that herd. The moved in animals do not get compensation if deemed a reactor during the restricted period, i.e. they remain ineligible so long as the herd remains restricted. However, there are a number of exceptions to the one clear test rule as follows: newly established herds; introduction of a replacement stock bull(s) which requires a 30 day pre-movement test; emergency replacement suckler calf; movement into a TB free herd restricted pending a test because it is contiguous to infected fragments of a high risk bTB breakdown; or movement home to a restricted herd of a farmer's own test negative animals from a "B&B" or a rearing/grazing/feeding herd, to alleviate or prevent a welfare problem, which requires a 30 day pre-movement test. DAFM re-apply the restriction on inward moves following each reactor incident during a breakdown.

2.5.5. Detail

DAERA does not prohibit movement into a breakdown herd until it has had a clear test.

The 2015 FVO audit (FVO, 2015) commented in paragraph 54 of their report that: "the audit team could verify that no restriction policy is in place in the majority of cases to avoid introduction of cattle to restricted herds before they regain their OTF status, and this happens often at the convenience of herd keepers." Also, recommendation 5 of their draft report states, "To ensure that movements of susceptible animals into cattle herds where the presence of TB has been confirmed are prohibited with the exception of those that are authorised by the CAs on the basis of obvious animal welfare reasons."

2.5.6. Powers

DAERA has powers under Article 6(2) of the Tuberculosis Control Order (NI) 1999 to serve a notice prohibiting the movement of animals into a herd or onto a holding if a veterinary inspector knows or suspects that there is a *serious risk* of the spread of infection. DAERA also has the power under the same article to licence the movement of cattle into a herd to which a notice has been served and apply conditions to such movements.

It may be necessary to seek new powers to require herd keepers to comply by way of notice.

2.5.7. Impact

Immediate and full compliance with EU controls (ie stopping all moves into a TB breakdown herd until after a clear herd test), would have a disproportionate impact on dairy herds (reduced cash flow) and on beef finishing herds (cessation of business continuity) for little bTB benefit. Therefore the interim transition stage of no movements in until at least one full herd test after the breakdown (whether clear or not) and removal of reactors is preferred. A fresh assessment can be made after implementation and before decisions are taken to tighten procedures still further.

Based on 2014 data, there are between 1,800 and 2,000 herds that would be prevented from moving animals in until they had completed a herd test. Normally just over 50% of breakdown herds move animals in during the course of the breakdown. During 2014, this

ANNEX A

TOOLS & PROCESSES

was 900 herds involving 43,000 cattle. Approximately 510 herds purchased animals before the first test. Approximately 50% (850) herds had a clear first test and 22% (362) did not have a clear first test but had a clear second test.

2.5.8. <u>Timeline</u>

It is anticipated that the short and medium term recommendations could be introduced within 1-2 years of the strategy being agreed, subject to satisfactory IT changes, communication to staff and stakeholders and there being no need for legislative changes.

2.6. Reduce the number of NVL reactor animals required for a herd to be considered OTW

2.6.1. <u>Issue</u>

Currently a herd's Officially Tuberculosis Free (OTF) Status is withdrawn (OTW) where:

(a) TB is confirmed at post-mortem examination (PME) and/or by histopathology and/or culture in one or more animals;

(b) 6 or more non visible lesion (NVL) reactor animals (or unconfirmed suspect lesions at routine slaughter) are disclosed during the course of a breakdown;

(c) an animal shows clinical signs of bTB; or

(d) a veterinary risk assessment considers it epidemiologically prudent.

OTW status remains on a herd until <u>two</u> consecutive clear herd skin tests at least 60 days apart have been completed in accordance with Council Directive 64/432/EEC and cleansing and disinfection procedures are completed. OTW breakdowns also trigger further infection controls such as tracing and lateral risk testing. According to Annex A (3B) of Council Directive 64/432/EEC, tracing and checking is to be undertaken by the competent authority of any herd considered to be epidemiologically related to an OTW herd.

Where 5 or less NVL reactor animals (or unconfirmed suspect lesions at routine slaughter) are identified, the OTF status of the herd is suspended (OTS) - rather than withdrawn (OTW) - and the herd may be derestricted following <u>one</u> clear herd skin test completed at least 60 days post disclosure, and once cleansing and disinfection procedures are completed. Therefore disease control is much more rigorous and continues for a longer period in OTW breakdowns.

Epidemiological studies and the approach taken in other jurisdictions suggest that there would be a bTB control benefit from reducing the number of NVL reactors required before a herd is made OTW, triggering the additional bTB control measures described above.

The attached appendix 2 is an abstract from a TBSPG briefing paper on NVL reactors.

ANNEX A

TOOLS & PROCESSES

2.6.2. Recommendation

The group recommends that:

Herds with **two or more NVL reactors should be classified as OTW** and require two consecutive clear herd skin tests at least 60 days apart to regain OTF status; and that tracing and checking of epidemiologically related herds is carried out.

Further VEU analysis should be done with a view to **extending OTW classification to herds with one reactor based on epidemiological risk** assessment, where a favourable risk assessment would be required to be upgraded to OTS status.

2.6.3. Rationale for change

The specificity, at anim**al level, of the Single Comparative Intradermal Tuberculin test (SCITT) is** 99.98%, therefore 1 in 5,000 TB free animals tested is a false positive (Goodchild et al., 2015). However, where there is **more than one skin test positive** animal at a test, this increases the specificity at herd level further. The abattoir examination and subsequent dependent laboratory tests are comparatively insensitive (Corner, 1994; de Kantor *et al.*, 1987). Some infected animals will therefore have a positive skin test but remain negative at the "confirmatory" tests. However, the higher the number of NVL reactors that are disclosed, the greater is the confidence of infection being present.

2.6.4. Evidence

The epidemiological evidence presented by DAERA's VEU has indicated that the risk of future breakdown increases directly with the number of TB reactors during the breakdown and the size of the TB breakdown herd (VEU, 2013b). In contrast, confirmation of infection in reactor cattle, which is highly correlated to the presence of visible lesions at post mortem and to the number of reactors, was not predictive of the risk of future TB herd breakdown. This is a factor which is not addressed in the current policy for NVL reactors (unless there are more than five).

Several pieces of other research about the recurrence of infection in a herd have indicated that the number of NVLs is a highly important factor to consider (Doyle *et al.*, 2014; Karolemeas *et al.*, 2011; Olea-Popelka *et al.*, 2004; Wolfe *et al.*, 2010). There is a significant risk of falsely assuming that if infection is not confirmed by PME and/or laboratory tests the animal is not infected. Research has also indicated that the risk of future TB breakdown increases directly with the number of reactors during the breakdown. Indeed, even with compliance to the current legislative requirements for OTW herds, the bTB risk persists in many infected herds after de-restriction irrespective of of breakdown severity (Clegg et al., 2015; see proposed measure 14 for more detail).

The FVO Audit report (FVO, 2015) notes that "OTW status is always applied when more than five reactors to the SCITT are detected and in exceptional situations when – as a result of the epidemiological investigation of a breakdown – the risk is considered very high. If no *M. bovis* and/or lesion has been found yet and five or fewer reactors to the SCITT have been detected, the herd is classified as OTS, i.e. there is only a suspicion of the infection being present, without confirmation."

ANNEX A

TOOLS & PROCESSES

Although the FVO did not make any specific recommendation about the number of NVLs appropriate to OTW status the subject was touched upon in oral presentations and the FVO do expect to see appropriate tightening of our eradication programme. Not making NVL breakdowns OTW has been raised by EU Commission officials when submitting the annual UK TB eradication plans. The bovine tuberculosis subgroup of the Task Force on monitoring animal bTB eradication recommended to the UK in 2012 that either all breakdown herds be regarded as OTW, or that additional epidemiological information is used as a basis for the classification. They acknowledged that this was already applied to some extent, but recommended that it be extended further.

In the Republic of Ireland, OTW status is applied where 2 or more reactors are disclosed at a skin test or where a single reactor is identified in a high risk herd. This "singleton" policy considers not only the skin reaction of the animal but also other epidemiological information, e.g. the herd must not have been OTW in the 3 years prior to current disclosure and none of the contiguous herds must be concurrently confirmed breakdowns.

In Wales, OTFW (OTW) may be applied on epidemiological grounds where infection has not been confirmed. Such criteria include, if a breakdown herd is contiguous to an ongoing OTFW breakdown, has had its OTF status withdrawn in the preceding three years, or a Veterinary Officer identifies another valid reason. The Welsh Government has been applying OTFW status to all new TB breakdowns as a default position from 31 December 2015. OTFS (OTS) status is only applied following Veterinary Risk Assessment based on epidemiological evidence to suggest it is warranted.

From 6 April 2016, all breakdown herds in the High Risk Area of England require two consecutive skin herd tests with negative results at "severe" interpretation before regaining OTF status, regardless of post mortem and laboratory outcome. The disclosure test in these herds will also be reinterpreted at "severe" level of interpretation. This has been the policy in the TB Edge area of England since 2013.

Additionally from 6 April 2016, breakdown herds in the Low Risk Area of England which are contiguous to a herd with confirmed TB, or that had a previous breakdown in the last 4 years, or that were on annual testing because of their business pattern, will require two consecutive skin herd tests with negative results at "severe" interpretation before regaining OTF status, regardless of post mortem and laboratory outcome.

This approach could lead to a better focus on potential infection and to a potential decrease in further repeat breakdowns, eventually reducing costs to the bTB Programme through reduced compensation payments and testing. It would also bring Northern Ireland more into line with the Republic of Ireland and Great Britain.

It is therefore considered, based on the findings of the VEU study and in line with previously conducted research, that the number of NVL reactor animals required for a herd to be considered OTW, and therefore subjected to the same control measures as 'confirmed' TB breakdowns, should be reduced to two. The recommended policy based on the epidemiological evidence in this paper strongly agrees with the view of EU Commission officials and the evidence in previous studies conducted on this subject in both the north and south of Ireland and in Britain.

ANNEX A

TOOLS & PROCESSES

2.6.5. <u>Detail</u>

Herds with 2 or more NVL reactors during the course of a breakdown would automatically become OTW, thereby triggering additional bTB control measures.

Additional DAERA staff resource would be required in each year to deal with added workload arising from these breakdowns (not including identification of reactors from consequential breakdowns).

2.6.6. <u>Impact</u>

The bullet points below summarise the impact of the implementation of this proposal, based on figures from 2012.

- Approximately 100 additional OTW breakdowns

- 714 additional herd tests

- 304 additional individual animal tracing tests (involving approximately 556 animals).

- 25 additional reactors identified in the extra OTW breakdowns

- Tuberculin required for 55,902 additional animals to be tested

- APHIS changes

- Additional Field VO resource

- Additional administrative support

- 486 additional export notifications

2.6.7. <u>Timeline</u>

Implement within 12 months of the TBSPG strategy being agreed, subject to satisfactory IT changes.

2.7.   Allow limited moves from bTB breakdown herds in certain conditions

2.7.1. <u>Issue</u>

TBSPG recognise the overstocking and cash-flow difficulties which result when a herd is under TB restriction for an extended period. We have explored possible solutions which balance the needs of the breakdown herd without risking further spread of TB to neighbouring herds or to clean areas. Controlling this risk if cattle are to be grazed is very difficult.

2.7.2. <u>Recommendation</u>

TBSPG recommend that DAERA consider permitting limited moves from TB breakdown herds to approved rearing/finishing herds which are 100% housed and meet strict biosecurity conditions.

ANNEX A

TOOLS & PROCESSES

2.7.3. Impact

Such an approach would alleviate some of the difficulties associated with bTB herd restrictions. Strict biosecurity protocols would be required to prevent bTB spread from the rearing/finishing herd. Evaluation of this proposal after implementation would be required to provide assurance that such herds do pose an increased risk of local bTB persistence in the locality.

2.8. Introduce an Additional 6 Month Test for Derestricted Herds

2.8.1. Issue

Evidence suggests that herds with a recent history of infection are more likely to fail subsequent TB tests compared to herds with no history of infection, i.e. a recent history of infection is a significant risk factor. The most likely reasons for this are:

(a)   undisclosed infection remaining in the herd at the end of a breakdown

(b)   continuation of environmental risk factors

(c)   ongoing purchasing risk

Currently a Check Herd Test (CHT) is scheduled for all herds that have been cleared following a bTB episode. The CHT is usually scheduled for 6 months after OTF status has been restored. After the CHT has been completed, assuming it is clear and there are no remaining herd level risk factors, the next Annual Herd Test is scheduled for 12 months time.

2.8.2. Recommendation

The group recommends requiring a herd test 6 months after the CHT (check herd test carried out six months after de-restriction) following higher risk TB breakdowns, and define a higher risk TB breakdown as one with 2 or more skin test positive animals. This proposal brings forward the next test by 6 months for a subset of herds which are currently on an annual testing cycle but have been shown to have a significantly elevated risk of breakdown.

2.8.3. Rationale for Change

There is no legislative requirement to complete post de-restriction testing however, most Competent Authorities implement some level of additional testing after a herd becomes OTF to give greater assurance that there is no residual infection in the herd before it returns to the routine testing frequency.

In Northern Ireland, when confirmed (OTW) and unconfirmed (OTS) TB breakdown herds have satisfied the conditions required to regain OTF status, the herd is de-restricted and allocated a Check Herd Test (CHT)* with a due date of 5 to 7 months from the last herd test. Animals can be moved out of the herd unless this test becomes overdue. The next herd test in an Annual Herd Test (AHT)* and is scheduled for 12 months after a clear CHT test.

These tests are completed unless a higher risk test is required in the interim.

ANNEX A

TOOLS & PROCESSES

In annual testing areas of Great Britain (Wales and the Higher Risk Area in England), former OTS and OTW status herds must have a herd test 6 months after restoration of OTF status. If this test is negative the herd returns to annual testing. Animals moving out of any herd in an annual testing area must be pre-movement tested at the herd keeper's expense. (This includes during the period from restoration of OTF status until the herd returns to annual testing.)

In the Republic of Ireland, testing of herds after de-restriction is dependent on the severity of the breakdown:

• Herds with two or more reactors must complete two 6-monthly tests after de-restriction before returning to routine (annual) testing.

• Herds with a single TB confirmed reactor return to routine (annual) testing following a single 6-month test.

• Herds with a single unconfirmed reactor and no other risk factor return to routine testing immediately after de-restriction.

• In addition, after de-restriction a herd is given a 3 month window to move animals before herd movement restriction is re-applied for the ~3 months before the first 6 month test.

2.8.4. Options

To address the increased risk in recently de-restricted herds, 2 options have been considered:

• Option A: require a herd test 6 months after the CHT following all breakdowns.

• Option B: require a herd test 6 months after the CHT following higher risk breakdowns

Both options would identify infection in the de-restricted herd more quickly through more frequent testing of high risk herds over a longer period than at present. This is expected to reduce bTB spread in the longer term.

2.8.5. Evidence

There is ample evidence of continuing bTB infection risk in herds and animals for an extended period after herds are allowed to start trading again after a breakdown (Karolemeas et al., 2011; Dawson et al., 2014; Doyle et al., 2014; More and Good, 2015; More et al., 2015). In high risk bTB breakdowns this risk has been shown to extend for many years afterwards (Clegg et al., 2015). In the Australian situation, this risk was considered to extend to the life of the animal and it took a minimum of eight years to attain lowest risk status (More et al., 2015).   This measure does provide an additional point at which the infection status of these herds, which are known to be at increased risk of disclosing bTB infection, can be assessed. However, this will not protect other herds from the increased risk of purchasing infection from such herds after they are derestricted.

In Northern Ireland during 2014, 7.4% of CHTs had one or more positive animals, compared to 2.3% of AHTs. This demonstrates that herds with a recent history of infection

are more likely to fail subsequent TB tests compared to herds with no history of infection. DAERA VEU has considered the blanket approach (Option A) and concluded this would make little difference to bTB control (VEU, 2013c). It is the VEU view that a targeted implementation (Option B) is likely to be more effective. VEU have demonstrated that the risk of a future breakdown increases with an increasing number of reactors during the previous breakdown irrespective of confirmation status (VEU, 2013b). The breakdown rate at AHTs in 2014 where the previous test was an AHT was 2.0% (232 positive herds out of 11,351 herds tested). The breakdown rate at AHTs where the previous test was a CHT following 2 or more skin test positive animals in the previous 2 years was 8.7% (32 positive herds out of 369 herds tested).

(In this analysis the number of skin test positive animals in the 2 years prior to the CHT has been used as a proxy for the number of skin test positive animals in the TB breakdown period which resulted in the CHT. Associated herds have been counted separately.)

2.8.6. Impact

Based on 2014 figures, approximately 369 herd tests (plus any associated herd tests) would be brought forward by 6 months. However, infection undetected in the herd before de-restriction, or caused by environmental or business model risk factors would be identified more quickly, thereby reducing risk of intra-herd and inter-herd spread after de-restriction.

2.8.7. Timeline

It is estimated that this could be implemented within 12 months of agreement on the Strategy.

Other areas to be considered

The TBSPG expects that its recommendations would be strengthened and adapted as the implemention of the strategy unfolds to ensure the ongoing success of the programme. This would be dependent on the objective science based evaluation of the effectiveness of the measures that should be put in place and the use of the information to inform the policy decisions that would be required adapt the disease control strategies to the epidemiological situation.

Some additional measures were considered but not decided upon ahead of the launch of the strategy. These, and others, should be considered as part of the process outlined above, for example

- Pre movement testing - The TBSPG considered the merits of introducing some form of pre-movement testing and various risk based pre-movement options have been evaluated (VEU, 2015a, b). However, the only option where obvious benefit could be ascertained was very narrow and only impacted upon a very limited number of cattle movements i.e. in chronic bTB herd breakdowns (VEU, 2015b). It was therefore considered more effective to utilise resources on wider measures that enhanced detection of infection and reduced the risk of residual infection within infected herds, thereby reducing the risk of purchased infection once such herds start trading again. These measures include use of gamma interferon testing, application of severe interpretation, increased testing regimen before and after derestriction and wildlife

ANNEX A

TOOLS & PROCESSES

controls. Uptake of an informed purchasing approach by herd keepers may also help negate the risk from purchased infection (see Annex C; also Adkin et al. 2016a, b). The TBSPG does not, however, rule out the use of pre movement testing in the future and recommends that it is kept under review.

• Delaying herd tests in TB breakdowns until 60 days following removal of reactors rather than 60 days following the date of the last test

• Mitigating risk of previously skin test inconclusive cattle by restricting their movement off farm

• Contiguous testing around breakdowns assessed as having been caused by persistence of *M. bovis* in the locality – carryover/ contiguous spread/ wildlife.

It is recommended that DAERA continue to monitor and assess emerging technologies which may improve or even replace existing tools e.g. alternative tests.

ANNEX A

TOOLS & PROCESSES

3. ADDITIONAL CONTROL STRATEGIES

3.1. Genetic Susceptibility of bovines

3.1.1. Issue

The TB skin test (SCITT) measures an immune response, but there will be natural variation in how individual animals respond to exposure, including varying levels of exposure. The SCITT has high specificity, so it is highly likely a skin test positive is indeed infected, even if current post-mortem tests do not confirm it. However, not all exposed animals would be expected to respond to the skin test regardless of their genetic susceptibility. The resistance of some would mean that they may clear the pathogen without triggering an adaptive skin test response. The least susceptible (most resistant) animals are significantly less likely to be TB reactors on average. The bovine TB risk is ~20% genetic and the remainder is "environmental" risk factors (including force of infection, nutrition, concurrent infection, husbandry, animal behaviour etc). There is currently effectively a sire relative risk score available for certain sires within the Holstein breed. It is currently assumed that TB genetic resistance is not absolute i.e. it is not true to say that herd-keepers using lower TB risk sires will never have TB. Herd-keepers have accepted this risk previously when using genetic selection to improve udder health based on the somatic cell count phenotype. Additionally, selection for a high TB resistance score does not appear to be well correlated to economically important production traits (Bermingham et al., 2010) and tools are available for simultaneous selection of traits (Berry et al., 2011). The current sire relative risk score, and further developments, should make progeny relatively more resistant to the average exposure that they receive in the field, or relatively more resistant for longer, both of which would be acceptable progress. It is expected this work should lead to disclosure of cumulatively fewer TB reactors within-herd i.e. lower numbers of affected progeny on average.

3.1.2. Recommendation

The TBSPG recommends that the farming industry encourage the use of the "TB Advantage" index, and that TBEP monitor further developments in this important research area.

ANNEX A

TOOLS & PROCESSES

4.   bTB PROGRAMME INTEGRITY

4.1.   DNA Tagging

4.1.1. Issue

DNA tags are applied to TB reactor animals by DAERA staff either at disclosure or at valuation. The vast majority of TB reactors are tagged to assure continuity of reactor identity and therefore reduce errors and fraudulent activity and thus strengthen controls to reduce spread of infection. When a tag is applied, a small tissue sample is captured in a capsule. This is held by DAERA and is available for comparison when the animal is slaughtered. DAERA could therefore check that the animal valued, is the animal that is slaughtered. Currently animals made TB reactors by PVPs are not tagged until valuation but ideally all reactors should be DNA sampled at the time they are first identified to minimise the opportunity for fraudulent substitution of reactors for financial gain.

The reason that PVPs have not been required to apply the tags to date is that there was no contractual framework within which to make this happen. This aspect has been resolved by the new contractual arrangement for the delivery of bTB testing services that DAERA introduced on 11 April 2016. However, before implementation can proceed legislation will first have to be changed to give Approved Veterinary Surgeons (AVS) / PVPs powers to apply DNA tags.

4.1.2. Recommendation

The use of DNA tagging is an important tool in ensuring that TB reactor identification, valuation and removal is well correlated. There is a gap in the process and this should be resolved to ensure that all animals with positive readings at test read off have a DNA tag applied. To achieve this objective, it is recommended that **AVS should apply DNA tags** to any animals that they detect with TB reactor readings at the level of interpretation specified for the test.

4.1.3. Rationale for change

To assure continuity of reactor identity and therefore reduce errors and fraudulent activity and thus strengthen controls to reduce spread of infection.

4.1.4. Evidence

DNA tags are applied to more than 97% of reactor animals and the main reason that a small number of animals are not DNA tagged is because of health and safety issues. Stakeholders have advised that there is a need to have animals DNA tagged at test read off. A post-implementation review carried out following the introduction of the DNA tagging of TB reactors in England, has found that such tagging is proving to be a strong deterrent to cattle identity switching, and is also helping to reduce the number of herds under long-term restrictions. The results show that prior to DNA tagging, in herds where suspicious patterns were noted, 13% of the total number of reactors identified had double replacement ear tags ordered after the TB test reading.

Following the introduction of DNA ear tagging, this dropped to 1%. In herds where more systematic patterns were noticed, the percentage of TB reactor identities that had double

ANNEX A

TOOLS & PROCESSES

replacement ear tags ordered after the reading of the TB skin test fell from 22% to 1.5%. This represents a significant change in behaviour.

Any steps to reduce errors, fraudulent or otherwise, should be supported and experiences should be shared across jurisdictions.

4.1.5. Detail

Legislative change would be required. DAERA's new contractual arrangements for provision of testing services include provision for the application of DNA tags. It would be necessary to set up systems, purchase equipment and train PVPs in parallel with changing the legislation.

4.1.6. Impact

Whilst this change may not have a significant impact on overall infection levels, it would be a deterrent for anyone considering retaining a TB reactor animal reducing the possibility of identity errors occurring and contributing to controlling spread of infection.

In 2013/14, PVPs would have tagged 5598 reactors in 1570 herds.   There would be an initial outlay for DAERA for taggers, submission forms and additional tags.

In addition, there will be a requirement to train AVS in this procedure and an associated cost with this.

4.1.7. Timeline

TBSPG recommend that this is implemented as soon as possible following the necessary legislative amendment.

4.2.   TB Reactor – Quality Assurance Checks

4.2.1. Issue

The TBSPG has heard evidence that there are occasions when there are cattle presented for valuation and slaughter which have not given positive skin readings as a natural response to the injection of tuberculin commonly referred to as "Volunteered Reactors". The extent to which this occurs is not known but anecdotally it would appear to TBSPG that the occurrence is frequent enough to warrant a recommendation which will quantify the extent of the problem and mitigate against it happening.   This is fraud; it tarnishes the majority of the farming community, impacts on programme costs, skews reported infection levels and negatively affects bTB control.

4.2.2. Recommendation

It is recommended that action is taken to design and implement a preliminary field trial of counter measures to:

• Develop our knowledge of re-examining TB reactor lumps;

• Develop our understanding of post skin test Gamma Interferon testing, in particular correlation with skin test results;

ANNEX A

TOOLS & PROCESSES

- Develop field procedures

- Enable a policy decision on the best overall approach to take regarding volunteered reactors, which should incorporate studies to further evaluate this measure.

4.2.3. Rationale for change

Volunteered reactors are animals that are presented as reactors for valuation and slaughter which have not given positive skin readings as a natural response to the injection of tuberculin. They are due to physical interference with the test, or substitution of cattle for the real reactors, or false reporting of test responses. The main trigger for local suspicion is a significant number (5+) of reactors with no visible lesions at slaughter, especially repeated episodes. Such fraud may be organised or opportunistic and sustained or intermittent. It is important to understand the extent to which this occurs and to introduce counter measures to minimise the extent of this potentially costly practice.

4.2.4. Evidence

The number of animals for which compensation is paid as a result of this fraudulent activity is not known. In the Republic of Ireland, introduction of measures to tackle the problem have been unofficially reported as a success. The Republic of Ireland have informally estimated a reduction of 10-15% (verbal communication) in reactor numbers as a result of their Quality Assurance (QA) approach however a figure for potential benefit has not been established yet for Northern Ireland.

4.2.5. Detail

Important measures that would reduce the number of volunteered reactors have been considered by TBSPG and by DAERA and these include DNA tagging, compensation changes and assessment of testing data. In terms of specific action to identify potential cases, a field trial is necessary to:

(a) Develop our knowledge of re examining TB reactor lumps;

(b) Develop our understanding of post skin test Gamma Interferon testing, in particular correlation with skin test results;

(c) Enable a policy decision on the best overall approach to take with volunteered reactors.

The field trial should proceed within a year of the report's recommendations being agreed, delivered on a scale that would be determined by the available resource, and subject to a positive business case.

4.2.6. Impact

The purpose of the trial is to quantify the potential impact of the implementation of this measure. As well as providing important information and scientific evidence the trial itself may cause a reduction in volunteered reactors.

ANNEX A

TOOLS & PROCESSES

4.2.7. <u>Timeline</u>

The field trial should proceed within a year of the report's recommendations being agreed. The outcome and review of the field trial will enable DAERA in consultation with TBEP to consider full roll out across the country in the following 12-18 months. Timescale will be influenced by DAERA resources.

ANNEX A

TOOLS & PROCESSES

5.   ADDITIONAL DECISION MAKING SUPPORT

5.1.   Genotyping of *Mycobacterium bovis*

5.1.1. <u>Issue</u>

DAERA/AFBI has a unique set of molecular strain typing data gathered over several years (herd level data from 2003 to present, animal-level data from 2010 to present).

Variable Number Tandem Reports (VNTR) data have arguably been under utilised within the programme and the absence of comprehensive analyses means that there is not a full awareness of the contribution that strain typing makes/could make to the understanding of TB, disease controls and policy development. AFBI is a recognised world leader in the development and application of this technology.

Currently all cattle and badger *M. bovis* positive cultures are genotyped and the results made available to DAERA veterinary officers each month via the DAERA intranet. Informally information is provided interactively on a case by case basis at the discretion of the DAERA officer.

Molecular typing is an established yet evolving technology with the potential to provide ever more resolved epidemiological information to develop our understanding about infection maintenance and spread and with which to monitor aspects of the Northern Ireland TB Programme.

Whole Genome Sequencing (WGS) is seen as an important new technology, which has multiple applications; the most immediate of which is integration of bacterial whole-genome sequencing and epidemiology to track pathogen transmission. (See the appendix 1 which provides further detail on the scientific background and use of VNTR and GWS).

The direction of travel is towards integrating WGS with classical epidemiological data and modelling, which has the potential to significantly improve our understanding of bTB maintenance and spread. This should provide the highest possible resolution of the transmission dynamics in this cattle-cattle and cattle-badger system. VNTR typing should still be used in a cost-effective manner to target micro-epidemics for detailed sequencing analyses.

5.1.2. <u>Recommendation</u>

The group recognises the value of VNTR typing and recommends that **DAERA continues to VNTR type all culture positive cattle and badgers** and works to expand its use of the information, especially relating to practical application on an area basis through the auspices of the Geographic Information System (GIS) which is currently under development (that is, genotype data for cattle and wildlife superimposed on maps of breakdown herds and their surrounding area). Expertise in this area must be maintained and developed in line with technological advances.

5.1.3. <u>Rationale for change</u>

Develop a better epidemiological understanding of the infection at all levels and potentially adapt local measures accordingly. The development of a GIS system would allow

visualisation of all data and assist in the investigation of localised infection outbreaks (see under 12).

Maintaining and developing the use of VNTR would facilitate meeting a number of 2015 FVO Audit recommendations, particularly those relating to epidemiological investigations and use of epidemiological data.

It also fits with the Group's direction of travel regarding regional and local groups, sharing of information and concentration on infection clusters.

5.1.4. Evidence

There is widespread official support for strain typing, including from:

(a) **Food and Veterinary Office (FVO) auditors**, as per extracts from the 2014 FVO United Kingdom and Republic of Ireland Audit reports as well as the FVO Audit report from 2015 (FVO, 2014a, 2014b, 2015).

(b) UK - Contribution of molecular epidemiology to the control of bTB

(c) There is an extensive use of genotyping after bTB confirmation to better understand the geographical dynamics of the infection and contribute to ascertain the probable cause of infection. Spatial and temporal mapping of the range of spread of *M. bovis* genotypes provides a very valuable insight into the transmission patterns of the infection and significantly contributes to shape up prevention and control policies in the various bTB management areas in England and Wales. This has contributed to confirm and explain the geographical clustering of most genotypes, and the home-range maps drawn for each of them provide very relevant information to Animal and Plant Health Agency (APHA) staff about the importance of local routes of transmission and their local persistence (e.g. Brunton et al., 2015).

(d) **Republic of Ireland - Use of bacteriological culture and molecular typing**:

(e) The Task Force recommended greater use of bacteriological culture and molecular sub-typing diagnostic tools to substantiate the conclusions of the epidemiological investigations on the causes of the bTB infection detected, in particular when the involvement of wildlife is assumed to be the main source of infection in the geographical area under study (FVO, 2014b).

(f) Molecular epidemiology is also recommended in a **Task Force Working Document on Eradication of Bovine Tuberculosis in the EU**, *"Epidemiological analyses of available data may indicate different levels of risk in e.g. different herd types or other risk factors that need to be addressed. Expertise on epidemiology is needed at Member State level to identify and provide the most appropriate indicators and analyses for each epidemiological situation. Molecular epidemiology is also needed, in particular towards the final stages of eradication, in order to better determine the sources of infection and routes of spread"* (SANCO, 2013).

(g) **The Agriculture and Rural Development Committee** asked questions about the use of strain typing on a number of occasions and supported its use. The following recommendation was included in its 2012 review of bTB in Northern Ireland, *"The Committee recommends therefore that [the Department] bring to it as soon as*

TOOLS & PROCESSES

> *possible proposals that explore how the comprehensive and detailed information currently available on strains can be better interrogated and used in the programme to eradicate bovine TB"* (Anon, 2012).

(h) **Veterinary Officers** dealing with breakdowns value the scientific element and additional knowledge that it brings to breakdown investigations and information and advice that can be provided to the farmer and PVP. It is both informative and motivational to Veterinary Officers on the ground. Its significance in this regard should not be under estimated. AFBI also provides advice to DAERA staff regarding results and interpretation of molecular typing (VNTR) data.

(i) The **Ulster Farmers Union (UFU)** were supportive of AFBI's strain typing work in their submission to the 2009 Northern Ireland Audit Office bTB report, *"UFU welcomes the amount of research into TB which takes place in Northern Ireland and we have been encouraged by the strain typing work that has been undertaken at AFBI (Veterinary Sciences Division) to identify the unique clusters of infection throughout cattle and badger populations across Northern Ireland"* (NIAO, 2009).

5.1.5. Detail

Progression would be ongoing, and involve a number of strands, including development of the GIS and a new TB breakdown investigation report form. Governance boards would expect an epidemiological assessment of particular areas and an ongoing assessment of progress, or lack thereof. This will be an iterative process as the potential of the technology and our requirements are better understood.

An important output would be to define, monitor and analyse the geographical location or "home range" of a particular strain which would start to help to address questions for example about latency and reactivation and the role of (recorded) cattle movements. Assumptions about home range and movement (translocation) of molecular types need to be formally tested. Importantly, these data can be correlated using GIS with herd density, cattle density, cattle movements and seasonality. This is unique to Northern Ireland due to the size and completeness of both data sets. It may be possible to establish a figure for the transmission rate in certain circumstances within confidence intervals. This would be of significant value in the development of any future local infection models. Subsequently, it could be used in monitoring any effect of changes in farming practices or programme controls.

It can already be used to provide information about both chronic herds and herds with multiple strain types and help to distinguish these from recurrent infection or persistent environmental/location risks. It allows examination of herd risk factors where multiple strains are disclosed in comparison to those with few.

This is an initial step to further work to establish how the seeding or containment occurs in new high incidence areas.

It allows possible analysis of epidemic elements, most probably by describing areas where bTB control has failed, perhaps due to Programme shortcomings (e.g. inadequate tracing windows), some biological factor such as latency or farming risk practices like trading cattle.

The emergence of new strains suggests that local control measures are inadequate.

ANNEX A

TOOLS & PROCESSES

Investigating the role of wildlife utilises samples from the Test and Vaccinate or Remove (TVR) research project and the badger Road Traffic Accident (RTA) survey. The current VNTR analyses (at least on visual inspection) established that cattle and badgers tended to share the same molecular type of TB bacteria, at least on a regional level.

5.1.6. Impact

Better understanding, more buy in from vets and farmers, more informed decision making leading to a more effective programme.

As a result of the implementation of TBSPG recommendations that result in increased sensitivity of live animal testing there is likely to be an initial increase of between 600 -700 in the number of confirmed cases for VNTR strain typing.

The emerging application of Whole Genome Sequencing (WGS) technology will be monitored. The potential for its application is not yet clear but there could be staffing and technological investment implications for AFBI. However, WGS is being utilised in a DAARA funded Evidence and Innovation project looking at cattle and badger *M. bovis* isolates obtained from the TVR research area.

To make full use of the information technology available through strain typing and the developing GIS system (see under 12), a dedicated specialist would be required to analyse the information, advise and direct the response to infection and to train staff (and PVPs).

5.1.7. Timeline

Current coverage should be maintained with integration of molecular genotyping data into GIS as soon as possible to facilitate assessment on an area basis.

5.2. Geographic Information System (GIS)

5.2.1. Issue

DAERA has introduced a new GIS viewer to improve the efficiency of the breakdown mapping process. It is used to identify herds that are in proximity to a breakdown and for which additional testing may be required to reduce the spread of disease. There is significant potential to further develop this system to provide additional information which could facilitate the provision of epidemiological information, disease investigation communication and the provision of tailored advice. It should provide up to date information on badger sett locations, strain typing (including from wildlife), breakdown history and testing history to allow relevant people to see what is happening on an area basis as well as at an individual farm level, as well as the mapping element.

5.2.2. Recommendation

TBSPG recommends that GIS is a **resource to be developed** to meet the requirements of DAERA staff, PVPs and the governance groups as the strategy evolves.

ANNEX A

TOOLS & PROCESSES

Any GIS development needs to seamlessly link with other relevant national databases and also enable capture of additional information that will be pertinent to facilitating ongoing monitoring, evaluation and adaptable to meet the needs of future research priorities.

5.2.3. Rationale for change

Further development of the GIS would allow for the visualisation of the bTB situation at local, regional and national scale. It is intended that up to date information such as badger sett locations, strain typing (including from wildlife), breakdown history and testing history will be superimposed upon the mapping element to achieve this.

5.2.4. Impact

The further development of the GIS and, if possible, a linkage to NIFAIS in future would help to identify and describe disease patterns across Northern Ireland, identify risks earlier, plan appropriate intervention strategies and monitor progress. It would also facilitate management of cases, whether they are individual breakdowns or high incidence areas, and targeting of resource. It would demonstrate the use of the extensive molecular genotyping data (see under section 4) which is not currently available in a pictorial format at individual breakdown /locality level. It would facilitate identification of linkages between breakdowns through readily available up to date information on out farms / conacre. It will also facilitate the implementation of segregation notices to protect the herds contiguous to breakdowns.

5.2.5. Timeline

GIS updates should be released as they become available.

ANNEX A

TOOLS & PROCESSES

APPENDIX 1

Bovine TB – *Mycobacterium bovis* Whole-Genome Sequencing/Epidemiology

1. Molecular typing provides information about the genomic identity of the organism and how closely related it is to other organisms isolated from other hosts in the region; this information is important for effective epidemiological studies, including outbreak investigation. Currently Northern Ireland isolates of *M. bovis* are subject to molecular typing by spoligotyping & VNTR-typing in AFBI. These procedures add a significant extra dimension to the characterisation of *M. bovis* strains which can be used in outbreak investigations and for epidemiological research on the progression of the TB epidemic in Northern Ireland. For example, the approach has demonstrated strong evidence of geographical localisation and local associations between the strains of TB present in badgers and cattle.

2. The molecular typing data have essentially two applications:

    A. To investigate important aspects of bovine TB epidemiology, such as cattle-cattle transmission and cattle-wildlife transmission using descriptive, analytical and infection mathematical modelling studies.

    B. To help inform and optimize epidemiological investigations and contact tracings.

    Herd-level molecular typing data and isolates exist from 2003-present; animal-level data and isolates exist from 2010-present.

3. Recent data, summarised by Dr Hannah Trewby (University of Glasgow) and AFBI for 2003-2010 show the numbers of the various *M. bovis* spoligotypes, and VNTR-types, from typed (confirmed) breakdowns by year in Northern Ireland.

Year	Number of Unique Spoligotypes	Number of Unique VNTR - types	Number of typed breakdowns	Total No. of breakdowns (includes confirmed and unconfirmed)
2003	12	57	1347	2902
2004	13	61	1621	2954
2005	12	61	1432	2556
2006	9	72	1285	2033
2007	10	72	1235	1862
2008	11	72	1115	1789
2009	10	72	1080	1771
2010	9	72	934	1617
Total (unique) 2003 – 2010	16	185	10049	17484

ANNEX A

TOOLS & PROCESSES

4. It is apparent from the above table that, while there is great diversity in strain types, which is currently being used by epidemiologists to track infection progression, there is also considerable clustering of the more prevalent types. This clustering limits the ability of these techniques to discriminate between some outbreaks. The geographical dimension adds a further important factor which adds value to the approach.

5. This is where the higher resolution of bacterial **W**hole- **G**enome **S**equencing (WGS) offers further potential to discriminate between outbreaks in which multiple spoligo- and VNTR-types are present. WGS will enhance our limited understanding of how the TB epidemic is maintained and transmitted, and the critical points where control might be more usefully deployed. The results of WGS are likely to have a significant impact on the strategic deployment of scarce resources, including more sensitive diagnostics and additional control measures. Furthermore, such epidemiological information has the potential to significantly improve our understanding of bTB control investigations, delineating spatial, temporal and interspecies dynamics, retrospectively. Notably, WGS theoretically has the potential to indicate the direction of transmission between cattle and badgers in some outbreaks.

6. The whole genome sequence of *M. bovis (*Fig 1) was first published in 2003 (Garnier et al., 2003). As indicated, the sequence consists of 4,345,492 base pairs and it is this sequence and its functional units that convey the unique characteristics of the organism.
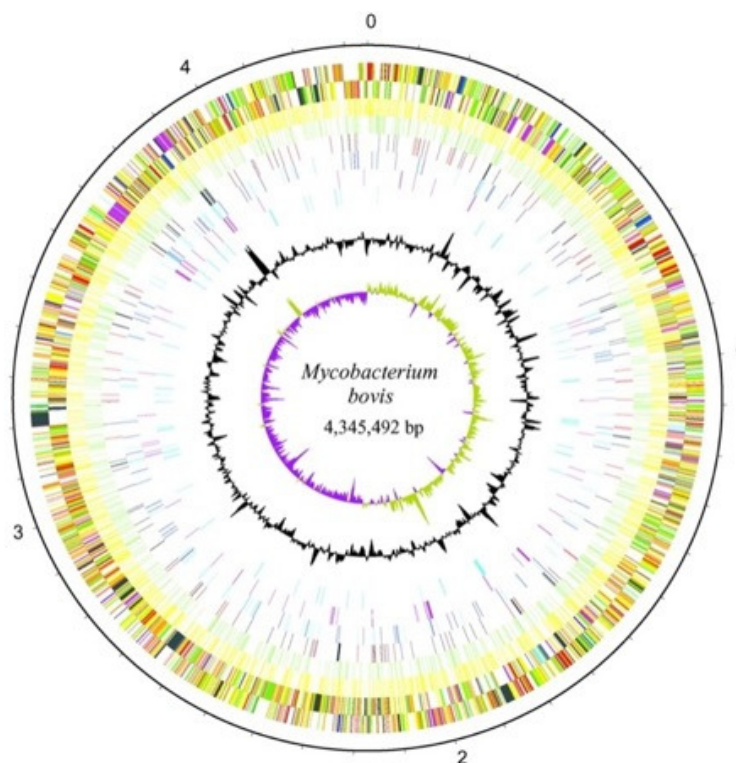

Fig 1. Sequence of one isolate (AF2122/97) of M. bovis which is a fully virulent 1997 Great Britain isolate from an infected cow suffering caseous lesions in lung and bronchomediastinal lymph nodes.

ANNEX A

TOOLS & PROCESSES

7.   It is the variation in this sequence in the population of *M. bovis* isolates collected locally, nationally and internationally that is currently being probed using WGS. It has also been shown that this sequence is highly-related to other members of the mycobacteria family e.g. *M. tuberculosis* (causal agent for human TB). However, unlike rapidly-evolving viruses and some bacteria, TB bacteria appear to mutate exceptionally slowly. In order to attempt to understand maintenance and transmission dynamics it is necessary to more fully integrate family trees (derived from WGS data), mutation rates and other epi-data (tests, movements, contacts etc) and modelling approaches, preferably from longitudinal studies taking place over many years with dense sampling of the host populations involved.

8.   WGS of *M. bovis* has already produced some significant high profile analysis, particularly related to *M. bovis* transmission dynamics in Northern Ireland, through Dr. Robin Skuce and AFBI colleagues using isolates denoted by DAERA from TB outbreaks on farms in Northern Ireland and working with collaborators in the University of Glasgow (Biek et al, 2012; Trewby et al., 2016).

9.   It is of note that the BBRSC/DEFRA[1] have recently awarded a multi-million pound project to researchers in Cambridge University, the Sanger Institute and APHA Weybridge to investigate bTB maintenance and transmission dynamics using WGS, *inter alia.* on isolates from the RBCT study.

10.   WGS in combination with powerful mathematical and statistical tools offers significant potential in addressing some of the issues raised in para 6, above. However, this potential needs to be fully researched especially as the associated technologies are still evolving nationally and internationally. DAERA/AFBI have an important role in this evolution because of the unique data-bases available and also the urgent need to resolve problems related to TB dynamics in NI. Development of capability and capacity in microbial WGS would also support the Northern Ireland strategy which recognises genomics as an important enabling technology, especially at a local level, in an integrated and strategic approach to the eradication of *M. bovis* in the cattle population.

11.   In addition, there is potential to investigate the existence and potential impact of super-shedders *i.e.* sources which have a disproportionate influence on infection propagation and to track and understand better the maintenance/spread though populations and the landscape/environment. This has already been used to good effect in the biomedical field where Roetzer et al. (2013) concluded that WGS was superior to conventional genotyping for the tracing and investigating of *M. tuberculosis* micro–epidemics. WGS provides a measure of the *M. tuberculosis* mutation rate over time in its natural host. More recently Walker et al. (2013) again in UK human studies, indicated that WGS could delineate outbreaks and allowed improved inference about direction of transmission between cases. The technique identified super-spreaders and predicted the existence of undiagnosed cases, potentially leading to earlier treatment of infected patients and their contacts. Such sentiments have direct carry over into issues concerning bovine TB control. A recent review by Wlodarska et al. (2015) usefully summarises the potential role of diagnostic techniques including WGS in the diagnosis of *M. tuberculosis* in humans.

---

[1] J Wood et al University of Cambridge. Exploring the richness of Mycobacterium bovis strain diversity to decipher the epidemiology of bovine tuberculosis ecology

ANNEX A

TOOLS & PROCESSES

12. In a small, pilot study in relation to the Northern Ireland cattle/badger *M. bovis* studies, Biek et al. (2012) indicated that WGS can provide additional insights into TB epidemiology even where optimal contact data are not available, and that more extensive sampling and analysis, especially over time, has the potential to allow quantification of the extent and direction of transmission between and within cattle and badgers.

13. The final conclusion of Trewby et al. (2015) is highly relevant. "We *suggest that continued advances in mathematical models integrating epidemiological and genetic information will allow a more confident resolution of the factors involved in the spread of M. bovis, giving a better understanding of the interplay between epidemiological and genetic factors for this important and troublesome pathogen".*

14. How should we use WGS?

    In addressing this question, it is noted that there is a DAERA project investigating TB dynamics using genomic epidemiology in the TVR study area. This project could potentially be a good test-bed for this approach. TBSPG are supportive of this project continuing for several years in order to acquire enough data for a definitive analysis. However:

    A. WGS has significant potential in further characterising *M. bovis* beyond the capability of current Spoligotyping / VNTR typing. However, it will not replace that approach yet on grounds of cost and speed of data analysis. Deployment beyond the research environment may therefore be confined initially to providing further resolution to those types where it is currently not possible to resolve strain types. WGS is considered to be a game-changing technology in clinical microbiology for several applications (Tang and Gardy, 2014; Robinson et al., 2013). Despite the step-change in resolution, this approach will still be confounded to some extent by the slow mutation rate of TB bacteria *i.e.* resolution of transmission dynamics within-herd may be somewhat limited. Consequently, it will be important to understand the diversity of TB bacteria within the same host and over as long a time scale as possible. Nevertheless, there is proven additional resolution available, particularly between-herd, as demonstrated by the Biek et al. (2012) and Trewby et al. (2015).

    B. The primary role at this juncture will be as a research tool where it has considerable potential in informing thorny epidemiological conundrums such as:

       (a) The impact of recorded (and possibility unrecorded) cattle movements

       (b) The risk factors for herds in a infection cluster

       (c) The spatio-temporal interaction with wildlife

       (d) Multiple infections in the same animal

       (e) Multiple infections in the same herd.

       (f) The role of super-spreaders

       (g) Infection type distributions and potential geographical influences

ANNEX A

TOOLS & PROCESSES

      (h)   Whether TB strains have different traits (transmissibility etc)

C. Research will no doubt continue to develop the application of the technology in conjunction with advanced mathematical modelling and DAERA should continue to participate though AFBI in links with the University of Glasgow (and others if appropriate).

D. Specifically, further work is needed to better investigate the flow of the various strains of *M. bovis* between cattle and wildlife and it would be expedient to convene a workshop specifically on this topic to further explore the potential for WGS to be used in the control and eradication of bovine TB in Northern Ireland. (see link below2 to a recent workshop at the University of Glasgow on WGS). The enhanced resolution of this problem has important implications for the Northern Ireland bovine TB Eradication Plan.

---

2 http://www.gla.ac.uk/research/az/boydorr/meetingsevents/2015-bovinetuberculosis/

ANNEX A

TOOLS & PROCESSES

APPENDIX 2

(a) Non Visibly Lesioned (NVL) animals arise when an animal is positive to either the SCITT or gamma test but no lesion is identified on carcass inspection at the abattoir.

(b)   The detection rate at the abattoir can be as low as 25% of infected animals. This implies that detection at the abattoir is a very poor means of confirming infection status. We know from previous studies that lesions can both vary in position and size (from the microscopic to grossly visible). In addition, detection depends on the thoroughness of the inspection e.g. as evidenced in Great Britain when a more rigorous inspection regime was introduced.

(c) Detection at the abattoir is most probable in animals which have been infected for some time i.e. the lesions have had time to develop. The SCITT and Gamma Interferon test (even prior to the SCITT) tests are more likely to detect infection at an earlier stage. (See diagram in the ANNEX illustrating this point)

(d) The poor sensitivity of the SCITT itself (approx. 60%) means that inevitably some infected animals escape detection so having at least two positive animals would be sufficient to confirm infection on the farm.

On scientific grounds **it is agreed** that the infection status of herds should be determined on the results of the SCITT not on whether lesions are found in the abattoir. Except in the case of course where lesions are found in the abattoir in the absence of a positive SCITT or Gamma Interferon test.

Source - R de la Domenech et al 2006 Res Vet Sci 81 190- 210
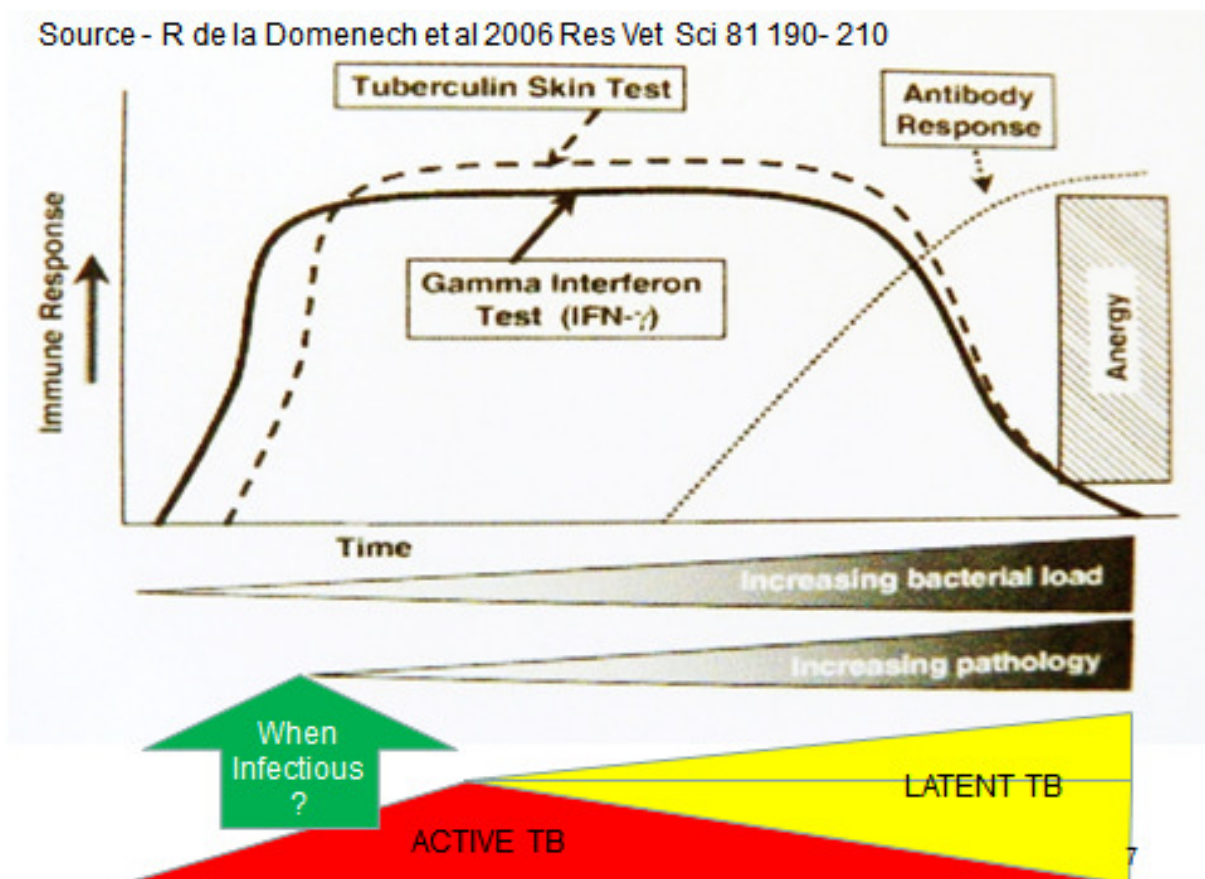
ANNEX A

TOOLS & PROCESSES

Experimental data clearly demonstrate that following infection there is a period when neither the SCITT nor the Gamma Interferon test will show a positive response. However, it has been shown that the Gamma Interferon test will respond earlier than the SCITT. At the later stages of the infection the response to these tests diminish and in some cases an antibody response can be observed which will increase as the infection progresses further.

While infection is progressing the bacterial load increases as does the development of lesions which can be detected on inspection at the abattoir. However, early bTB lesions may not be sufficiently developed to be detected on inspection.

While the animal is infected when carrying the *M. bovis* organism it is not necessarily infectious i.e. secreting the organism. It is not known whether the organisms are secreted continuously or intermittently nor indeed whether they are secreted in a state which can be cultured (i.e. detected). Recent human studies indicate that many excreted organisms are non - culturable i.e. are in a latent state which can be reactivated i.e. become culturable.

The TB organism is known to exist in at least two different states i.e. active (e.g. growing) and latent (inactive). The properties of the latent state in bTB (caused by *M. bovis*) are much less well understood than that of the latent state in human TB (caused by *M. tuberculosis*).

ANNEX A

TOOLS & PROCESSES

REFERENCES

Abernethy, D.A., Denny, G.O., Menzies, F.D., McGuckian, P., Honhold, N. and Roberts, A.R., 2006. The Northern Ireland programme for the control and eradication of *Mycobacterium bovis*. *Veterinary Microbiology*, *112*(2), pp.231-237.

Adkin, A., Brouwer, A., Downs, S.H. and Kelly, L., 2016a. Assessing the impact of a cattle risk-based trading scheme on the movement of bovine tuberculosis infected animals in England and Wales. *Preventive Veterinary Medicine*, *123*, pp.23-31.

Adkin, A., Brouwer, A., Simons, R.R.L., Smith, R.P., Arnold, M.E., Broughan, J., Kosmider, R. and Downs, S.H., 2016b. Development of risk-based trading farm scoring system to assist with the control of bovine tuberculosis in cattle in England and Wales. *Preventive Veterinary Medicine*, *123*, pp.32-38.

Álvarez, J., Perez, A., Bezos, J., Marqués, S., Grau, A., Saez, J.L., Mínguez, O., de Juan, L. and Domínguez, L., 2012. Evaluation of the sensitivity and specificity of bovine tuberculosis diagnostic tests in naturally infected cattle herds using a Bayesian approach. *Veterinary Microbiology*, *155*(1), pp.38-43.

Anon. (2012). Northern Ireland Assembly Agriculture and Rural Development Committee: Review into Bovine Tuberculosis. Report: NIA 83/11–15Agricultural and Rural Development Committee, http://www.niassembly.gov.uk/assembly-business/committees/archive/agriculture-and-rural-development/reports/review-into-bovine-tuberculosis/

Bermingham, M.L., More, S.J., Good, M., Cromie, A.R., Higgins, I.M. and Berry, D.P., 2010. Genetic correlations between measures of *Mycobacterium bovis* infection and economically important traits in Irish Holstein-Friesian dairy cows. *Journal of Dairy Science*, *93*(11), pp.5413-5422.

Berry, D.P., Bermingham, M.L., Good, M. and More, S.J., 2011. Genetics of animal health and disease in cattle. *Irish Veterinary Journal*, *64*, p.5.

Biek, R., O'Hare, A., Wright, D., Mallon, T., McCormick, C., Orton, R.J., McDowell, S., Trewby, H., Skuce, R.A. and Kao, R.R., 2012. Whole genome sequencing reveals local transmission patterns of *Mycobacterium bovis* in sympatric cattle and badger populations. *PLoS Pathog*, *8*(11), p.e1003008.

Brunton, L.A., Nicholson, R., Ashton, A., Alexander, N., Wint, W., Enticott, G., Ward, K., Broughan, J.M. and Goodchild, A.V., 2015. A novel approach to mapping and calculating the rate of spread of endemic bovine tuberculosis in England and Wales. *Spatial and Spatio-temporal Epidemiology*, *13*, pp.41-50.

Carrique-Mas, J.J., Medley, G.F. and Green, L.E., 2008. Risks for bovine tuberculosis in British cattle farms restocked after the foot and mouth disease epidemic of 2001. *Preventive Veterinary Medicine*, *84*, pp.85-93.

Clegg, T.A., Blake, M., Healy, R., Good, M., Higgins, I.M. and More, S.J., 2013. The impact of animal introductions during herd restrictions on future herd-level bovine tuberculosis risk. *Preventive Veterinary Medicine*, *109*(3), pp.246-257.

ANNEX A

TOOLS & PROCESSES

Clegg, T.A., Good, M. and More, S.J., 2015. Future risk of bovine tuberculosis recurrence among higher risk herds in Ireland. *Preventive Veterinary Medicine*, *118*, pp.71-79.

Clegg, T.A., Good, M., Duignan, A., Doyle, R. and More, S.J., 2011b. Shorter-term risk of *Mycobacterium bovis* in Irish cattle following an inconclusive diagnosis to the single intradermal comparative tuberculin test. *Preventive Veterinary Medicine*, *102*(4), pp.255-264.

Clegg, T.A., Good, M., Duignan, A., Doyle, R., Blake, M. and More, S.J., 2011a. Longer-term risk of *Mycobacterium bovis* in Irish cattle following an inconclusive diagnosis to the single intradermal comparative tuberculin test. *Preventive Veterinary Medicine*, *100*(3), pp.147-154.

Corner, L.A., 1994. Post mortem diagnosis of *Mycobacterium bovis* infection in cattle. *Veterinary Microbiology*, *40*(1), pp.53-63.

Dawson, K.L., Stevenson, M.A., Sinclair, J.A. and Bosson, M.A., 2014. Recurrent bovine tuberculosis in New Zealand cattle and deer herds, 2006–2010. *Epidemiology and Infection*, *142*, pp.2065-2074.

De Kantor, I.N., Nader, A., Bernardelli, A., Girón, D.O. and Man, E., 1987. Tuberculous infection in cattle not detected by slaughterhouse inspection. *Journal of Veterinary Medicine, Series B*, *34*(1-10), pp.202-205.

De la Rua-Domenech, R., Goodchild, A.T., Vordermeier, H.M., Hewinson, R.G., Christiansen, K.H. and Clifton-Hadley, R.S., 2006. Ante mortem diagnosis of tuberculosis in cattle: a review of the tuberculin tests, γ-interferon assay and other ancillary diagnostic techniques. *Research in Veterinary Science*, *81*(2), pp.190-210.

Doyle, L.P., Courcier, E.A., Gordon, A.W., O'Hagan, M.J.H. and Menzies, F.D., 2016. Bovine tuberculosis in Northern Ireland: Risk factors associated with duration and recurrence of chronic herd breakdowns. *Preventive Veterinary Medicine*, *131*, pp. 1-7.

Doyle, L.P., Gordon, A.W., Abernethy, D.A. and Stevens, K., 2014. Bovine tuberculosis in Northern Ireland: Risk factors associated with time from post-outbreak test to subsequent herd breakdown. *Preventive Veterinary Medicine*, *116*(1), pp.47-55.

Duignan, A., Good, M. and More, S.J., 2012. Quality control in the national bovine tuberculosis eradication programme in Ireland. *Rev. Sci. Tech*, *31*, pp.845-860.

EU Commission, Accepted by the Bovine tuberculosis subgroup of the Task Force on monitoring animal disease eradication. EU Veterinary Programmes. SANCO/10067/2013. Pp. 20.

Frankena, K., White, P.W., O'keeffe, J., Costello, E., Martin, S.W., Van Grevenhof, I. and More, S.J., 2007. Quantification of the relative efficiency of factory surveillance in the disclosure of tuberculosis lesions in attested Irish cattle. *Veterinary Record*, *161,* pp. 679–684.

FVO (2014a). Final Report Of An Audit Carried Out In The United Kingdom From 15 To 26 September 2014 In Order To Evaluate The Effectiveness Of And Progress Made By The Programmes Co-Financed By The European Union To Eradicate Bovine Tuberculosis.

ANNEX A

TOOLS & PROCESSES

Food and Veterinary Office, DG(SANCO) 2014-7055. Pp. 27. http://ec.europa.eu/food/audits-analysis/audit_reports/details.cfm?rep_id=3424

FVO (2014b). Final Report Of An Audit Carried Out In Ireland From 21 To 28 May 2014 In Order To Evaluate The Effectiveness Of, And Progress Made By The Programmes Co-Financed By The European Union To Eradicate Bovine Tuberculosis. Food and Veterinary Office, DG(SANCO) 2014-7054. Pp. 16. http://ec.europa.eu/food/audits-analysis/audit_reports/details.cfm?rep_id=3430

FVO (2015). Final Report Of An Audit Carried Out In The United Kingdom From 01 June 2015 To 05 June 2015 In Order To Evaluate The Effectiveness Of And Progress Made By The Programmes Co-Financed By The European Union To Eradicate Bovine Tuberculosis In Northern Ireland. Food and Veterinary Office, DG(SANTE) 2015-7570 – MR. Pp. 47. http://ec.europa.eu/food/audits-analysis/audit_reports/details.cfm?rep_id=3560

Garnier, T., Eiglmeier, K., Camus, J.C., Medina, N., Mansoor, H., Pryor, M., Duthoy, S., Grondin, S., Lacroix, C., Monsempe, C. and Simon, S., 2003. The complete genome sequence of *Mycobacterium bovis*. *Proceedings of the National Academy of Sciences*, *100*, pp.7877-7882.

Good, M.,Duignan, A. and More, S.J., 2011. The impact of the national full herd depopulation policy on the recurrence of bovine tuberculosis in Irish herds during 2003 to 2005. *Veterinary Record*, *169,* pp. 581- 585..

Goodchild, A.V., Downs, S.H., Upton, P., Wood, J.L.N. and de la Rua-Domenech, R., 2015. Paper: Specificity of the comparative skin test for bovine tuberculosis in Great Britain. *Veterinary Record*, *177*, p.258.

Gormley, E., Doyle, M., Duignan, A., Good, M., More, S.J. and Clegg, T.A., 2013. Identification of risk factors associated with disclosure of false positive bovine tuberculosis reactors using the gamma-interferon (IFNγ) assay. *Veterinary Research*, *44*(1), p.1-8.

Karolemeas, K., McKinley, T.J., Clifton-Hadley, R.S., Goodchild, A.V., Mitchell, A., Johnston, W.T., Conlan, A.J.K., Donnelly, C.A. and Wood, J.L.N., 2011. Recurrence of bovine tuberculosis breakdowns in Great Britain: Risk factors and prediction. *Preventive Veterinary Medicine*, *102*(1), pp.22-29.

Lahuerta-Marin, A., Gallagher, M., McBride, S., Skuce, R., Menzies, F., McNair, J., McDowell, S.W. and Byrne, A.W., 2015. Should they stay, or should they go? Relative future risk of bovine tuberculosis for interferon-gamma test-positive cattle left on farms. *Veterinary Research*, *46*(1), pp.90-97.

Lahuerta-Marin, A., McNair, J., Skuce, R., McBride, S., Allen, M., Strain, S.A., Menzies, F.D., McDowell, S.J. and Byrne, A.W., 2016. Risk factors for failure to detect bovine tuberculosis in cattle from infected herds across Northern Ireland (2004–2010). *Research in Veterinary Science*, *107*, pp.233-239.

More, S.J. and Good, M., 2015. Understanding and managing bTB risk: Perspectives from Ireland. *Veterinary Microbiology*, *176*, pp.209-218.

ANNEX A

TOOLS & PROCESSES

More, S.J., Radunz, B. and Glanville, R.J., 2015. Review: Lessons learned during the successful eradication of bovine tuberculosis from Australia. *Veterinary Record*, *177*, pp.224-232.

NIAO (2009). The control of bovine tuberculosis in Northern Ireland. REPORT BY THE COMPTROLLER AND AUDITOR GENERAL

NIAO (2009). The control of bovine tuberculosis in Northern Ireland. REPORT BY THE COMPTROLLER AND AUDITOR GENERAL N8-09, 18 March 2009

Olea-Popelka, F., Freeman, Z., White, P., Costello, E., O'Keeffe, J., Frankena, K., Martin, W. and More, S., 2012. Relative effectiveness of Irish factories in the surveillance of slaughtered cattle for visible lesions of tuberculosis, 2005-2007. *Irish Veterinary Journal*, *65*, pp.1-5.

Olea-Popelka, F.J., White, P.W., Collins, J.D., O'Keeffe, J., Kelton, D.F. and Martin, S.W., 2004. Breakdown severity during a bovine tuberculosis episode as a predictor of future herd breakdowns in Ireland. *Preventive Veterinary Medicine*, *63*(3), pp.163-172.

Robinson, E.R., Walker, T.M. and Pallen, M.J., 2013. Genomics and outbreak investigation: from sequence to consequence. *Genome Medicine*, *5*(4), p.36

Roetzer, A., Diel, R., Kohl, T.A., Rückert, C., Nübel, U., Blom, J., Wirth, T., Jaenicke, S., Schuback, S., Rüsch-Gerdes, S. and Supply, P., 2013. Whole genome sequencing versus traditional genotyping for investigation of a *Mycobacterium tuberculosis* outbreak: a longitudinal molecular epidemiological study. *PLoS Med*, *10*(2), p.e1001387.

SANCO (2013). Working Document on Eradication of Bovine Tuberculosis in the EU NIA 92/08-09, 18 March 2009.://www.niauditoffice.gov.uk/the_control_of_bovine_tuberculosis_in_ni.pd

Shittu, A., Clifton-Hadley, R.S., Ely, E.R., Upton, P.U. and Downs, S.H., 2013. Factors associated with bovine tuberculosis confirmation rates in suspect lesions found in cattle at routine slaughter in Great Britain, 2003–2008. *Preventive Veterinary Medicine*, *110*, pp.395-404.

Tang, P. and Gardy, J.L., 2014. Stopping outbreaks with real-time genomic epidemiology. *Genome Medicine*, *6*, p.104.

Trewby, H., Wright, D., Breadon, E.L., Lycett, S.J., Mallon, T.R., McCormick, C., Johnson, P., Orton, R.J., Allen, A.R., Galbraith, J. and Herzyk, P., 2016. Use of bacterial whole-genome sequencing to investigate local persistence and spread in bovine tuberculosis. *Epidemics*, *14*, pp.26-35.

USDA (2009). Analysis of bovine tuberculosis surveillance in accredited Free States**.** United States Department of Agriculture Animal and Plant Health Inspection Service Veterinary Services. January 30, 2009 pp. 39.

ANNEX A

TOOLS & PROCESSES

VEU (2013a). Descriptive analysis of Northern Ireland Tuberculosis restricted incidents in the period from 2005 to 2012. September 2013, pp. 76.

VEU (2013b). Is it justified to reduce the number of NVL reactors required from > 5 to 2 or 3 to treat a bovine tuberculosis (bTB) breakdown in the same way as bTB breakdowns with confirmed reactors? August 2013, pp. 33.

VEU (2013c). Evidence base for introducing an additional 6-month test after a CHT. November 2013, pp. 10.

VEU (2015a). Use of severe interpretation in the control of bovine TB in Northern Ireland. DARD Veterinary Epidemiology Report, January 2015, pp.10.

VEU (2015a). Bovine tuberculosis pre-movement test in Northern Ireland: Summary and options to be considered. DARD VEU Report, March 2015. Pp.45.

VEU (2015b). Bovine tuberculosis pre-movement test in Northern Ireland: Supplementary material Pre-movement test in chronically bTB infected herds. DARD VEU Report, September 2015. Pp.4.

VEU (2015b). TB Testing in N. Ireland: Comparison of Test Results for Different Groups of Veterinary Surgeons: Update incorporating 2014 data. June 2015, pp.10.

VEU (2015c). Comparison of full and partial herd depopulations in the control and eradication of bovine tuberculosis. January 2015, pp. 18.

VEU (2015d). Post-Mortem Surveillance for Bovine Tuberculosis in Northern Ireland. May 2015, pp. 33.

Walker, T.M., Ip, C.L., Harrell, R.H., Evans, J.T., Kapatai, G., Dedicoat, M.J., Eyre, D.W., Wilson, D.J., Hawkey, P.M., Crook, D.W. and Parkhill, J., 2013. Whole-genome sequencing to delineate *Mycobacterium tuberculosis* outbreaks: a retrospective observational study. *The Lancet: infectious diseases*, *13*(2), pp.137-146.

Wlodarska, M., Johnston, J.C., Gardy, J.L. and Tang, P., 2015. A microbiological revolution meets an ancient disease: improving the management of tuberculosis with genomics. *Clinical Microbiology Reviews*, *28*(2), pp.523-539.

Wolfe, D.M., Berke, O., Kelton, D.F., White, P.W., More, S.J., O'Keeffe, J. and Martin, S.W., 2010. From explanation to prediction: a model for recurrent bovine tuberculosis in Irish cattle herds. *Preventive Veterinary Medicine*, *94*(3), pp.170-177.