CVO statement on the reduction in the number of new TB incidents in Great Britain

1. Ben Bradshaw asked me in June to carry out an urgent review in light of emerging evidence of a fall in the numbers of new TB incidents.

Report on the reduction in TB incidence

- 2. The headline TB statistics are set out in Annex A. Annex B includes a number of graphs that are referred to throughout this report. The figures are based on data extracted on 28 July. They are provisional figures and will change as all results for the period become available. Given the seasonal variation in TB incidence any set of statistics is to some extent a snapshot in time; analysis of longer term trends will be essential.
- There have been 1,769 new TB incidents during the period 1 January 30 June 2006. Over the same period in 2005 there were 2,178 new TB incidents. This represents a reduction of 19%.
- 4. This reduction is against a background of an increase of 16% in the number of tuberculin tests carried out in cattle herds. The herd incidence rate (the proportion of tests on unrestricted herds which resulted in a confirmed new incident) has decreased more sharply. The incidence of confirmed herd breakdowns for January June 2006 was 2.5% compared to 4.7% over the same period in 2005 (see Annex B Graph 1).
- In addition to a reduction in the number of new TB incidents, there has been an absolute reduction in the number of animals reacting to the skin test. The number of reactors has reduced by 28% - from 13,968 from January - June 2005 to 10,014 over the same period in 2006. This equates to 3.3 reactors per 1,000 animal tests (see Annex B – Graph 2).
- 6. The herd prevalence rate has marginally reduced. 3.5% of herds were under TB restrictions because of a TB breakdown on 30 June 2006, in comparison to 3.8% of herds at the same point in 2005. A further 3.2% of herds were restricted for other reasons linked to the TB control regime. 93% of GB cattle herds were officially TB free at the end of June 2006 compared to 94% in 2005.
- 7. These data show that there has been a real reduction in the number of new TB incidents over the last 12-18 months, and the levels are now comparable with those at the same period in 2004. Despite this reduction, levels of TB remain high in comparison with other EU countries and well above levels that have previously been experienced in the UK. There has been a long term trend of increase in disease incidence over the last decade, with a sharper increase since the Foot and Mouth Disease outbreak in 2001.

- 8. Underneath this national picture of a reduction in disease there are regional differences. There has been a reduction in both the number of new TB incidents and levels of TB incidence in most counties, although there have been exceptions to this general trend in a small number of counties. As an illustration, Annex B Graph 3 sets out the different patterns of disease in a number of counties in the southwest and western region of England.
- 9. There has also been a suggestion of an increase in the number of TB incidents identified through examination at the slaughterhouse, which might suggest that the skin test was becoming less efficient at identifying disease, or that the Meat Hygiene Service was improving its surveillance. Initial analysis from VLA does not bear this out. Graph 4 illustrates the number of new incidents detected at the slaughterhouse.

What might have caused this reduction?

10. I have considered a number of factors that might have affected the number of new TB incidents. This has involved detailed analysis by my officials in TB Division and VLA epidemiologists. I have also exposed this analysis to external challenge by inviting Howard Dalton, Defra's Chief Scientific Adviser, to convene a small group of independent experts, to review our analyses. Follow up analysis has been undertaken as a result of comments from that group (set out in Annex D). I have also sought to ground the emerging conclusions by drawing on the practical experience of farmers, practising vets and the SVS from the high incidence county of Cornwall.

Tuberculin

- 11. There has been commentary from some observers that the fall in the number of new TB incidents has been caused by the change in the supply of tuberculin used in the skin test. The tuberculin used in Great Britain has historically been manufactured at VLA Weybridge, but since October 2005 there has been a progressive switch over to tuberculin produced by a Dutch manufacturer, Lelystad. This is a due to production difficulties at the Weybridge site but it is likely that we will have to use both tuberculins in combination for the foreseeable future. Although this switch started in October 2005, until early 2006 the majority of the tuberculin used in GB was produced in Weybridge; by March 2006 most of the supply came from Lelystad. This pattern of use is shown in graph 5.
- 12. VLA have been monitoring the impact of this change of supply, with their analysis focusing on three questions:
- Is the Dutch tuberculin performing significantly differently from Weybridge tuberculins?
- If so, has the number of TB incidents identified declined as a result of the change in tuberculins?

• If so, how big has the impact been and should mitigating action be implemented?

13. VLA's fuller analysis is at Annexes C and D. The key findings are:

- A small but statistically significant difference in the performance of the two tuberculins has been detected¹;
- The Dutch tuberculin detects proportionately more cattle with Visible Lesions (VL);
- There is no statistically significant difference between the average skin thickness measurements in confirmed reactor cattle produced by the different products;
- There is no statistically significant difference in the proportion of reactors and inconclusive reactors detected in routine whole herd tests by the two products;
- There is no statistically significant difference in the number of reactors disclosed at the first positive herd test;
- The percentage of VL animals appears to vary with tuberculin type for animals with 3-4mm bovine-avian tuberculin reactions;
- The average (unadjusted) number of reactors disclosed per animal tested appears to vary across Animal Health Offices;
- Annual testing has increased substantially especially from 2004, resulting in a steady increase in the proportion of confirmed new incidents (CNIs) in these targeted areas. The absolute number of CNIs has decreased in 2006.
- The skin test must be conducted properly to be effective, since the potential impact calculated from Vet Net data of a 1-2mm reduction in the bovine minus avian reaction difference will have a marked effect on detection (modelling suggests that a 2mm difference in swelling will mean 24% of incidents are missed or detected at a later stage); and,
- The VLA view is that the Lelystad product is marginally less potent than the current Weybridge product but may be more specific. Their view is that it is not sub-standard and it has passed the relevant potency tests.
- 14. This analysis, which was reviewed by Howard Dalton's expert group, suggests that the two tuberculins are functioning in a slightly different manner and this could be a small contributory factor to the reduction in the number of new incidents. However, the evidence to date suggests the difference is not significant enough to account for the whole fall in the number of new TB incidents we have experienced; it may have made a contribution, but this is not expected to be large. Tuberculin is a biological product and there has always been variability, even between batches from the same manufacturer, which are produced and assayed to the same

¹ The comparison of the tuberculin data indicates to date that the proportion of visible lesion animals taken in the TB control programme differs significantly between summed Weybridge and Dutch PPD batches, with the Weybridge results having a smaller % of VLs.

standards (under EU licence conditions). Variations in performance are a standard feature of biological products such as tuberculin; the variations identified here are within acceptable limits and within the ranges seen historically between batches of Weybridge product (see graphs 6 and 7); it does not call into question the efficacy of the new Dutch tuberculin.

Cattle controls

- 15. I have also considered whether the reduction in disease could be driven by the success of our national programme of cattle controls. The control system based on the tuberculin skin test has been effective historically in reducing the weight of infection in the national herd (and in eradication of the disease from other countries). The number of animals tested in recent years has increased significantly. This is because we have rigorously reviewed the parish test intervals annually, which has led to more higher risk herds being tested more frequently. We have also gradually introduced a zero tolerance policy on overdue tests since late 2004, fully implementing this from February 2005, which has also increased the number of animals being tested. We have therefore been identifying and removing infection from the national herd at a greater rate than in previous years. As the rate of transmission of the disease is relatively low, the control measures we have in place should deliver a reduction in the incidence of disease.
- 16. A number of other policy changes have also been introduced over the last year, which may have reduced the risk of the spread of disease or led to changes in behaviour. The compensation system was changed in England on 1 February 2006. Pre-movement testing has been introduced across GB (along with post-movement testing in Scotland) to reduce the risk of spread of disease through cattle movements. These changes are relatively recent and they cannot have had a significant effect on the reduction in TB we have experienced I am encouraged by results to date. Up to 21 July 125 reactors and 271 inconclusive reactors had been identified from specific pre- or post-movement tests across GB.

Changes in the cattle industry

17. There have been a number of changes in the cattle industry over the last 9 months which may have influenced behaviour and changed the profile of animals being submitted for TB testing. For example, replacement of the Over Thirty Month rule by a system of testing for BSE in November 2005 and the introduction of the Older Cattle Disposal Scheme in January 2006, together with changes in the slaughter arrangements for casualty animals, have had an impact on the cattle market. Stakeholders have suggested that there may have been a rush to dispose of older animals before these changes were made, which may have reduced the number of older animals, which have a higher likelihood of disclosing TB, being presented for testing in the last 6 months. However, data on the age profile of the national herd does not substantiate this. If these changes have had an impact, it will be temporary.

Seasonality

18. TB is a cyclical disease, with rates of incidence varying seasonally and over longer timescales. The seasonal variation appears to reflect both testing patterns associated with housing and turnout and likely patterns of transmission. There is always a fall in incidence over the first half of the year, with the fall this year being more pronounced than in recent years; the key issue going forward is the extent of the upturn that would be expected in the autumn. It is difficult to draw any conclusions about any changes in incidence until there is evidence about whether the patterns are sustained over the entire annual cycle.

Other factors

19. Other suggestions have been put forward to explain the drop in the statistics. One suggestion is climatic conditions over the last 12-18 months. There is a range of theories about what impact climatic conditions may have on the risk of disease transmission and they are poorly understood. These effects cannot be readily analysed.

Conclusions

20. Having considered carefully the analysis that has been carried out and subjected it to challenge by experts I have reached the following conclusions:

i) There has been a real reduction in the number of new TB incidents in Great Britain over the last 6 months in comparison to the trend over the last 12-18 months. The number of new incidents is now similar to the same period in 2004, although there is some variation in the regional picture.

ii) It is too early to draw any firm conclusions as to whether this is a temporary change or the start of a sustained reduction. TB is a disease with long incubation, and the incidence varies seasonally. We would need to consider whether this pattern of decline is maintained over a full year before reaching any firmer conclusions.

iii) The reduction is likely to be caused by a complex combination of factors. Our analysis to date has enabled us to rule out some factors, and we may be able to improve our understanding further as the amount of data increases, but it is highly unlikely that it will be possible to explain the decline with any precision.

iv) There is evidence of a small difference in performance between the Weybridge and the Dutch tuberculins, but the evidence to date suggests it is not significant enough to be the principal cause of the reduction in the number of new TB incidents; it may have made a contribution but it would not be large. These differences need to be considered within the broader

context of variation between performance of different tuberculin batches and alongside improvements in the way the tuberculin test is carried out by the veterinary profession.

v) There has not been a significant increase in the number of TB incidents identified through slaughterhouse controls, which would have been an indication that the skin test was missing infected animals. This is despite increased scrutiny by meat inspectors now that carcases from older cattle can enter the food chain. This aspect of TB surveillance is critical in conjunction with the tuberculin test.

21. The following steps follow from the evidence and conclusions:

i) Measures to identify and remove disease in the cattle population remain critical to our ability to control bovine TB. The approach set out in the TB Strategy remains valid. Our approach has increased the number of tests carried out and introduced a zero tolerance approach to overdue tests. All the evidence suggests that over time this increase in the number of tests and the regularity of testing will reduce levels of infection in the national herd and help minimise the risk of TB establishing in new areas.

ii) The skin test remains the foundation of our TB control programme and is required by EU legislation. It is an effective test when carried out properly. The report being published today from DNV Consulting on Bovine TB testing procedures in England and Wales has identified some areas of concern about how the test is being carried out by the veterinary profession but concludes that these do not fundamentally undermine the integrity of the national testing programme. None the less, I attach a high priority to ensuring that Defra, the SVS and the wider veterinary profession continue to work in partnership to reduce the risk of disease by delivering our cattle testing programme, and to address the specific issues raised in the DNV report.

iii) We can improve our cattle controls still further. From October we will roll out use of the gamma interferon test more widely. When used in a targeted way to supplement the skin test this will increase the sensitivity of our testing regime and allow us to remove more infected animals at an earlier stage of infection.

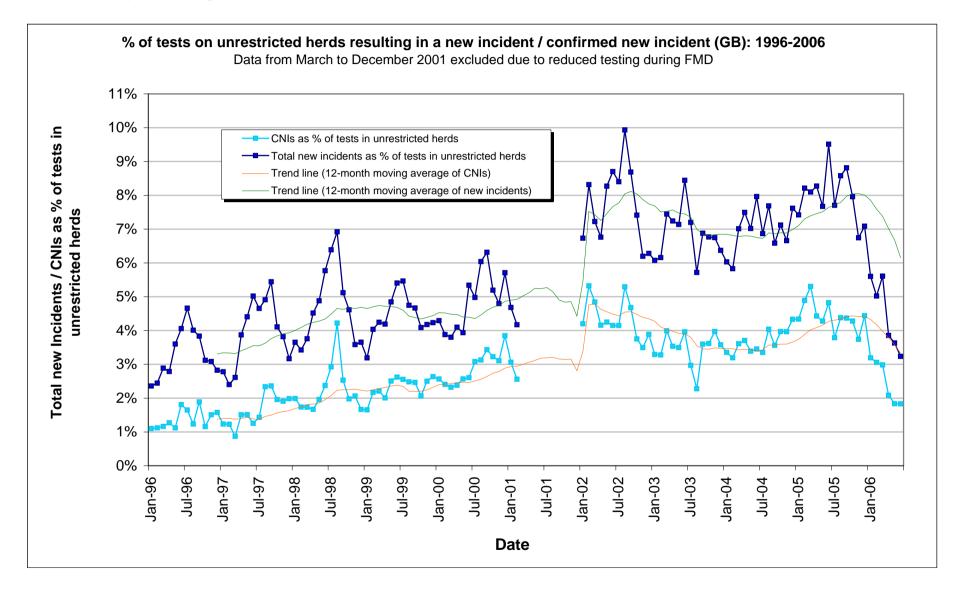
iv) Both the tuberculin products being used for skin testing in Great Britain are fit for purpose. The differences in performances are within the range of inter-batch variation that we have seen historically. We will consider whether there is action that needs to be taken in the field to minimise the impact of any batch to batch variation because this phenomenon may be amenable to further investigation under field or laboratory conditions. Given the degree of uncertainty in this area we will continue to monitor tuberculin performance closely. We will also consider what further analyses might be carried out on the effect of tuberculin batch variation on identification of disease. v) I will continue to monitor the position carefully and consider how the evidence can be used to target our efforts to tackle TB more effectively. Continued scrutiny of the number of cases identified in slaughterhouses and through gamma blood testing will remain particularly important.

Annex A

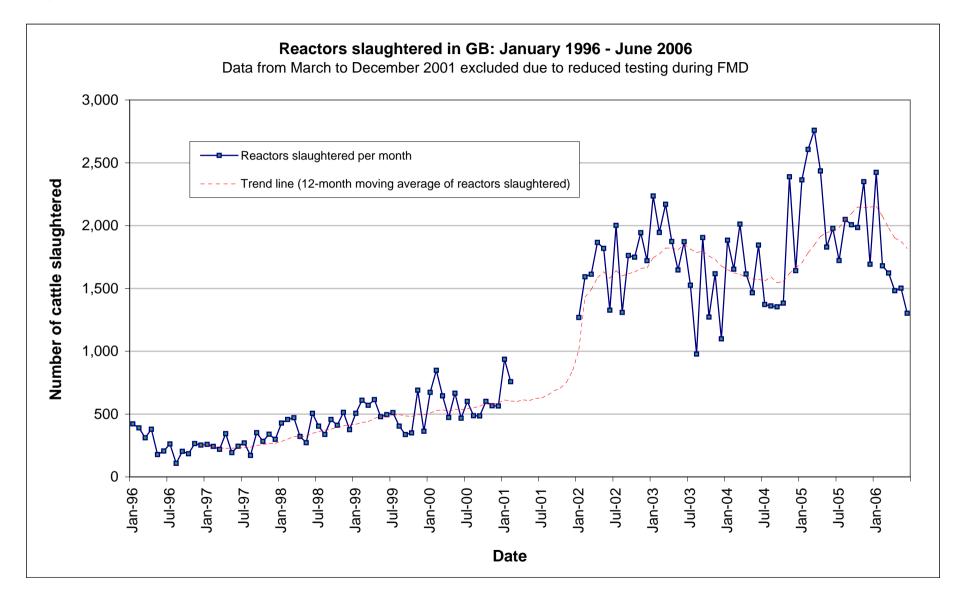
HEADLINE TB STATISTICS: JANUARY – JUNE 2006

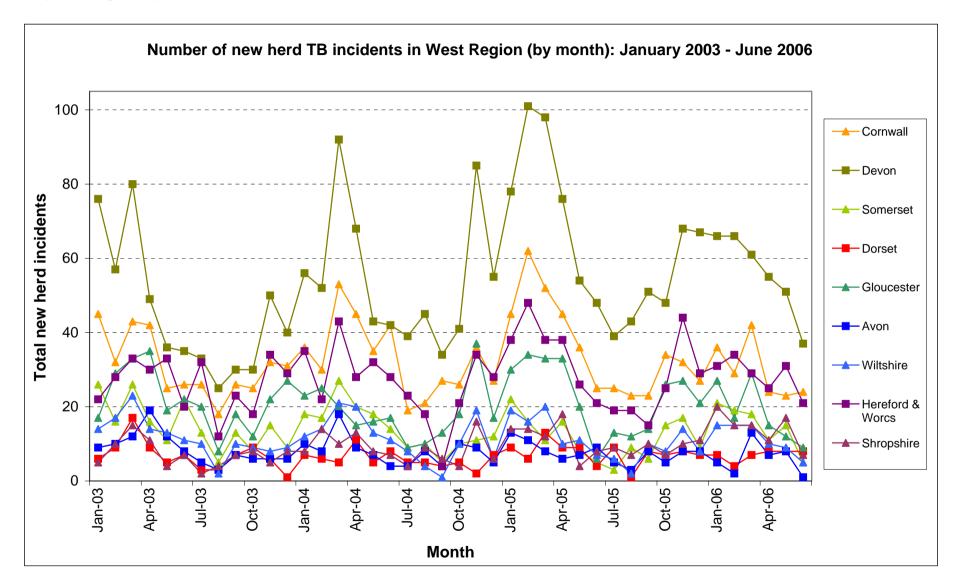
Herd Incidence Rate (confirmed breakdowns only)	2.5%	Confirmed new TB herd breakdowns as a percentage of tests on unrestricted herds tested in GB between 1 January - 30 June 2006.				
Reactors per 1,000 animal tests	3.3	Tuberculin test reactors per 1,000 animal tests in GB between 1 January – 30 June 2006.				
Herd Prevalence Rate	3.5%	Percentage of GB cattle herds under TB restrictions on 30 June 2006 because of a TB breakdown (does not include herds under restriction for an overdue tuberculin test).				
Herd TB Incidence (all breakdowns)	4.5%	New TB herd breakdowns as a percentage of tests on unrestricted herds tested in GB between 1 January - 30 June 2006. Note : the provisional 19% reduction in the number of herd breakdowns in January - June 2006 compared to the same period in 2005, combined with an increase in the number of herds tested, equates to a provisional decrease in herd TB incidence of 44%.				
% TB-Free Herds	93.3%	Percentage of GB cattle herds officially TB-free on 30 June 2006 (the remainder includes herds placed under TB restrictions for any reason, e.g. an overdue tuberculin test, a TB breakdown, disclosure of inconclusive reactors within three years of the conclusion of a confirmed incident, etc.).				

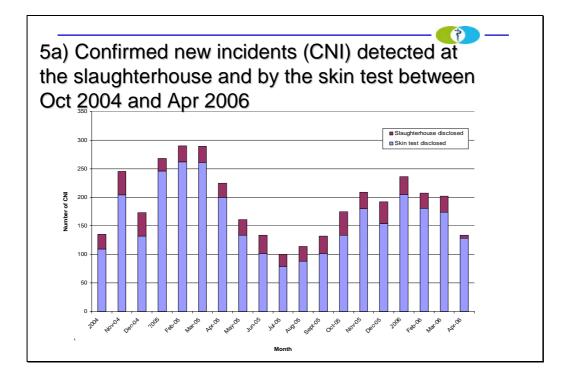
Annex B. Graph 1: Change in TB incidence



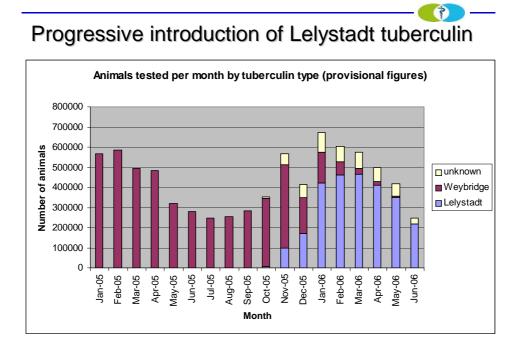
Graph 2: Numbers of reactors

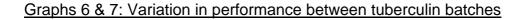


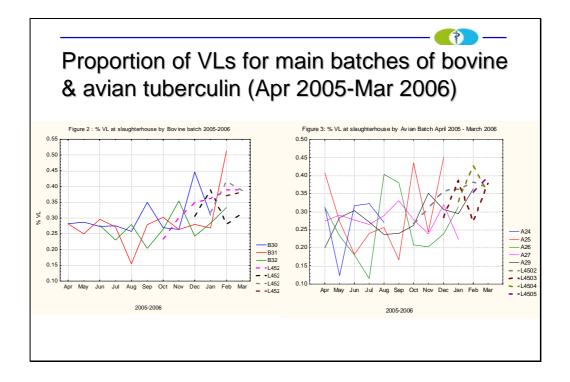


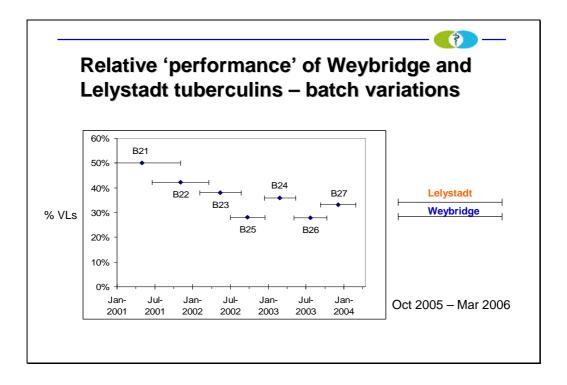


Graph 5: Changing source of tuberculin supply









VLA analyses: monitoring the comparative performance of the Dutch and Weybridge tuberculins (October 2005 to March 2006)

VLA analyses addressed the following questions:

- Is the Dutch tuberculin performing significantly differently from Weybridge tuberculins?
- If so, has the number of TB incidents identified declined as a result of the change in tuberculins?
- If so, how big has the impact been and should mitigating action be implemented?

Key findings arising from the 6 month study can be summarised as follows:

- A small but statistically significant difference in the performance of the two tuberculins has been detected*(slide 1);
- There is no variation in average SICCT² reaction in Visible Lesioned (VL) reactors (slide 2);
- Lelystadt PPD detected significantly more VL reactors than Weybridge PPD, but no significant differences for other reactor types (slide 3);
- The percentage of VL animals appears to vary significantly with tuberculin type for animals with 3-4mm bovine-avian reactions (slide 4);
- There is no statistically significant difference in the number of reactors at the disclosing test (slide 5);
- The average (unadjusted) number of reactors disclosed per animal tested appears to vary across SVS Regions and Animal Health Offices (slides 6 and 7);
- The number of confirmed new incidents detected at slaughterhouse has not changed significantly since October 2004 (slides 8 and 9);
- It is absolutely clear that the bTB test must be conducted properly to be effective, since the potential impact calculated from Vet Net data of a 1-2mm reduction in the bovine minus avian PPD reaction difference will have a marked effect on detection (a 2mm difference in swelling will mean 24% of incidents are missed or detected later); and,
- The VLA view is that the Lelystadt product is marginally less potent than the current Weybridge product but may be more specific. Their view is that it is not sub-standard, is in the normal range seen between batches of PPD from whichever manufacturer, and it has passed the relevant potency tests (slides 10 and 11).

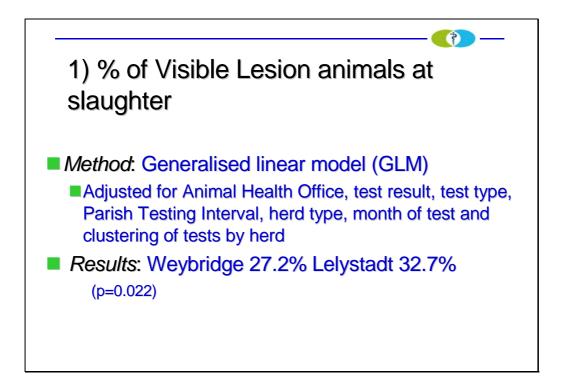
² Single Intradermal Cervical Comparative Test

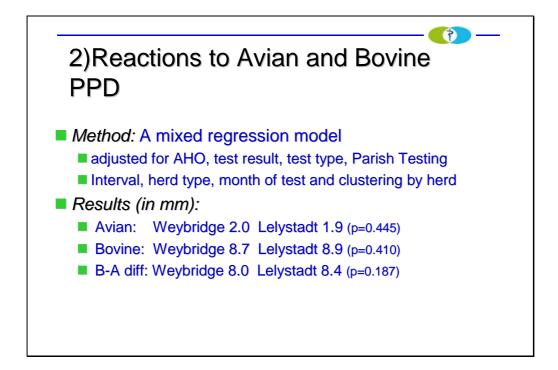
*The comparison of the tuberculin data indicates to date that the proportion of visible lesion animals taken in the TB control programme differs significantly between summed Weybridge and Dutch PPD batches, with the Weybridge results having a smaller % of VLs.

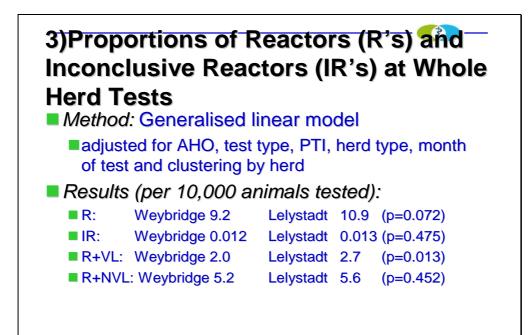
This can be interpreted in two ways. 1) the sensitivity of the combined Dutch PPDs is less because of failing to pick up NVLs, (animals which could be in the early stage of disease), which may or may not be confirmed with culture, to the same extent as the Weybridge PPDs. This would result in underdetection of cases, resulting in a transcient decline in cases reported, despite there being no true decline in cases. 2) the specificity of the Dutch PPDs is better than the Weybridge PPDs. This would result in fewer false positive reactions and so fewer unconfirmed incidents. In this case, any decline in confirmed incidents would be real and not due to under-detection.

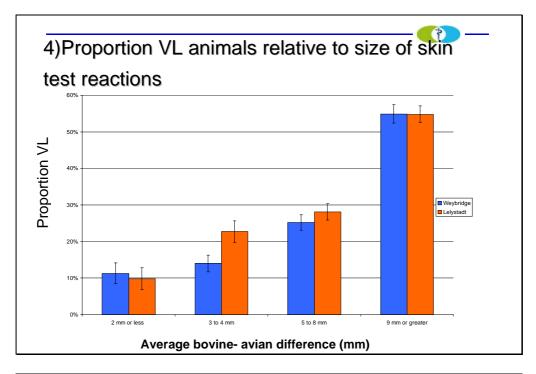
The data that we have gives some indication that there are subtle differences in performance between the Dutch and current Weybridge PPDs (suggesting that the Dutch bovine/avian PPD combination is not so good at detecting infection), which suggests that 1) rather than 2) is the case. However, at this time the data are slight.

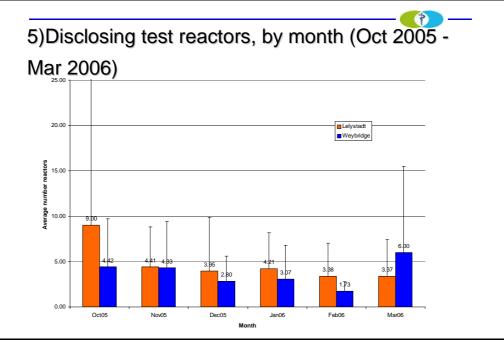
Detailed results are presented below:

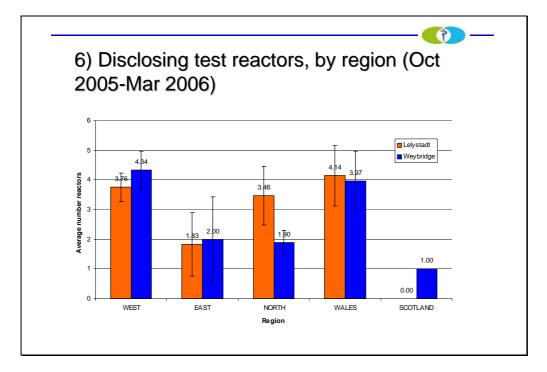


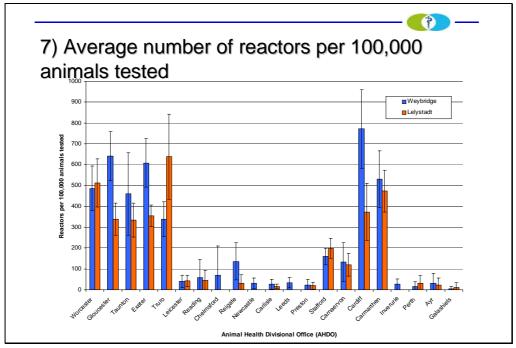


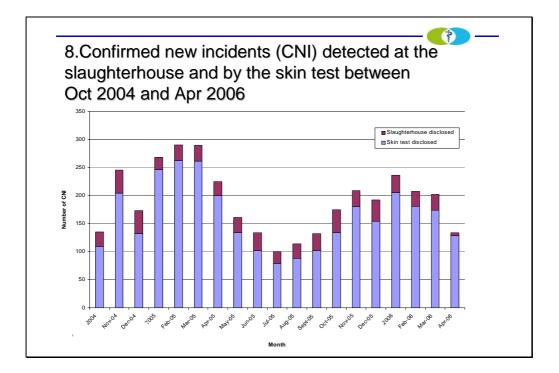


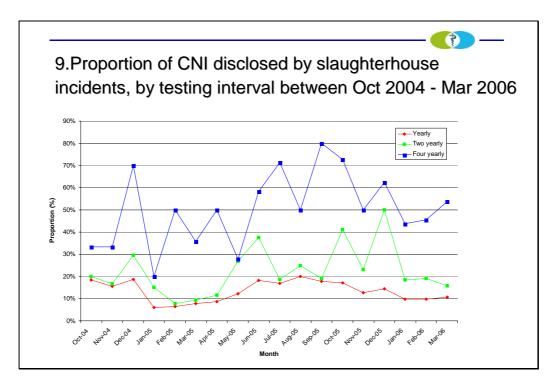


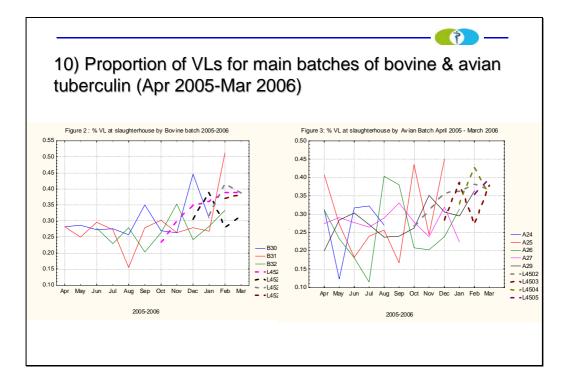


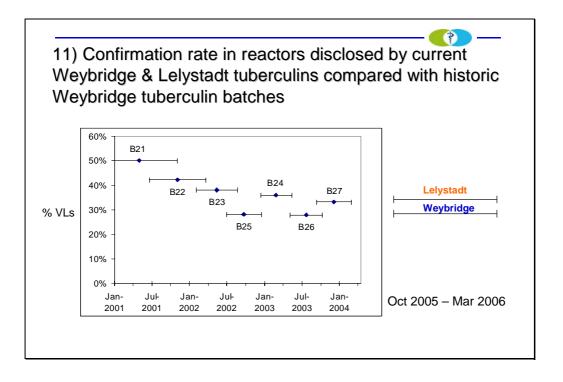












Annex D - additional VLA analyses requested at the Chief Scientific Adviser's meeting on 17 July

Following discussion on the possible causes of the reduction in number of new TB incidents, further analyses were carried out to explore if changes in parish test intervals and test types might be distorting the figures.

Number of reactors taken at the *start* of each confirmed new incident (CNI) disclosed between October 2005 and March 2006, by disclosing test

Summary

Overall, the average number of reactors taken at the disclosing test for CNI disclosed between October 2005 and March 2006 was 3.6 (standard deviation: 4.8), significantly less than the average (4.4 S.D: 6.7) for CNI disclosed between October 2004 and March 2005 (P < 0.001) (Table 1).

However, when comparing the average number of reactors taken by disclosing test type between the two six-month time periods, these differences were generally not significant, except for CNI disclosed by twelve-month contiguous tests (VE-CON12; relative change in mean: -39%; P = 0.01) and reactors taken at the first whole herd test following the disclosure of a slaughterhouse case (relative change in mean: -46% P = 0.02). For routine herd tests, difference in average number of disclosing test reactors taken was borderline significant (VE-RHT; relative change in mean: -44%; P = 0.05). (Table 1).

Data source

Data were extracted from Vetnet on 20 July 2006 (last test date recorded on 4^{th} July 2006).

Time frame: two six-month time periods were compared for CNI disclosed between October 2004 to March 2005 and October 2005 to March 2006 (inclusive).

Findings

The average number of reactors taken at the disclosing test was examined for the most frequently recorded test types (on Vetnet) for CNI commencing between CNI between October 2005 and March 2006 (inclusive) as compared with that CNI disclosed between October 2004 and March 2005 (Table 1).

Overall, the average number of reactors taken at the disclosing test for CNI disclosed between October 2005 and March 2006 was 3.6 (SD: 4.8), significantly less than the average for CNI disclosed between October 2004 and March 2005 (4.4 S.D: 6.7; P < 0.001).

Although, the average number of reactors taken by disclosing test type was generally lower for CNI disclosed between Oct 2005-March 2006 compared with that one year earlier, these differences were not significant at the 5%-

level, except for CNI disclosed by twelve-month contiguous tests (VE-CON12; -39%; P = 0.01) and reactors taken at the first whole herd test following the disclosure of a slaughterhouse case P = 0.02). For routine herd tests, difference in average number of disclosing test reactors taken was borderline significant (VE-RHT; -44%; P = 0.05).

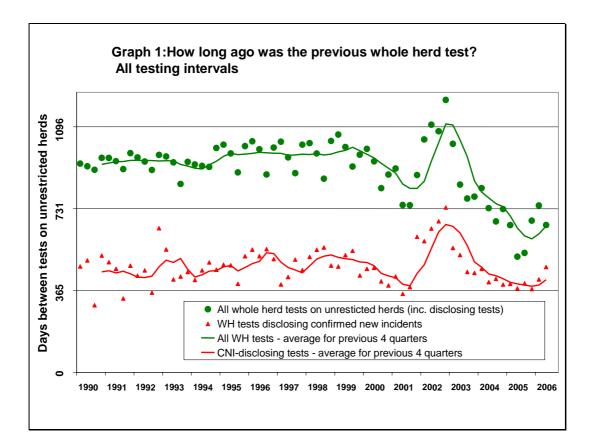
Numbers of			Number of reactors per confirmed incident				
Disclosing test type ^{1,2}		Reactors taken	Mean (standard deviation)			P-value for	
	Confirmed new incidents		Oct 2005 – Mar 2006	Oct 2004 – Mar 2005	Change in mean (%)	significance of difference between means	
VE-WHT	312	1,244	3.99 (4.40)	4.24 (7.66)	-6.0%	0.61	
VE-6M	224	1,079	4.82 (5.31)	5.57 (5.88)	-13.5%	0.15	
VE-SLH ²	198	405	2.05 (5.35)	3.76 (8.74)	-45.6%	0.02	
VE-IR	142	227	1.60 (1.77)	1.92 (1.85)	-16.6%	0.12	
VE-12M	125	639	5.11 (5.67)	6.32 (8.41)	-19.1%	0.16	
VE-CON	61	352	5.77 (6.90)	5.14 (5.32)	12.2%	0.54	
VE-CON12	51	133	2.61 (2.51)	4.27 (4.87)	-38.9%	0.01	
VE-RHT	34	79	2.32 (2.36)	4.15 (5.23)	-44.0%	0.05	
VE-CON6	25	103	4.12 (4.63)	5.32 (7.44)	-22.6%	0.48	
VE-CT	20	81	4.05 (3.80)	2.72 (2.30)	+49.0%	0.16	
VE-WHT2	7	21	3.00 (3.00)	5.67 (6.30)	-47.1%	0.23	
Other	45	107	2.38 (2.32)	2.44 (2.82)	-2.7%	0.91	
Total	1,244	4,470	3.59 (4.83)	4.36 (6.68)	-17.6%	<0.001	

Table 1. Average number of reactors at the start of each CNI disclosed between October2005 and March 2006 (inclusive) by disclosing test type

^{1,2}VE-WHT: whole herd test; VE-6M: six-month test ²VE-SLH: slaughterhouse disclosed breakdown: refers to reactors taken at the first whole-herd test *following* disclosure of a slaughterhouse case; VE-IR: IR-retest: reactors taken at disclosure test of an individual animal test, predominantly IR retests, but also includes tests such as tracing tests (VE-TR) and private tests (VE-PRI); VE-12M: twelve month test; VE-CON: contiguous herd test; VE-CON12: contiguous herd test (twelve-month); VE-RHT: routine herd test; VE-CON6: contiguous herd test (six-month); VE-CT: check-test; VE-WHT2: whole-herd test (twenty-four months)

<u>Graphs 1 and 2</u> show that annual testing has increased substantially over the years, especially from 2004. This can be seen in the reduction in days between routine herd tests (Graph 1). Importantly, the proportion of Confirmed New Incidents (CNI's) in yearly tested parishes has increased steadily since FMD, indicating that increases in testing have been targeted at the correct areas (Graph 2). The absolute number of CNIs has decreased in

2006 despite the increase in testing. So, although the rates will tend to overemphasise the reduction in TB cases, there is an absolute decline.





Graph 2: Number of confirmed new incidents recorded on VetNet in previous12 months, according to parish testing interval in force (current and in first quarter of 2002). Note – there can be a delay of 3 to 6 months in confirming an incident

