2017 NATIONAL BOVINE TUBERCULOSIS ERADICATION PROGRAM UPDATE

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ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY SERVICES
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Topics Included

▪ TB occurrences in U.S. in 2017, program status

▪ Status of Gamma interferon test

▪ Status of DPP

▪ Outcomes of TB Summit
Bovine TB Program Update
National TB Prevalence/Incidence 2017

- 10 new affected herds / 913,000 total US cattle herds
  = .00001 or .001% or 10 : 1 million herds

- This is great, right? ...or is it?
  ...where are these few new cases coming from?
Percentage of U.S. Cattle Responding to the Skin Test, 1917 - 2017

Affected Cattle and Cervid Herds, FY 1987-2017
Affected Herds, By State, FY 1998-2017

149 herds - 63% beef, 29% dairy, 1% mixed, 7% captive cervid
Affected Herds, By State, FY1998-2017\(^1\), Without Michigan Herds

\(^1\)75 herds – 49% beef, 39% dairy, 3% mixed, 9% captive cervid

*TB detected in 2007 or later for the first time in many years
How do we find bTB-affected herds? (FY 2003 to 2017)

Case findings (112 Total)

1) High Risk Area on-farm testing in MI/MN

2) Epidemiologic tracing

3) Slaughter trace back

4) Routine on-farm testing outside MI/MN

11/15/2017
Hurdles to U.S. TB Eradication

- Pockets of wildlife infection
- Undetermined sources of infection (New WGSs?, human transmission?)
- Annual introduction from Mexican feeders & “ropers”, and undocumented movement of Mexican origin “ropers” from state to state
- Non-uniform detection at slaughter plants
- Poor animal ID/Traceability/correlation at slaughter
- Changes in cattle production: larger herds, heifer raisers, recipient suppliers
- Decreased regulatory budgets
## FY 2016 Affected Herds

<table>
<thead>
<tr>
<th>State</th>
<th>County</th>
<th>Herd Type</th>
<th>Size</th>
<th>Disclosed By</th>
<th>Herd Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>Alpena</td>
<td>Beef</td>
<td>81</td>
<td>Annual test</td>
<td>State Depop</td>
</tr>
<tr>
<td>MI</td>
<td>Oscoda</td>
<td>Beef</td>
<td>180</td>
<td>Annual test</td>
<td>Test &amp; remove</td>
</tr>
<tr>
<td>IN</td>
<td>Franklin</td>
<td>Beef</td>
<td>49</td>
<td>Slaughter</td>
<td>Depopulation</td>
</tr>
<tr>
<td>MI</td>
<td>Alcona</td>
<td>Beef</td>
<td>65</td>
<td>Trace/Epi</td>
<td>Test &amp; remove</td>
</tr>
<tr>
<td>MI</td>
<td>Alcona</td>
<td>Beef</td>
<td>215</td>
<td>Movement</td>
<td>Pending</td>
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</table>

11/15/2017
<table>
<thead>
<tr>
<th>State</th>
<th>County</th>
<th>Herd Type</th>
<th>Size</th>
<th>Disclosed By</th>
<th>Herd Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>Montmorency</td>
<td>Beef</td>
<td>175</td>
<td>Annual test</td>
<td>Test and remove</td>
</tr>
<tr>
<td>MI</td>
<td>Alpena</td>
<td>Dairy</td>
<td>300</td>
<td>Annual test</td>
<td>Test and remove</td>
</tr>
<tr>
<td>IN</td>
<td>Franklin</td>
<td>Beef</td>
<td>50</td>
<td>Area testing</td>
<td>Undetermined</td>
</tr>
<tr>
<td>NM</td>
<td>Eddy</td>
<td>Dairy</td>
<td>7000</td>
<td>Slaughter</td>
<td>Undetermined</td>
</tr>
<tr>
<td>SD</td>
<td>Harding</td>
<td>Beef</td>
<td>670</td>
<td>Slaughter</td>
<td>Depopulation</td>
</tr>
<tr>
<td>MI</td>
<td>Lake</td>
<td>Beef</td>
<td>10</td>
<td>Trace/epi</td>
<td>Depopulation</td>
</tr>
<tr>
<td>SD</td>
<td>Harding</td>
<td>Beef</td>
<td>403</td>
<td>Trace/epi</td>
<td>Test and remove</td>
</tr>
<tr>
<td>SD</td>
<td>Butte</td>
<td>Beef</td>
<td>60</td>
<td>Trace/epi</td>
<td>Test and remove</td>
</tr>
<tr>
<td>MI</td>
<td>Alcona/Alpena</td>
<td>Beef</td>
<td>40</td>
<td>Annual test</td>
<td>Test and remove</td>
</tr>
<tr>
<td>NM</td>
<td>Eddy</td>
<td>Dairy</td>
<td>6000</td>
<td>Epidemiology</td>
<td>Undetermined</td>
</tr>
</tbody>
</table>

*One large TX dairy remains on test and remove since 2015*
M. bovis Positive Cattle from Slaughter Surveillance, FY 2001–2017

1470 total cases including 60 in adult cattle; 410 cases in fed cattle including 309 cases (66%) in Mexican origin fed cattle
FY 2017 Slaughter Surveillance Cases

15 Histocompatible cases

13 Confirmed *M. bovis* cases

2 Not *M. bovis*

5 Adult cattle cases

1 NM dairy

1 CA dairy

3 to single SD beef

8 Fed cattle cases

3 MX (NL, YU, BCN), 2 MX (UNK)

2 MI, 1 AZ

11/15/2017
FY 2017 Slaughter Surveillance Cases (ID/Lesion Correlation)

15 Histocompatible cases

13 Confirmed *M. bovis* cases

2 Not *M. bovis*

8 Fed cattle cases

5 Adult cattle case

5 ID/Lesion match

4 ID/Lesion match, 2 no match, 2 no tissue
## Historical Slaughter ID/TB Lesion Correlation

<table>
<thead>
<tr>
<th>Year</th>
<th>Histo Comp Cases</th>
<th>No Match (wrong ID)</th>
<th>No Tissue</th>
<th>No ID</th>
<th>PCR (Neg) not M. bovis</th>
<th>Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>15</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2*</td>
<td>9 (69%)</td>
</tr>
<tr>
<td>2016</td>
<td>14</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>2015</td>
<td>12</td>
<td>0</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>2014</td>
<td>16</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>2013</td>
<td>29</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>12 (41%)</td>
</tr>
<tr>
<td>2012</td>
<td>16</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>3 (18%)</td>
</tr>
<tr>
<td>Totals</td>
<td>87</td>
<td>6 (7%)</td>
<td>21 (24%)</td>
<td>11 (13%)</td>
<td>19 (22%)</td>
<td>23 (26%)</td>
</tr>
</tbody>
</table>

*both matched, 73% match rate including these two
ID/Lesion correlation at slaughter efforts

- Working group formation
- Systematic DNA matching at NVSL to look for issues in absence of TB
- Development of training materials
TB Granuloma Submissions and Submission Rate, FY 2000 – 2017

*Extrapolated yearly total from first 3 quarters

19/15/2017
Granuloma Lesion Submission in “Top 40” Adult Cattle Slaughter Plants, October 1, 2016 – June 30, 2017

≥ 1 lesion/2,000 adult cattle slaughtered (33)
< 1 lesion/2,000 adult cattle slaughtered (7)
Live Animal Testing

SKIN TESTING, CATTLE AND BISON
GAMMA INTERFERON TESTING
CERVID SKIN AND SEROLOGY TESTING
Caudal Fold Testing (CFT) in Cattle and Bison, FY 2006-2017

FY 2017 partial year through August 31, 2017; 44 States reporting (missing states AL, FL, NY, NV, TN, WV), n=779,035 CFT tests administered. Source: Veterinary Services District Offices and SCS database.
Caudal Fold Test Response Fraction by State, Cattle and Bison, FY 2017¹

¹ n=779,035 CFT tests administered during October 1, 2016 – August 31, 2017. Missing state data = AL, FL, NY, NV, TN, WV. Source: Veterinary Services District Offices and SCS database.
Interesting Bovine TB cases Fiscal Year 2017

- Pending California dairy herd test
- New Mexico dairies
- South Dakota beef outbreak
- Indiana longhorn – and fed slaughter case
Pending California dairy test

Slaughter case at California plant, 6/28/2017
- DNA match of ear tag tissue with lesion tissue
- All cattle in slaughter lot were from the same dairy
- Dairy has approximately 4,200 head in milking herd
- Dairy under quarantine and surveillance of cull cows
- WGS of *M. bovis* isolate, unique, with closest match Mexican dairy cattle

Location of the dairy is southern California desert
- Highest heat index in the US
- California postponed testing until mid-October 2017
New Mexico dairies

Slaughter trace back from Texas plant, 12/6/2016, WGS unique isolate

TB infection confirmed in first dairy (Dairy #1, 5000 cows) by testing late January/early Feb 2017
  ▪ Additional slaughter case
  ▪ 16 TB compatible cows
  ▪ Sister dairy (Dairy #2, 4500 cows) tested negative

Second test of dairies early May 2017
  ▪ Dairy #1
    ▪ Additional 12 TB-compatible cows
    ▪ 44 TB-compatible calves 5-6 months of age
  ▪ Dairy #2
    ▪ No evidence of infection in cows after 3 tests
    ▪ 58 TB-compatible calves 5-6 months of age

Interesting part, apparent spread Dairy #1 to Dairy #2 via waste milk
South Dakota beef outbreak

3 adults slaughter cases within 1 week (early February 2017)
- Two different slaughter plants in Nebraska
- Traced back to two different feedlots in Nebraska and South Dakota
- Cows had entered feedlots in fall of 2016
- WGS, unique

All three traces lead to 640 head cow-calf herd in NW SD

Source herd was at calving time
- Very challenging to get depopulation accomplished quickly
- Depopulation completed early April 2017

Traces
- Excluding feeders, indemnity thus far for 465 animals, 71 herds, 13 states, about $455,000: AR (1), CO (21), IA (3), KS (5), MN (5), MO (1), MT (3), ND (3), NE (1), NM (3), SD (20), WI (2), WY (3)
- 2 cows found infected in 2 receiving herds in SD
  - These new TB-affected herds are under testing plans
Indiana Longhorns

Small herd found by area test, confirmed 12/26/2016
- Whole Genome Sequence related to cervid TB in 2009
- Owner has personal attachment to animals, under state quarantine

Trace of confirmed infected animal in found in Michigan herd
- Laboratory confirmed March 21, 2017
- Came by way of an Indiana roping-stock dealer

Slaughter case on 5/9/2017 at Texas slaughter plant. Closely matching IN stains of *M. bovis*
- Traced to group of roping steers in Arizona
- Still under investigation how connected to Indiana
Status of Gamma Interferon Test
Approved as supplemental test – either CCT or interferon gamma

Commercial test kit (Bovigam™) by ThermoFischer

Single tube of blood taken 3-30 days after CFT injection

Seven approved state labs: CA, CO, MI, NV, PA, TX, WA, and NVSL

Approved for use in cattle only

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1FY 2017 thru 9/27/2017. Source: CA, CO, MI, NV, TX, WA and NVSL; does not include tests performed in PA.
History of recent gamma interferon test problems

2002 to July 31, 2015, commercial gamma interferon kit utilization
  ▪ January 2015 – July 2015, detection, investigation and discovery of low activity lots (#201 and #301) of CSL PPD in commercial kits

August 1, 2015-August 31, 2016, non-kit implementation of ROW components of test including Lelystad PPD
  ▪ Very high and unexpected false-positive rate observed

September 1, 2016 to May 12, 2017, replacement of Lelystad PPD with an NVSL PPD
  ▪ Low and unexpected sensitivity observed in known TB-affected herds

May 13, 2017 to present, gamma interferon use suspended
  ▪ Activities underway to restore use of test at NVSL, Field Offices, and CHC
Major Components of Gamma Interferon Assay Studied at NVSL/ARS since January 2017

Antigens: PPDs and more specific M. bovis antigens
- IDVet, Lelystad, Spain, Perugia, VLA, NVSL, Observe, CSL, Polybatics
- Dilution studies, side-by-side comparisons
- End of October 2017 completion expected
- Field testing in TB-infected herds ongoing

ELISA assays for gamma interferon
- Prionics/Thermo-fisher ROW, IDVet, VMRD
- Side-by-side comparisons, dilution series, limits of detection
- Early October 2017 completion expected

Expected outcome
- Selection of best PPD and ELISA components for U.S. program use
In addition to working out laboratory parameters to optimize the test, program use of Gamma interferon will require setting a cutoff point that yields the best combination of sensitivity and specificity AND that corresponds to comparative cervical test (CCT) performance.

Evaluating SENSITIVITY of gamma interferon testing since March 2016
- U.S. TB-infected herds, continuing to the end of December 2017, and beyond
- CCT done in parallel with gamma
- PPDs have included Lelystad (2 serials), IDVet, Polybatics, and NVSL

Evaluating SPECIFICITY of gamma interferon testing
- Study of data from August 1, 2015 - August 31, 2016 where Lelystad was used in field. Compare result with sensitivity-appropriate cutoff
- Propose limited field specificity studies with TB-negative herds with potential data collection before 2018
Sensitivity of CCT and gamma interferon in 3 infected dairies since March 2016

<table>
<thead>
<tr>
<th>Follow-up Test</th>
<th>N$^1$</th>
<th>Cutoff</th>
<th>Sensitivity</th>
<th>Specificity$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT</td>
<td>952</td>
<td>Susp or React</td>
<td>77%</td>
<td>91%</td>
</tr>
<tr>
<td>γ Lely New</td>
<td>161</td>
<td>0.1</td>
<td>96%</td>
<td>50%</td>
</tr>
<tr>
<td>γ Lely Old</td>
<td>460</td>
<td>0.1</td>
<td>88%</td>
<td>73%</td>
</tr>
<tr>
<td>γ NVSL</td>
<td>270</td>
<td>0.1</td>
<td>54%</td>
<td>95%</td>
</tr>
<tr>
<td>γ IDVet</td>
<td>310</td>
<td>0.1$^3$</td>
<td>93%</td>
<td>72%</td>
</tr>
</tbody>
</table>

$^1$Only caudal-fold test positive cattle were tested with CCT and gamma. And not all animals received all follow-up tests. Sensitivity/Specificity based on visible lesions that were histocompatible

$^2$These are Tb-exposed cattle from infected herds; therefore, specificity is not what might be expected in free herds

$^3$Difference between bovine and avian optical densities is depicted for all gamma PPDs. IDVet specifies a different calculation (S/P ratio)
Receiver Operating Characteristic Curves of Comparative Cervical Test (CCT) Versus Gamma Interferon Testing with 4 PPDs, in 3 US Dairies Infected with Bovine Tuberculosis (March 2016 to June 2017)
Area Under Receiver Operating Characteristic (ROC) Curves* and 95% Confidence Intervals for 4 Different PPDs in Gamma Interferon Testing for Bovine Tuberculosis in 3 Infected US Dairies (March 2016-May 2017)

*Area under ROC curve. A measure of discriminatory ability of a test, in this case, to detect visible lesions of tuberculosis
Steps for releasing gamma interferon test for state laboratory and general use

Complete laboratory evaluations and selection of major test components
  ▪ Target October 2017

Field sensitivity/specificity studies to have confidence in cutoff point performance, and as compared with CCT
  ▪ Target December 2017

NVSL establishment of quality control parameters for major components of the test
  ▪ Target January 2018

NVSL coordination of purchasing and distribution of components
  ▪ Target January 2018

NVSL performance testing of outside laboratories
  ▪ Target March 2018
Status of Captive Cervid Testing Including DPP
Serological TB testing of cervids was implemented in February 2013

Testing is done using the DPP VetTB Assay

- Approved species are elk, red deer, white-tailed deer, fallow deer, and reindeer
- All testing is performed at NVSL
- Future validation for mule deer and sika deer is under consideration
Cervid Serological TB Testing

- 12,588 cervids have been tested in FY 2017
- 4 reactors have been necropsied in FY 2017
- Histopathology on the reactors were negative, 1 is pending and all cultures for M. bovis are pending
- 5 animals were euthanized or died without a 2nd DPP test and further histopathology and culture were negative.
Cervid Serologic TB Testing, FY 2017
Testing With DPP as Primary and Secondary Test

<table>
<thead>
<tr>
<th>Species</th>
<th>No. DPP Tests for each species</th>
<th>No. ( % ) 1st DPP Positive</th>
<th>No. ( % ) 2nd DPP Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elk</td>
<td>2630</td>
<td>9 (.34%)</td>
<td>2 (.08%)</td>
</tr>
<tr>
<td>Red deer</td>
<td>109</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>White-tailed deer</td>
<td>9578</td>
<td>8 (.08%)</td>
<td>1 (.01%)</td>
</tr>
<tr>
<td>Fallow deer</td>
<td>197</td>
<td>3 (1.5%)</td>
<td>1 (.51%)</td>
</tr>
<tr>
<td>Reindeer</td>
<td>74</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>12,588</strong></td>
<td><strong>0.16%</strong></td>
<td><strong>0.03%</strong></td>
</tr>
</tbody>
</table>

Note: All DPP results based on OD reader cut off points previously established. No DPP positive animals necropsied have cultured positive for *M. bovis*. 
## Cervid Serologic TB Testing, FY 2017

Testing With DPP as Primary and Secondary Test

<table>
<thead>
<tr>
<th>Species</th>
<th>No. of necropsies completed</th>
<th>No. of cultures with no growth completed</th>
<th>No. of cultures pending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elk</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Red deer</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>White-tailed deer</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Fallow deer</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Reindeer</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>9</strong></td>
<td><strong>5</strong></td>
<td><strong>4</strong></td>
</tr>
</tbody>
</table>
Cervid Skin testing, FY 2013-2017

Single Cervical Tests$^1$:
- FY 2017: 4,427, 40 Responders
- FY 2016: 2,086, 19 Responders
- FY 2015: 6,121, 43 Responders
- FY 2014: 6,049, 71 Responders
- FY 2013: 9,229, 160 Responders

$^1$ >90% states reporting
Outcomes of TB Summit

FORT COLLINS, CO

JULY 26-27, 2017
TB Summit Readout

July 26-27, 2017, Fort Collins, CO

Objectives:

▪ Identify needs, gaps, and barriers to eradication and control of bovine TB in U.S. cattle.

▪ Identify alternative approaches to indemnity and the indemnification process.

▪ Identify appropriate biosecurity measure that are protective against bovine TB and discuss methods of incorporating them nationally.

▪ Initiate discussions to create a path forward to improving conditions and removing roadblocks of the National TB Program.
Large group discussions – Major themes

- Risk of introduction from cattle of Mexican origin
- "Islands" of infection
- Heifer Raisers
- Indemnity
- Human to Animal or Animal to Human transmission
- Education
- Biosecurity guidelines: prevention of introduction and reducing spread on-farm
Discussion and Breakouts

▪ Panel Discussion
▪ Breakouts
▪ Indemnity
▪ Biosecurity
▪ Roles and Collaboration
Mark Schoenbaum
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