附件 1

Consumers Union®

May 1, 2012

Margaret Hamburg, Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Commissioner Hamburg:

USDA's announcement last week that a fourth case of bovine spongiform encephalopathy (BSE) has been identified in the United States, in a dairy cow in Central California, is a warning flag that current safeguards against BSE are not adequate and FDA should take additional steps to protect the health of animals and of the beef-eating public.

Consumers Union, the policy and advocacy arm of Consumer Reports, is concerned that if additional steps are not taken now, this deadly disease could circulate and amplify within U.S. cattle. FDA should immediately prohibit feeding bovine blood, poultry litter, and all brains and other "specified risk materials" to cows, as all of these could carry the BSE infective agent.

USDA has confirmed to news media that the current case is an "L-type" atypical strain of BSE.[1] FDA therefore must be especially vigilant, because this may well not be a "spontaneous" case, but rather may well have been infected through feed, and it may be particularly infectious in humans.

The L-type BSE strain has previously been identified in cattle in Europe[2] and in Canada.[3] This would suggest that the current case may have been contracted through feed.

Studies further suggest that the L-type BSE can infect humans, possibly even more easily than "classical" BSE. A study using humanized mice (mice genetically engineered to have brain prions like humans) suggested that L-type BSE could infect humans.[4] Another

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[1] Thompson, H. 2012. California BSE prion comes with a different twist. *Nature News Blog*, April 27. At: http://blogs.nature.com/news/2012/04/california-bse-prion-comes-with-a-different-twist.html

[2] Brown, P, McShane, LM, Zancusso, G and L Detwiler. 2006. On the question of sporadic or atypical bovine spongiform encephalopathy and Creutzfeldt-Jacob disease. *Emerging Infectious Diseases*, 12(12): 1816-1821. At: http://wwwnc.cdc.gov/eid/article/12/12/pdfs/06-0965.pdf

[3] Dudas, S et al. 2010. Molecular, Biochemical and Genetic Characteristics of BSE in Canada. *PLOS* One, At: http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0010638

[4] Kong, Q, et al. 2008. Evaluation of the human transmission risk of an atypical bovine spongiform encephalopathy prion strain. *Journal of Virology*, pp. 3697-3701.

also shown that either mice[12] or sheep[13] infected with BSE can transmit the disease to other mice or sheep via blood transfusion. Since milk replacer is fed to weaning animals, which appear to be more susceptible to BSE than older animals, FDA, as a preventive measure, should prohibit bovine blood products in cattle feed.

FDA should ban all ruminant brains, spinal cords, and other "specified risk materials" from animal feed, regardless of the age of the ruminant these materials come from.

As a further safeguard, FDA should prohibit all brains, spinal cords and other potentially risky "specified risk materials" in animal and pet food. In 2008, FDA banned brains and spinal cords from cattle older than 30 months, in animal and pet food. This ban was too narrow; it should include a broader range of risky materials, such as tonsils and eyes, including all the tissues FDA banned for human consumption in 2004.[14] Risky materials from younger cattle also should be prohibited in animal and pet food. In the United Kingdom, BSE has been found in at least 49 cows under 30 months of age.[15] Therefore FDA should extend the ban on risky materials to include such materials from all cattle, regardless of age.

We would appreciate having an opportunity to discuss these recommendations with you and your staff. Thank you for your consideration.

Sincerely,

Michael Hansen, Ph.D.
Senior Scientist

Jean Halloran
Director, Food Policy Initiatives

cc USDA Secretary Tom Vilsack

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and J.W. Ironside. 2004. Preclinical vCJD after blood transfusion in a *PRNP* codon 129 heterozygous. *Lancet*, 364: 527-528.

[12] Taylor, D.M., Fernie, K., Reichl, H.E. and R.A. Somerville. 2000. Infectivity in blood of mice with a BSE-derived agent. Letter to the Editor. *Journal of Hospital Infection*, 46: 78-79.

[13] Hunter, N., Forster, J., Chong, A., McCutcheon, Parnham, D., Eaton, S., MacKenzie, C. and F. Houston. 2002. Transmission of prion diseases by blood transfusion. *Journal of General Virology*, 83: 2897-2905.

[14] FDA. 2004. Interim Final Rule on Use of Materials Derived from Cattle in Human Food and Cosmetics. 69 FR 134, pp. 42256-42274. At: http://www.gpo.gov/fdsys/pkg/FR-2004-07-14/html/04-15881.htm

[15] http://vla.defra.gov.uk/vla/vla_ati_020205.htm

USDA

USDA, APHIS
BSE Surveillance Program Overview

Dean Goeldner
Senior Staff Veterinarian
Veterinary Services
Animal and Plant Health Inspection Service
U.S. Department of Agriculture
May, 2012

Safeguarding Animal Health

1

USDA

History of BSE Surveillance in U.S.

- Active BSE surveillance since 1990
- Enhanced surveillance from 2004 to 2006
  - One-time intensive effort
  - Over 800,000 animals tested
  - BSE prevalence determined to be very low
- Ongoing surveillance implemented in 2006

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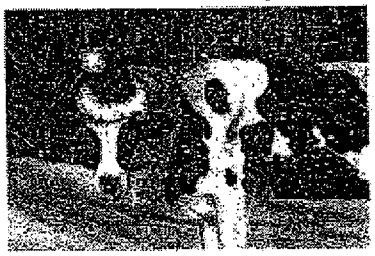
2

USDA

4 Positive BSE Findings in U.S.

- December 2003 – Washington State dairy cow imported from Canada
- Texas cow – 2005*
- Alabama cow – 2006*
- California cow – 2012*

*Note- the TX, AL, and CA cows were atypical, not classical, BSE.



USDA

Objectives of BSE Ongoing Surveillance

- Continue to assess and monitor change in BSE status of US cattle
- Provide mechanisms for detection of **one infected animal per million adult cattle with 95% confidence**
- Meet /exceed international surveillance practices recommended by the OIE

USDA

OIE

- Surveillance standards based on points that reflect likelihood of a BSE finding
- Surveillance designed to at minimum detect 1 case in 100,000 adult cattle with 95% confidence
- Countries with "large" cattle populations should accumulate ≥ 300,000 OIE points over a 7 year period (~42,857 OIE points per year)

World Organisation for Animal Health

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OIE Point Values for BSE Surveillance

AGE

SURVEILLANCE STREAM

Table 2. OIE point values for each surveillance stream, by cattle age

	Clinical suspect	Casualty slaughter	Fallen stock	Routine slaughter (Apparently healthy)
Age ≥ 1 year and < 2 years	N/A	0.4	0.2	0.01
Age ≥ 2 years and < 4 years	260	0.4	0.2	0.1
Age ≥ 4 years and < 7 years	750	1.6	0.9	0.2
Age ≥ 7 years and < 9 years	220	0.7	0.4	0.1
Age ≥ 9 years	46	0.2	0.1	0.0

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Points can be accumulated over 7 years

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BSE Ongoing Surveillance

- Target populations
  - ➢ All cattle with CNS signs (including rabies negatives cases)
  - ➢ Cattle >30 months of age
    - ❖ Condemned during antemortem inspection
    - ❖ Cattle without CNS signs but having clinical signs associated with BSE
    - ❖ Cattle sent to rendering or 3D/4D facilities

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BSE Ongoing Surveillance

Targeted cattle come from 4 sampling streams:

- ➢ On farm deaths
- ➢ Condemned at slaughter
- ➢ Renderers and 3D/4D operators
- ➢ Public health and veterinary diagnostic labs

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U.S. BSE Surveillance Summary

Fiscal year of sample collection	Total valid samples tested	Clinical Suspects	Casualty (Downer)	Fallen stock	Routine (healthy) slaughter	OIE points
2011	40,482	2,272	10,849	27,361	0	997,360
2010	44,301	2,375	13,099	28,827	0	948,593
2009	44,217	2,376	14,093	27,748	0	1,036,849
2008	43,145	2,442	14,224	26,479	0	1,121,624
2007	43,336	3,339	12,821	27,175	1	1,487,215
2006	314,801	1,416	20,703	272,778	19,904	775,126
2005	413,647	1,527	50,557	381,557	6	899,642
Total	943,929	15,747	136,346	771,925	19,911	7,266,410

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BSE Testing

- Obex collected and submitted in BSE kits provided by the National Veterinary Services Laboratory (NVSL)
  - Kits include submission and data collection forms
- Samples tested by ELISA at one of seven BSE-approved laboratories in the National Animal Health Laboratory Network (NAHLN)
- Sample material from inconclusive tests sent to the NVSL for confirmation

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Veterinary Services Laboratory Submissions (VSLS)

- Sample submitter or APHIS personnel enters surveillance submission and data collection information into VSLS system electronically on BSE VSLS webpage
- Testing laboratories enter test results into VSLS
- Test reports generated as needed (e.g., number of samples collected and tested reported monthly to Sec. of Agriculture and on APHIS website)

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Key Points about BSE Testing

- Testing does not protect human or animal health
  - SRM removal and feed bans do this *if* infectivity is present.
- Testing is for surveillance purposes
  - Some countries used tests to restore consumer confidence
    - Not science-based application of testing
- Extensive evidence suggests testing all animals is inefficient at finding cases
  - Not supported by epidemiological data
  - Expensive
  - Impractical in a *test-and-hold* situation
  - Poor surveillance yield

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BSE Mitigation Measures

Protection of human health

- Removal of SRMs at slaughter
- Ban on slaughter of non-ambulatory cattle
- Prohibition of air-injection stunning
- Additional process controls in advanced meat recovery systems
- Prohibition of mechanically separated beef

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BSE Mitigation Measures

Protection of animal health

- 1997 FDA Feed Ban: prohibits mammalian protein in ruminant feed
- 2008 FDA Feed Ban Enhancement: prohibits high-risk cattle material (brain and spinal cords) in all animal feed. Effective April 27, 2009; compliance date October 26, 2009

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Conclusion

- From FY 2007-11, no positive cattle were identified from surveillance designed to identify one infected animal out of a population of one million with 95% confidence
- BSE Ongoing Surveillance will continue to test from multiple surveillance streams to capture high risk animals
- US BSE surveillance is 10 times more sensitive than the OIE recommendations

USDA

Thank You

- Dean Goeldner, DVM
- Senior Staff Veterinarian
- USDA/APHIS-Veterinary Services
- 4700 River Road, Unit 43
- Riverdale, MD 20737
-
- telephone: 301-851-3511
- email: dean.goeldner@aphis.usda.gov

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Questions?

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17

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USDA, APHIS
BSE Response Plan

Lisa A. Ferguson, DVM
National Center for Animal Health Programs
U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services
May 9, 2012

USDA

History

- United States has had a BSE response plan in place since at least 1998.
- It has been utilized in previous BSE occurrences and has been updated several times.
- In response to the April, 2012 detection in California, the 2009 version of the response plan has been updated again (2012).

USDA

Initial Laboratory Response

- The BSE response begins when an inconclusive test result to an ELISA screening test is reported by an approved BSE testing lab.
- BSE test samples, including tissues for DNA comparison testing, are forwarded to the National Veterinary Services Laboratories (NVSL) in Ames, Iowa for confirmation.

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Test Result Confirmation

- NVSL uses Western blot and immunohistochemistry (IHC) as confirmatory tests.
- Upon confirmation by NVSL, including DNA matching of genetic material, actions progress to a full scale response.

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Initial Field Activities

- Field activities are conducted and coordinated jointly by Veterinary Services and State personnel.
- Carcass, identification devices and records are secured and preserved.
- Last farm of residence for the positive animal is visited to obtain further information (age, clinical and feed history, etc.).

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Incident Complexity Analysis Team

- An incident complexity analysis team is dispatched to assess the extent and complexity of the incident.

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Notifications

- Federal and State authorities
- Congress
- Stakeholders
- Media
- Public
- OIE (within 24 hours of confirmation)

Objective

- The objective of the BSE investigation is to trace at-risk cattle.

USDA

At-risk Cattle

- Animals that in their first year of life were housed with the positive animal during its first year of life and exposed to the same, possibly contaminated feed source; and
- Progeny born to the positive animal in the 2 years prior to the BSE diagnosis or onset of BSE signs.

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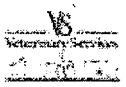

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Cattle of Interest

- At-risk cattle
- Potential at-risk cattle
- Cattle that cannot be distinguished from at-risk cattle

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Hold Orders and Quarantines

- BSE is not a contagious disease.
- A hold order or quarantine is initially placed on all cattle on the last premises of residence for the positive animal.
- The hold order or quarantine is modified as quickly as possible to apply only to cattle of interest.

USDA

Next Steps

- The investigation may lead to additional premises, additional at-risk cattle, additional cattle of interest and additional quarantines.
- At-risk cattle are depopulated and tested.
- Preferred carcass disposal is by incineration or alkaline digestion. Lined landfills may be used if regulations permit.

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Outcomes

- At-risk cattle are traced to the greatest extent possible.
- However, at some point the investigation will be terminated.

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Organization

- Field investigation is run from an Incident Command Post (ICP) in the State where the positive animal was identified.
- Incident Command System procedures allow for a flexible and scalable response as needed.
- Reports are sent daily to Regional and National staff and on to APHIS leadership.
- Regional and National staff provide support to the field investigation.

USDA

Feed Investigations

- Feed investigations are the responsibility of and conducted by the Food and Drug Administration's Center for Veterinary Medicine in conjunction with State authorities.
- Feeding histories obtained are shared with these authorities.
- Priority is placed on feed used during the first year of the positive animal's life.

USDA

Thank You

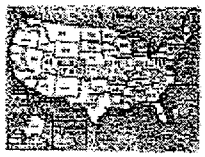
- Lisa A. Ferguson, DVM
- Deputy Director for Science and Technology
- USDA/APHIS-Veterinary Services
- 4700 River Road, Unit 43
- Riverdale, MD 20737
- telephone: 301-851-3301
- email: Lisa A. Ferguson@aphis.usda.gov

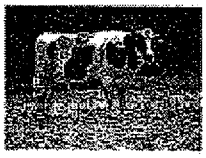
Questions?

Safeguarding Animal Health

USDA

Overview of the 2012 Bovine Spongiform Encephalopathy (BSE) Case in the United States





Jonathan Zack, DVM
Director, Preparedness and Incident Coordination
U.S. Department of Agriculture (USDA)
Animal and Plant Health Inspection Service (APHIS)
Veterinary Services (VS)
Emergency Management and Diagnostics (EMD)
May 9, 2012

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Sampling of the Cow

- April 18: Workers from a rendering company pick up the carcass of a Holstein cow.
  - Dead at a dairy farm in Tulare County, California.
- Routine brain (obex) sample collected as part of USDA BSE surveillance program.
  - Carcass held at rendering company transfer station.
  - Carcass did not complete the rendering process.

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Diagnostic Testing in California

- April 19: Obex sample delivered to the California Animal Health and Food Safety Laboratory (CAHFSL).
  - ➢CAHFSL located in Davis, California.
- Later on April 19: CAHFSL reported an "inconclusive" test result to USDA.
  - ➢Enzyme-linked immunosorbent assay (ELISA) BSE screening test used.

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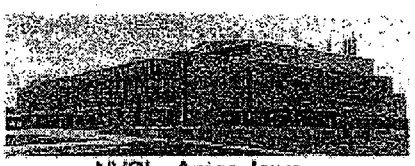
Shipment of Inconclusive Sample

- April 20: CAHFSL sent sample material to the USDA National Veterinary Services Laboratories (NVSL).
  - ➢Located in Ames, Iowa.
- April 21: Inconclusive sample material arrived at NVSL.
  - ➢Additional items also shipped to NVSL.
    - ❖Ear tags (collected by the renderer).
    - ❖Sample of hide containing a brand (registered to the Tulare County dairy).



NVSL–Ames, Iowa

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Diagnostic Testing at NVSL

- April 21: ELISA testing for BSE was positive.
- April 23: Immunohistochemistry (IHC) and Western blot (WB) testing were positive.
  - ➢Results indicated "L-type" (low-type) BSE, known as "atypical BSE" not "classical BSE".
- April 25: NVSL DNA genotyping matched branded hide, to tissue from ear tag, to positive obex sample.
  - ➢Confirms origin of cow – no errors were made in identifying the positive sample.

USDA

Investigation at Dairy of Origin

- Dairy records indicate cow was born in September 2001.
  - ➢10 years and 7 months old.
- Cow was pregnant, developed lameness, and was being treated.
  - ➢While undergoing treatment, she became recumbent (non-ambulatory).
  - ➢Cow was euthanatized on farm.

USDA

Locating "At-Risk" Cattle – Progeny in Last 2 Years

- Positive cow gave birth twice in the 2 years prior to illness/death.
  - ➢One calf born dead (stillborn).
  - ➢One calf, female, born alive and sold by dairy of origin.
- Progeny heifer was traced and located.
  - ➢BSE testing was negative.
  - ➢DNA genotyping is pending completion.

USDA

Locating "At-Risk" Cattle - Birth Cohort

- In first year of life, positive cow spent about 4 months on a calf ranch.
  - ➢No records from 10 years ago could be found for calf ranch.
- Inventory of cattle on the dairy of origin was completed.
- No at-risk birth cohort cattle have been found as of today.

USDA

Locating "At-Risk" Cattle - Birth Cohort (continued)

- Tracing of at-risk birth cohort cattle is continuing; looking for possible birth cohort cattle that left the herd of origin.
- A very small percentage of dairy cattle between 10-12 years old are likely to be alive at this time.
  - On average, North American dairy cows spend two and a half lactations in the milking herd (culled at 4.5 to 5 years of age)

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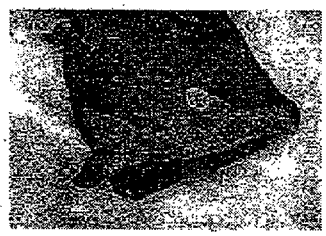
Disposal of Positive Carcass

- All material from the positive carcass, except the hide, was transported for disposal.
- Burial was in a secure hazardous waste disposal site in California.
- The hide is being held by California authorities.



Hide from the positive cow

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Feed Investigation

- April 26: Thorough investigation began into the feed associated with the positive cow.
- Investigation is ongoing, coordinated by the U.S. Food and Drug Administration (FDA) and feed authorities from the State of California.
- No immediate concerns have been identified to date.

Questions?

FDA BSE Feed Regulations

Entrance Conference for Taiwan Delegation
May 9, 2012

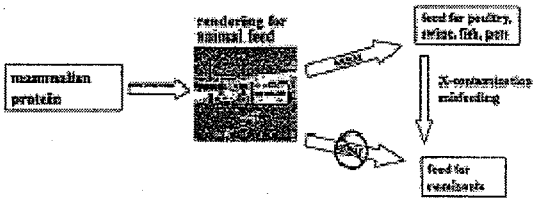
Bart Pritchett, DVM
FDA, Center for Veterinary Medicine
Division of Animal Feeds

Regulating Animal Feed

- FDA
  - Charged with enforcing the Federal Food Drug and Cosmetic Act
  - "Feed" means both human food and animal feed
  - Compliance with Federal laws is a requirement for interstate commerce and importation
- States
  - Cooperation through Association of American Feed Control Officials (AAFCO) to promote uniformity
  - FDA's work arrangements with states include contracts, partnerships, and cooperative agreements
  - 70% of FDA's feed inspection work is done by states under these types of arrangements

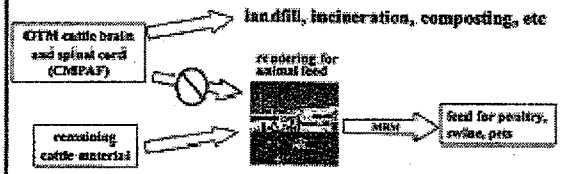
2

1997 BSE Feed Regulation (Feed Ban)



3

2008 Enhanced BSE Feed Regulation



2008 BSE Rule

- Published April 25, 2008
- Effective April 27, 2009
- Compliance Date: October 26, 2009
- Adds new section 21 CFR 589.2001 & amends 21 CFR 589.2000
- Prohibits for use in ALL animal feed the following material known as "cattle material prohibited in animal feed" (CMPAF):

Cattle Material Prohibited in Animal Feed (CMPAF)

- Brains and spinal cords from cattle ≥ 30 mos. of age
- Entire carcass of cattle not inspected and passed for human consumption
  - unless shown to be less than 30 months of age OR
  - brain and spinal cord removed
- Entire carcass of BSE-positive cattle, including tallow
- Tallow made from CMPAF that contains more than 0.15% insoluble impurities
- Mechanically separated beef made from CMPAF

Tallow Restrictions

- Tallow containing more than 0.15% insoluble impurities may no longer be used in feed for cattle

Source of tallow	Insoluble impurities Level	Feed use	Carryover statement required	Regulations
Any source (non-CMPAF or SRMs)	≤ 0.15%	Allowed in all animal feeds	None	21 CFR 589.2000 and 589.2001
Non-CMPAF	> 0.15%	Allowed in all but ruminant feeds	Do not feed to cattle or other ruminants	589.2000
CMPAF	> 0.15%	Not allowed in animal feed	Do not feed to animals	589.2000

7

Marking for Disposal

- CMPAF for disposal must be marked by an agent visible to the naked eye to indicate that it is not for use in animal feed
- The marking requirement does not apply to dead stock disposed of on the farm

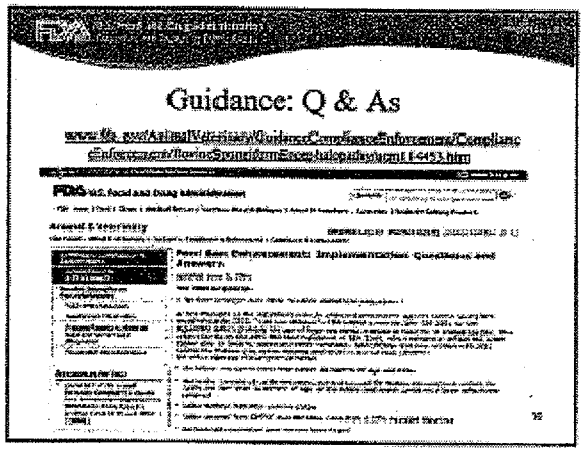
8

Impact on Renderers

- Major burden falls on rendering industry
  - Renderers that handle any cattle material must:
    - maintain records sufficient to demonstrate material rendered for use in animal feed does not contain CMPAF
  - Renderers that intend to render dead cattle for animal feed use must:
    - ensure that deads are under 30 months of age OR
    - ensure that brain and spinal cord are effectively removed
    - use separate equipment for handling CMPAF once it is removed
    - label materials containing CMPAF "Do Not Feed To Animals"
    - mark CMPAF with agent that is readily detected visually
    - maintain records sufficient to track CMPAF to ensure it does not enter animal feed
  - Comply with new restrictions on tallow

9

Guidance: Q & As



Guidance # 195

http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052419.pdf

#195

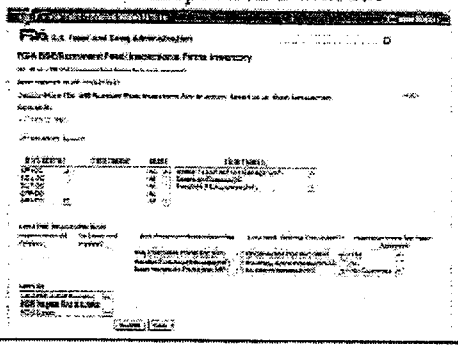
GUIDANCE FOR INDUSTRY

SMALL ENTITIES COMPLIANCE GUIDE FOR RENDERERS—SUBSTANCES PROHIBITED FROM USE IN ANIMAL FOOD OR FEED

Enforcement of the Feed Ban

- FDA and State Inspections
  - About 350 FDA HQ and field investigators
  - About 400 state inspectors
- More than 93,000 inspections since 1997
- ~ 8000 per year under current work plan
  - >70% conducted by state feed control officials
  - State inspection results submitted through FDA District BSE Coordinators
  - All inspections go into our FACTS database

Online Inspection Database



Feed Investigation of California BSE Case

- joint investigation by FDA and CDFA
- reviewed inspection history of rendering facility
  - inspected 12 times since 1998 (all NAI)
- identified firms that have supplied feed to dairy farm since 2001
- inspected each feed supplier
- reviewing inspection history of feed supplier for:
  - use of prohibited material
  - controls to prevent cross contamination

FDA BSE Feed Regulations

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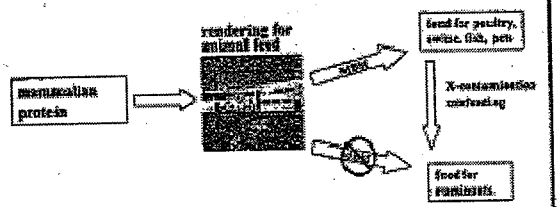

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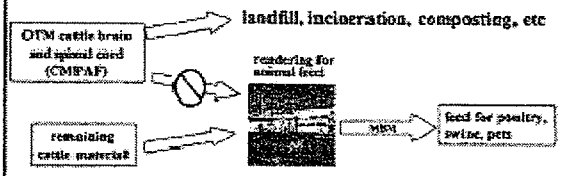

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- Effective April 27, 2009
- Compliance Date: October 26, 2009
- Adds new section 21 CFR 589.2001 & amends 21 CFR 589.2000
- Prohibits for use in ALL animal feed the following material known as "cattle material prohibited in animal feed" (CMPAF):

Cattle Material Prohibited in Animal Feed (CMPAF)

- Brains and spinal cords from cattle ≥ 30 mos. of age
- Entire carcass of cattle not inspected and passed for human consumption
  - unless shown to be less than 30 months of age OR
  - brain and spinal cord removed
- Entire carcass of BSE-positive cattle, including tallow
- Tallow made from CMPAF that contains more than 0.15% insoluble impurities
- Mechanically separated beef made from CMPAF

Tallow Restrictions

- Tallow containing more than 0.15% insoluble impurities may no longer be used in feed for cattle

Source of tallow	Insoluble Impurities Level	Feed use	Carriers statement required	Regulation
Any source (non-CMPAF or CNPAF)	≤ 0.15%	Allowed in all animal feeds	None	21 CFR §§9.3000 and §§9.3001
Non-CMPAF	> 0.15%	Allowed in all but ruminant feeds	Do not feed to cattle or other ruminants	§§9.3000
CMPAF	> 0.15%	Not allowed in animal feed	Do not feed to animals	§§9.3001

7

Marking for Disposal

- CMPAF for disposal must be marked by an agent visible to the naked eye to indicate that it is not for use in animal feed
- The marking requirement does not apply to dead stock disposed of on the farm

8

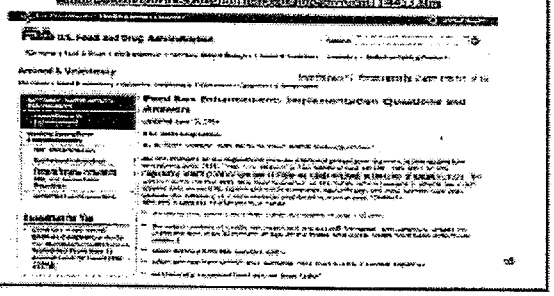
Impact on Renderers

- Major burden falls on rendering industry
  - Renderers that handle any cattle material must:
    - maintain records sufficient to demonstrate material rendered for use in animal feed does not contain CMPAF
  - Renderers that intend to render dead cattle for animal feed use must:
    - ensure that deads are under 30 months of age OR
    - ensure that brain and spinal cord are effectively removed
    - use separate equipment for handling CMPAF once it is removed
    - label materials containing CMPAF "Do Not Feed To Animals"
    - mark CMPAF with agent that is readily detected visually
    - maintain records sufficient to track CMPAF to ensure it does not enter animal feed
  - Comply with new restrictions on tallow

9

Guidance: Q & As

www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/BovineSpongiformEncephalopathy/ucm114453.htm



Guidance # 195

http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM050449.pdf

#195

GUIDANCE FOR INDUSTRY

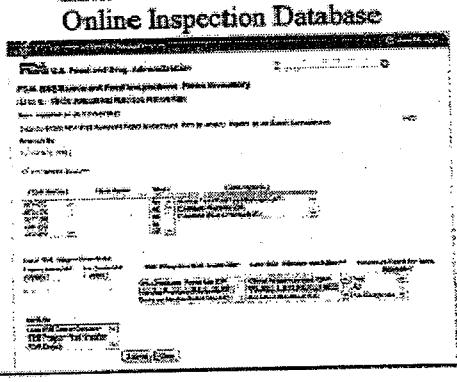
SMALL ENTITIES COMPLIANCE GUIDE
FOR RENDERERS—SUBSTANCES PROHIBITED FROM USE IN
ANIMAL FOOD OR FEED

Enforcement of the Feed Ban

- FDA and State Inspections
  - About 350 FDA HQ and field investigators
  - About 400 state inspectors
- More than 93,000 inspections since 1997
- ~ 8000 per year under current work plan
  - >70% conducted by state feed control officials
  - State inspection results submitted through FDA District BSE Coordinators
  - All inspections go into our FACTS database

12

Online Inspection Database



13

Feed Investigation of California BSE Case

- joint investigation by FDA and CDFA
- reviewed inspection history of rendering facility
  - inspected 12 times since 1998 (all NAI)
- identified firms that have supplied feed to dairy farm since 2001
- inspected each feed supplier
- reviewing inspection history of feed supplier for:
  - use of prohibited material
  - controls to prevent cross contamination

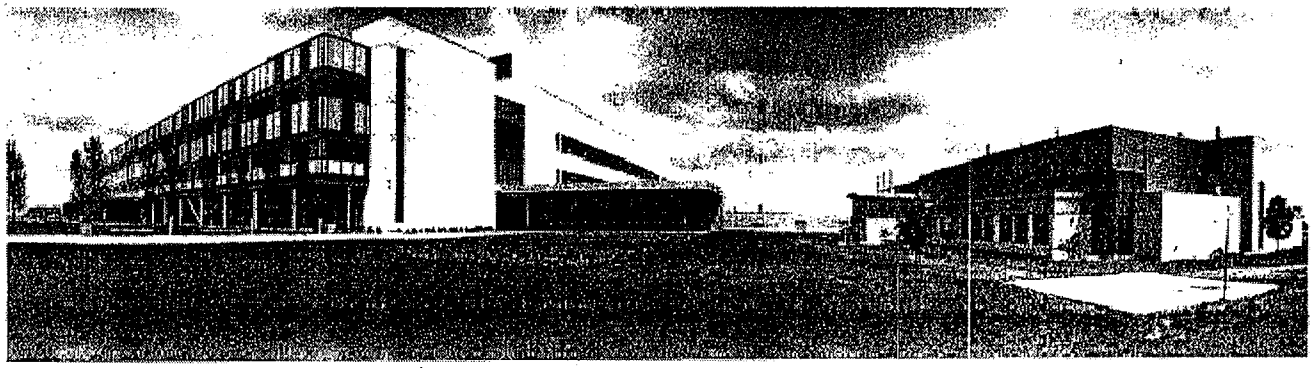
14

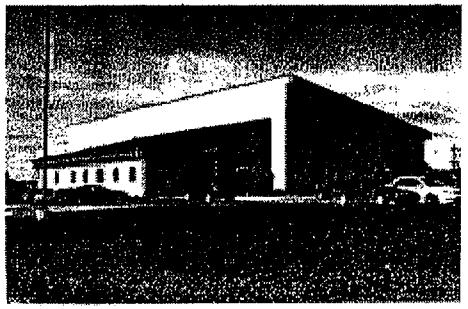
USDA

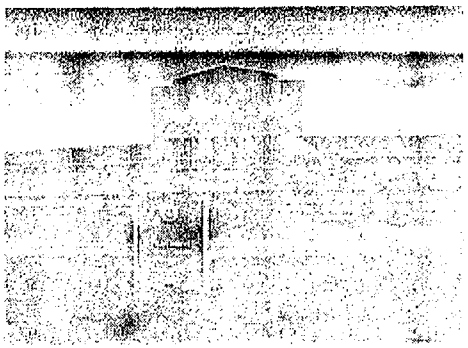
附件 3

National Veterinary Services Laboratories

Beth Lautner, D.V.M., M.S.
Director, National Veterinary Services Laboratories
Veterinary Services, Animal and Plant Health Inspection Service
May 10, 2012







USDA

NCAH
National Centers for Animal Health

National Veterinary Services Laboratories (NVSL), APHIS
Employs ~ 280

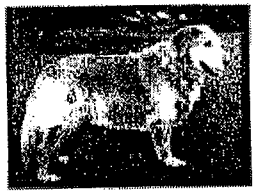
Center for Veterinary Biologics (CVB), APHIS
Employs ~ 205

National Animal Disease Center (NADC), ARS
Employs ~ 320

Together we meet the national needs for animal health research, diagnosis, and product evaluation.

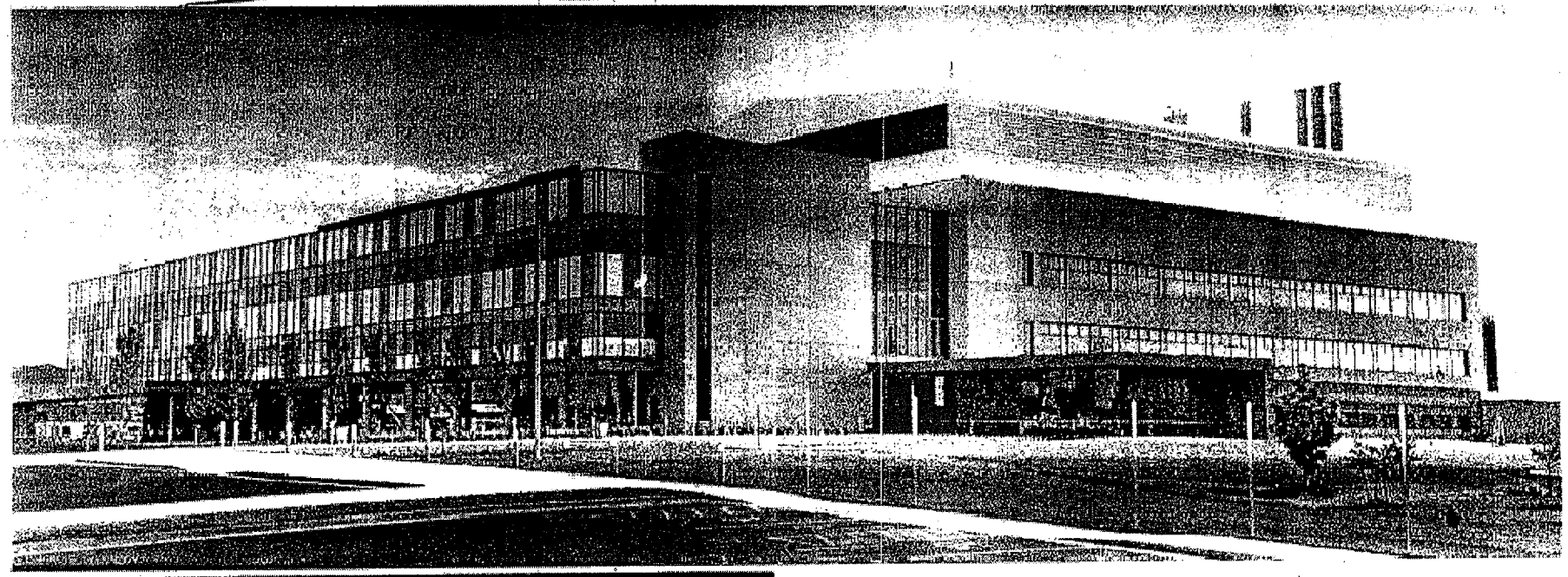


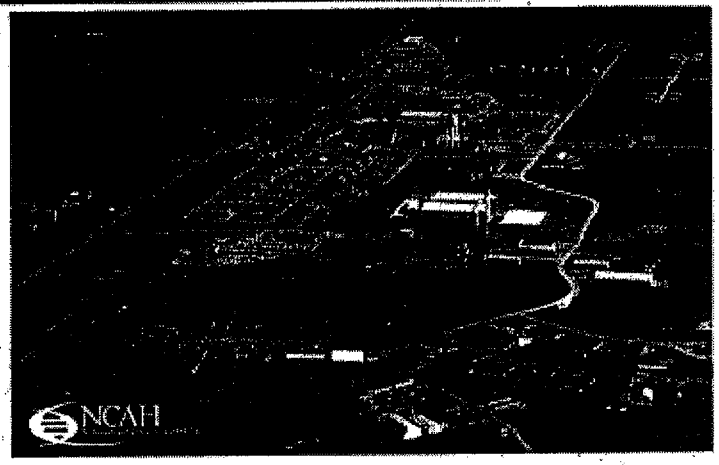


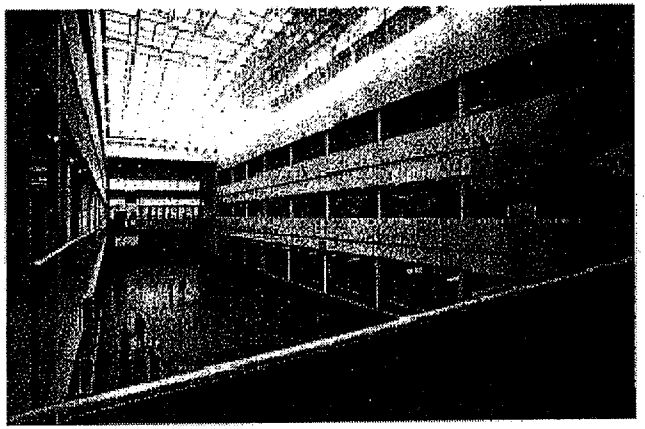


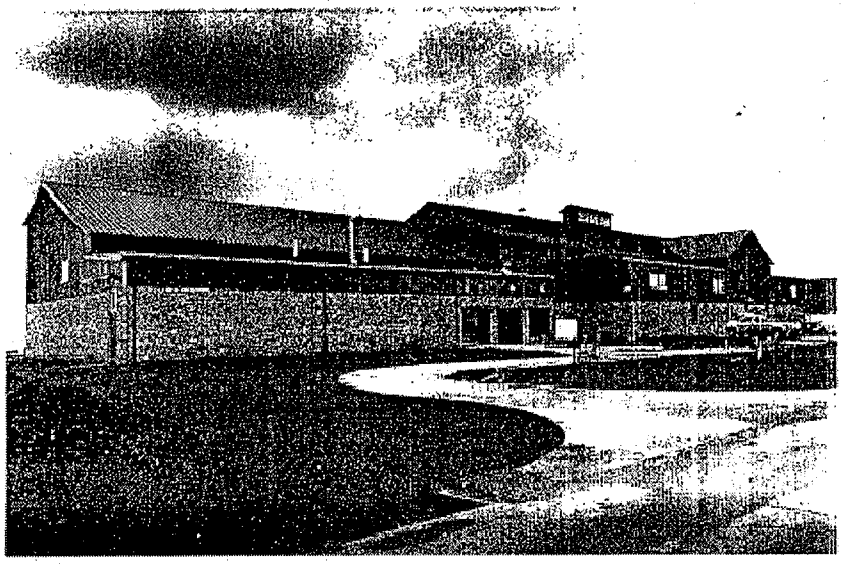

NCAH
National Centers for Animal Health

USDA

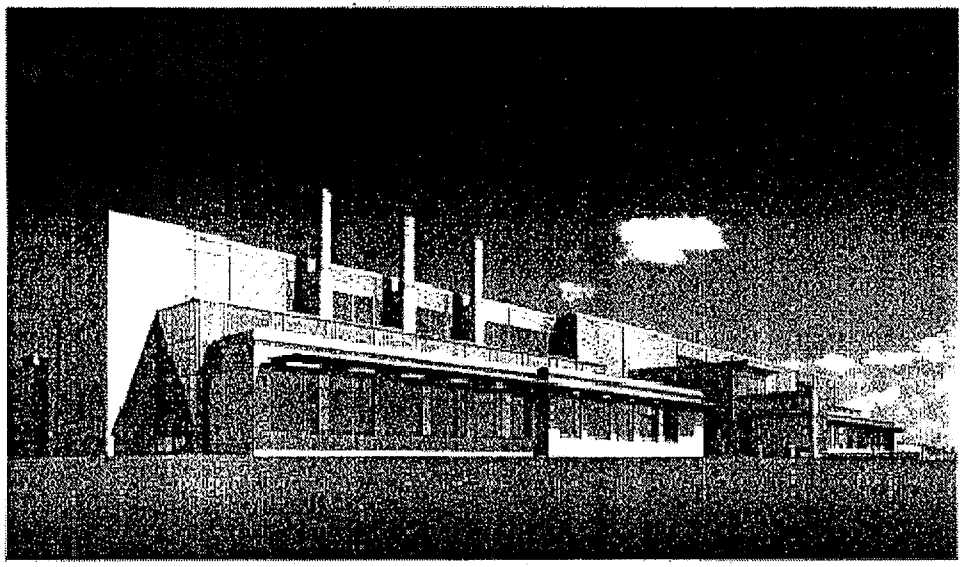








Low containment animal facility--2009



Phase 1 laboratory facility--2004

High containment animal facility--2007

NVSL Mission

- To safeguard U.S. animal health and contribute to public health by ensuring that timely and accurate laboratory support* is provided by a nationwide animal health diagnostic system.
  - Reference and confirmatory laboratory for USDA

FY11 – > 66,000 accessions and 533,000 tests approved.

* Includes both domestic and foreign animal diseases

NVSL Activities

- Conduct diagnostic testing
- Coordination of the National Animal Health Laboratory Network (NAHLN)
- Supply reference reagents to other laboratories
- Provide training in diagnostic techniques
- Conduct proficiency testing of other laboratories
- Conduct developmental projects to improve diagnostic techniques for diseases of significance
- Participate in World Organization for Animal Health (OIE) Collaborating Centre for the Diagnosis of Animal Diseases and Vaccine Evaluation in the Americas with CVB and Iowa State University
- Serve as OIE reference laboratory
  - high pathogenicity avian influenza, anthrax, pseudorabies, bluetongue, contagious equine metritis, equine encephalomyelitis, equine infectious anemia, leptospirosis, Newcastle disease, swine influenza, vesicular stomatitis and West Nile encephalitis

NVSL Structure

Laboratories

- Diagnostic Bacteriology Laboratory
- Diagnostic Virology Laboratory
- Pathobiology Laboratory
- Foreign Animal Disease Diagnostic Laboratory

Director's Office

- National Animal Health Laboratory Network
- Quality Assurance – ISO 17025 accreditation
- Calibration Laboratory

Program and Administrative Services

- NVSL program budget and user fees

Laboratory Resources Unit

- Shipping and receiving, biologics repository, warehouse, glassware, media prep

Administrative Unit

- NCAH Budget, Human Resources and Training, Procurement

Diagnostic Bacteriology Laboratory

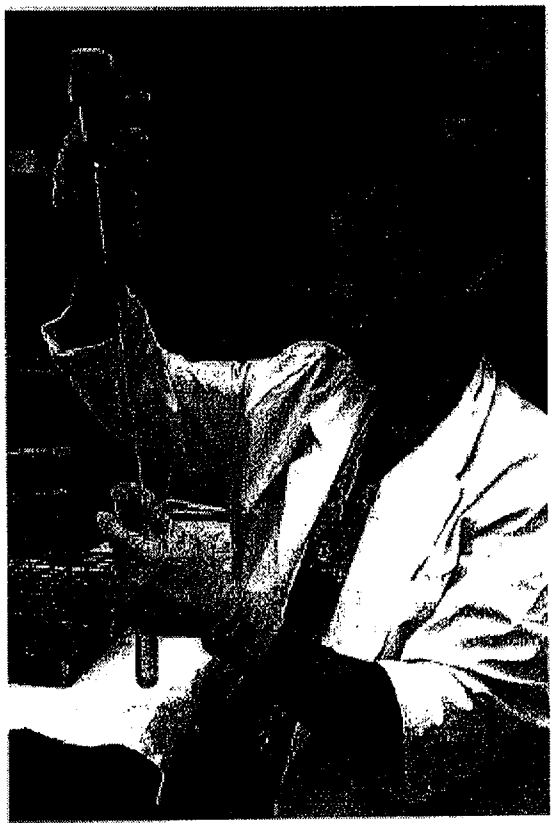
Dr. Matthew Erdman, Director

- Serology Section
  - Dr. David Kinker
- Bacterial Identification Section
  - Vacant
- Mycobacteria & Brucella Section
  - Dr. Suelee Robbe-Austerman

Diagnostic Bacteriology Laboratory

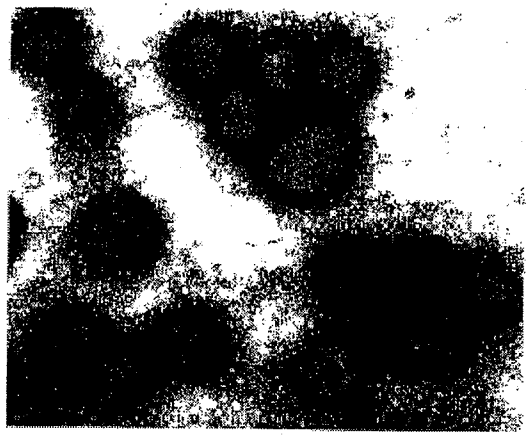
Partial List of Testing Capability

- Brucellosis
- Bovine tuberculosis
- Johne's disease
- Anthrax
- Salmonellosis
- Leptospirosis
- Contagious equine metritis
- Piroplasmosis
- Genotyping



Diagnostic Virology Laboratory
Dr. Beverly Schmitt, Director

- Avian Viruses Section
  - Vacant
- Bovine, Porcine & Aquaculture Viruses Section
  - Dr. Sabrina Swenson
- Equine/Ovine Viruses Section
  - Dr. Eileen Ostlund



Diagnostic Virology Laboratory

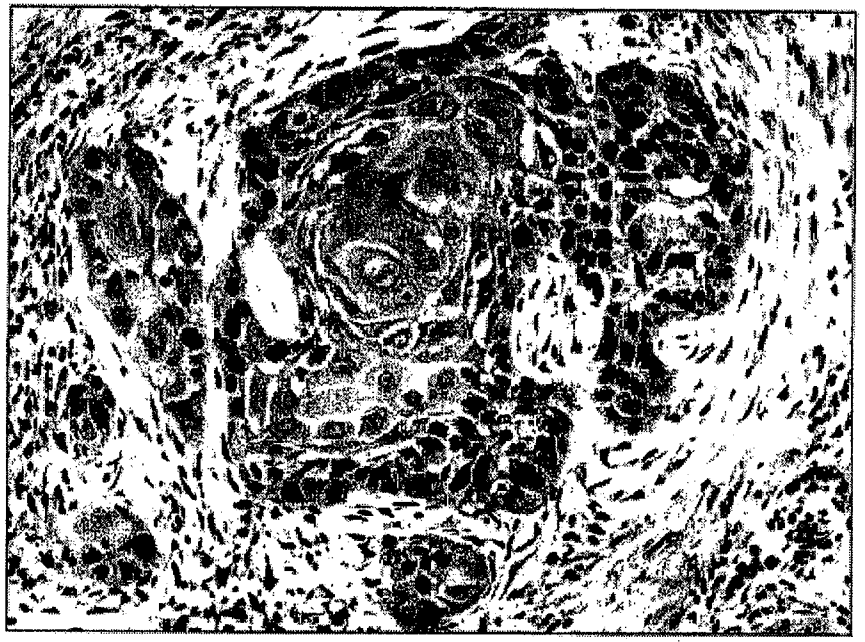
Partial List of Testing Capability

- Avian influenza
- Newcastle disease
- Pseudorabies
- Equine encephalomyelitis (Eastern, Western, Venezuelan)
- West Nile encephalitis
- Bluetongue
- Infectious salmon anemia
- Spring viremia of carp
- Equine infectious anemia

Pathobiology Laboratory

Dr. Arthur Davis, Director

- Pathology, Parasitology and Entomology Section
  - Dr. Mark Hall
- Chemistry and Analytical Services Section
  - Dr. Walter Hyde



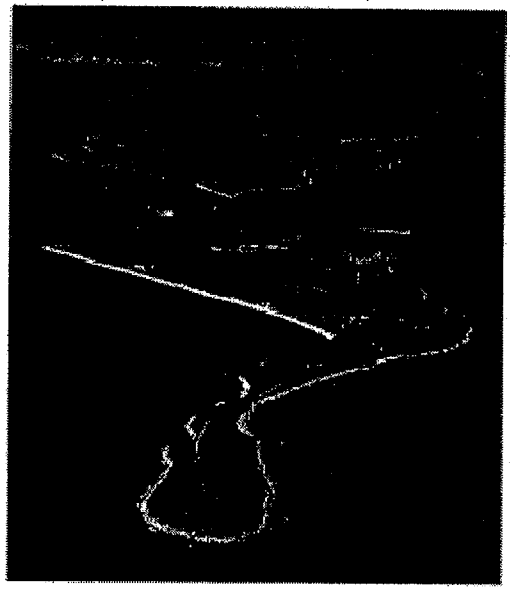
Pathobiology Laboratory

Diagnostics

- Bovine Spongiform Encephalopathy
- Scrapie
- Chronic Wasting Disease
- Bovine Tuberculosis
- Screwworm myiasis
- Tick identification

Foreign Animal Disease Diagnostic Laboratory

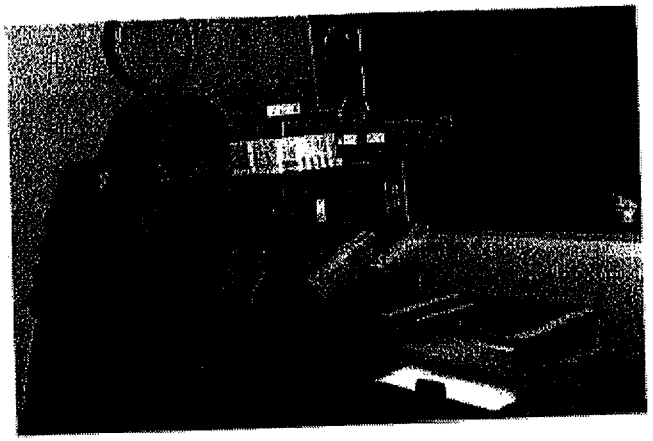
- Diagnostic Services Section
  - Dr. Fernando Torres-Velez
- Reagents and Vaccine Services Section
  - Dr. Wei Jia
- Proficiency and Validation Services Section
  - Dr. Mike McIntosh



Foreign Animal Disease Diagnostic Laboratory

Partial Listing of Testing Capability

- Foot and mouth disease
- Classical swine fever
- African swine fever
- Vesicular stomatitis



USDA

Quality Assurance

NVSL was the first laboratory in the world to be accredited to veterinary ISO 17025 standards by the American Association for Laboratory Accreditation (A2LA).

ISO International Organization for Standardization

ISO/IEC 17025 is the international standard for testing and calibration laboratories.

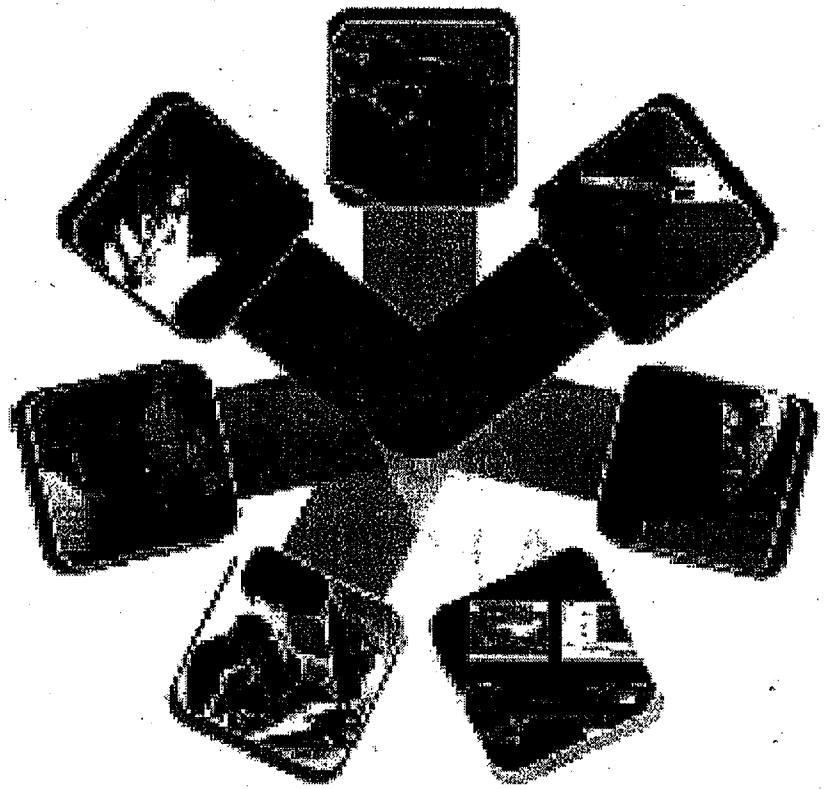
e91

Websites

- National Veterinary Services Laboratories
  www.aphis.usda.gov/animal_health/lab_info_services

- National Animal Health Laboratory Network
  www.aphis.usda.gov/animal_health/nahln

NAHLN Overview



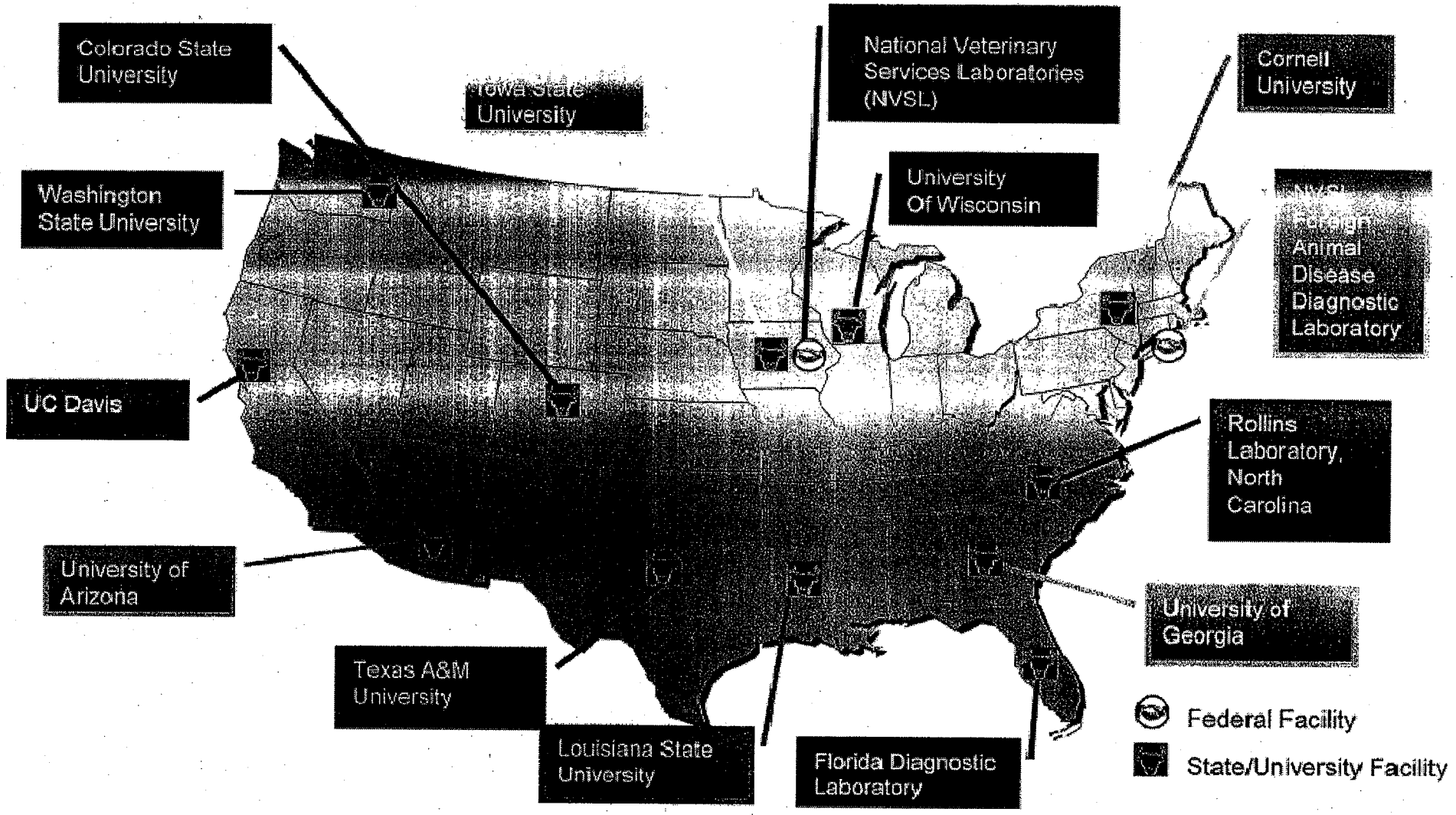
Barbara Martin, M.S.
NAHLN Coordinator
National Veterinary Services
Laboratories

National Animal Health Laboratory Network

- Formed in 2002
- Is a group of State funded veterinary diagnostic labs that deal with diseases of animals including endemic, exotic, zoonotic, and emerging diseases
- Is a **partnership** between:
  - **USDA**
    - Animal and Plant Health Inspection Service (APHIS)
    - National Institute of Food and Agriculture (NIFA)
  - **American Association of Veterinary Laboratory Diagnosticians** (AAVLD)
  - **NAHLN Laboratories**

The original 12 NAHLN laboratories

USDA



491

USDA

The Purposes of NAHLN

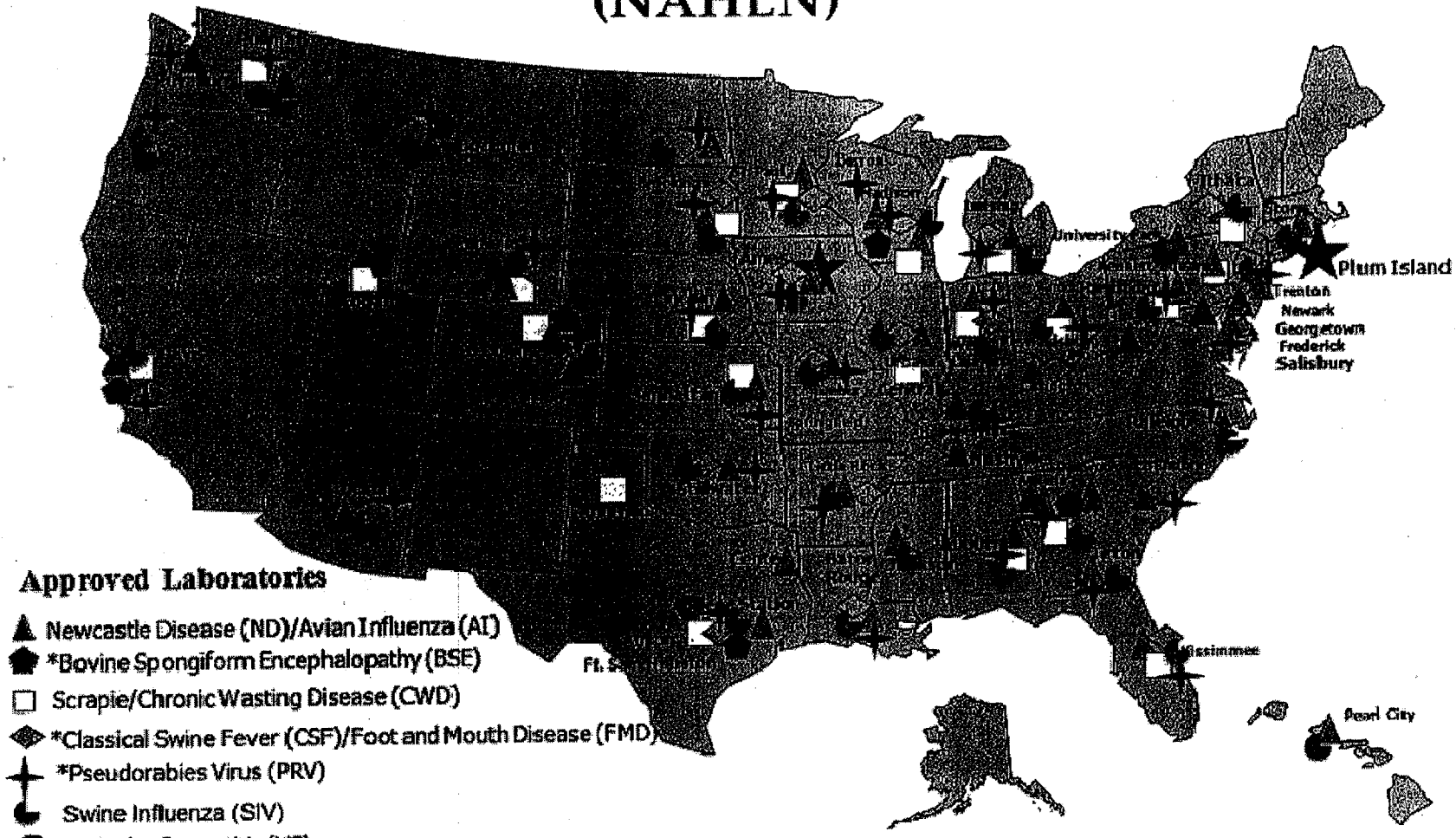
- Early detection
  - Targeted surveillance based on population density & risk
- Rapid response
  - Surge capacity to test outbreak samples
- Appropriate recovery
  - Large numbers of samples tested to show freedom

Founding Principles and Quality Requirements

- Quality standards
- Competency of laboratory personnel
- Standardized protocols and equipment
- Adequate biosafety/biosecurity
- Secure electronic communications and reporting
- Assessment of preparedness through scenario testing

USDA

National Animal Health Laboratory Network (NAHLN)



Approved Laboratories

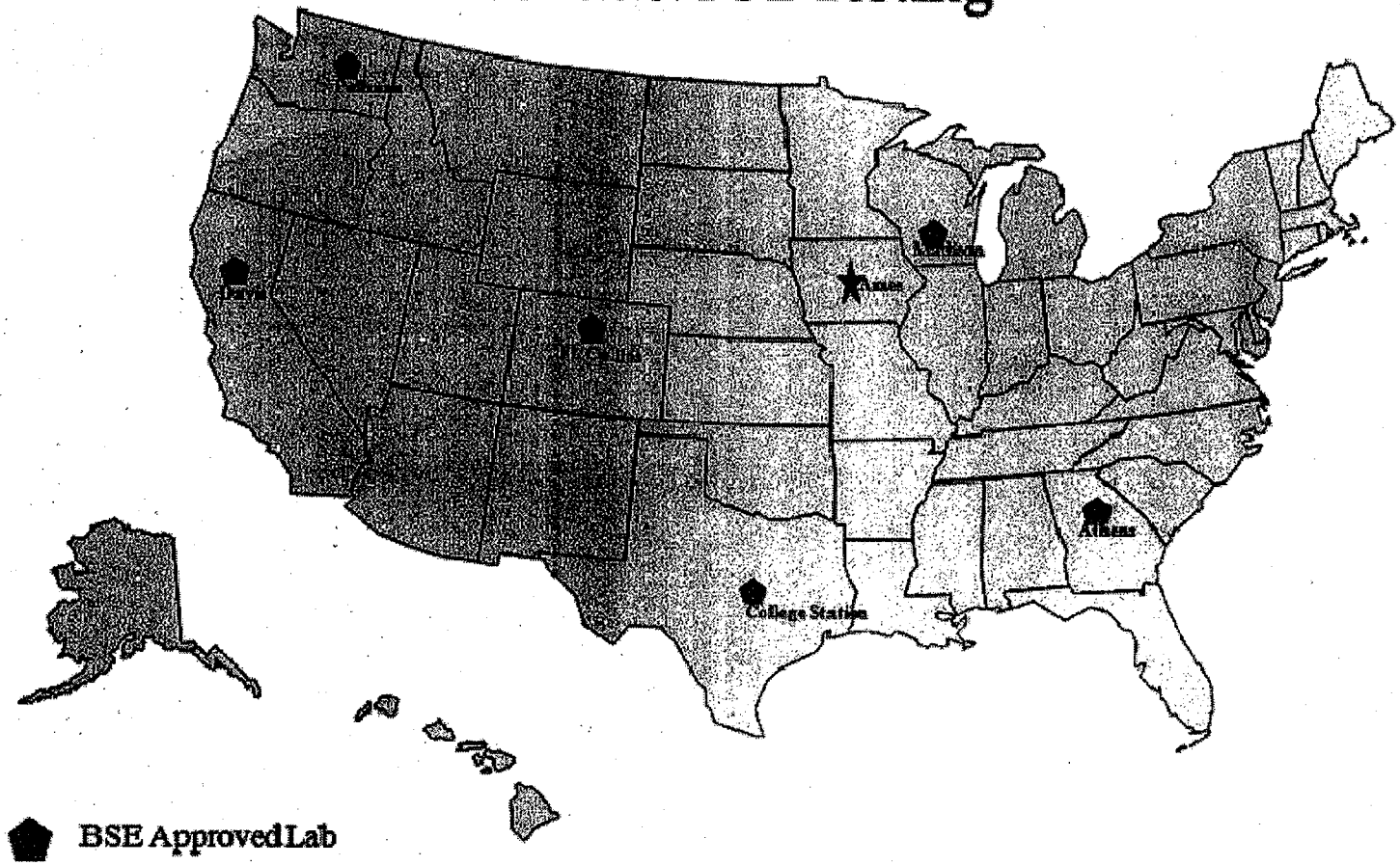
- Newcastle Disease (ND)/Avian Influenza (AI)
- *Bovine Spongiform Encephalopathy (BSE)
- Scrapie/Chronic Wasting Disease (CWD)
- *Classical Swine Fever (CSF)/Foot and Mouth Disease (FMD)
- *Pseudorabies Virus (PRV)
- Swine Influenza (SIV)
- Vesicular Stomatitis (VS)
- National Veterinary Services Laboratories

*For specified agents, not all laboratories are currently participating in surveillance testing

May 2012

USDA

Laboratories Approved to Conduct BSE Testing



BSE Approved Lab

NVSL Lab Site

May 2012

891

Applying Quality Requirements to BSE Testing

- Quality standards
  - All BSE labs are AAVLD accredited
    - 17025/OIE requirements
    - Required site visits
    - Quality Management System

- Standardized protocols and equipment
  - Licensed diagnostic kit
  - Controls and performance standards
  - Controlled copy of SOP
  - Maintenance and calibration of equipment

Applying Quality Requirements to BSE Testing

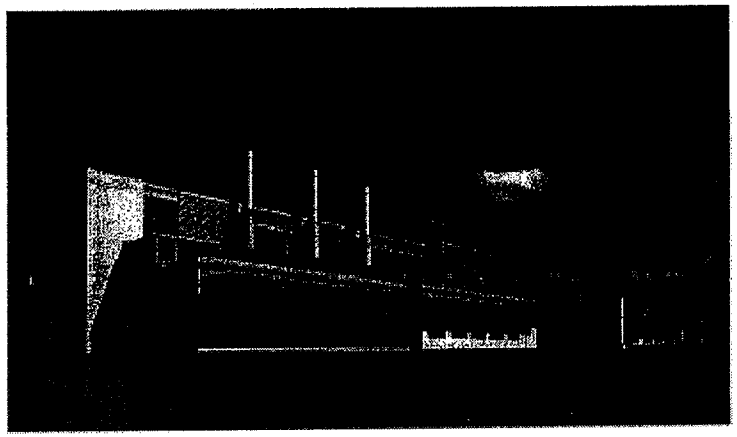
- Competency of laboratory personnel
  - NVSL – National Reference Laboratory
    - Provides training, proficiency test panels and confirmatory testing
  - Requirement - must successfully complete proficiency test process to participate in NAHLN surveillance activities
    - Annual competency assessment

- Adequate biosafety/biosecurity

- Secure electronic communications and reporting
  - Reporting requirements detailed in standard operating procedure and contract documents
  - Dedicated data system for BSE testing results from NAHLN laboratories

BSE Testing at NVSL

Bruce Thomsen, D.V.M., Ph.D., Diplomate ACVP
Supervisor, Pathology, Parasitology and Entomology Section
Pathobiology Laboratory
National Veterinary Services Laboratories



Current NVSL BSE Diagnostic Tests

- Enzyme Linked Immunosorbent Assay (ELISA) is used as screening test for surveillance on fresh brainstem (obex).

- Immunohistochemistry (IHC) and Western Blot (WB) are the approved confirmatory test methods.
  - IHC - formalin fixed tissues
  - WB - fresh tissue

First Case of BSE in the U.S.

1. December 2003
   - Six and one-half (6 ½) year-old Holstein cow with history of calving paralysis in Washington
   - Cow was imported from Canada in 2001
   - Classical form of BSE

173

Second and Third Cases of BSE in the U.S.

2. 2005
   - 12-year-old Brahman crossbred from Texas that died during transportation to packing plant
   - H-type (high-type) BSE

3. 2006
   - 10-year-old Santa Gertrudis crossbred, downer on farm, from Alabama
   - H-type (high-type) BSE

All four cases were strongly positive by Bio-Rad ELISA.

Mean Optical Densities

Case 1 (WA)

Mean 1.859 N= 2

Case 2 (TX)

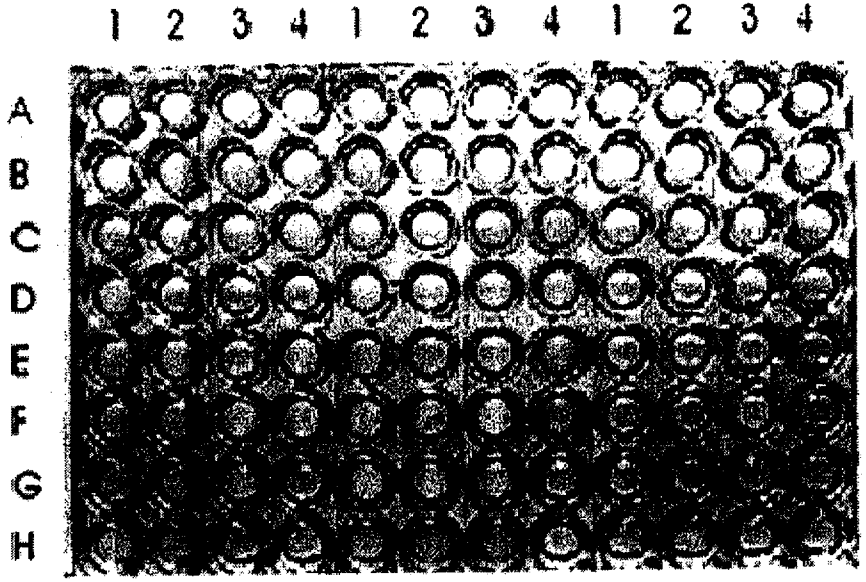
Mean 2.493 N=6

Case 3 (AL)

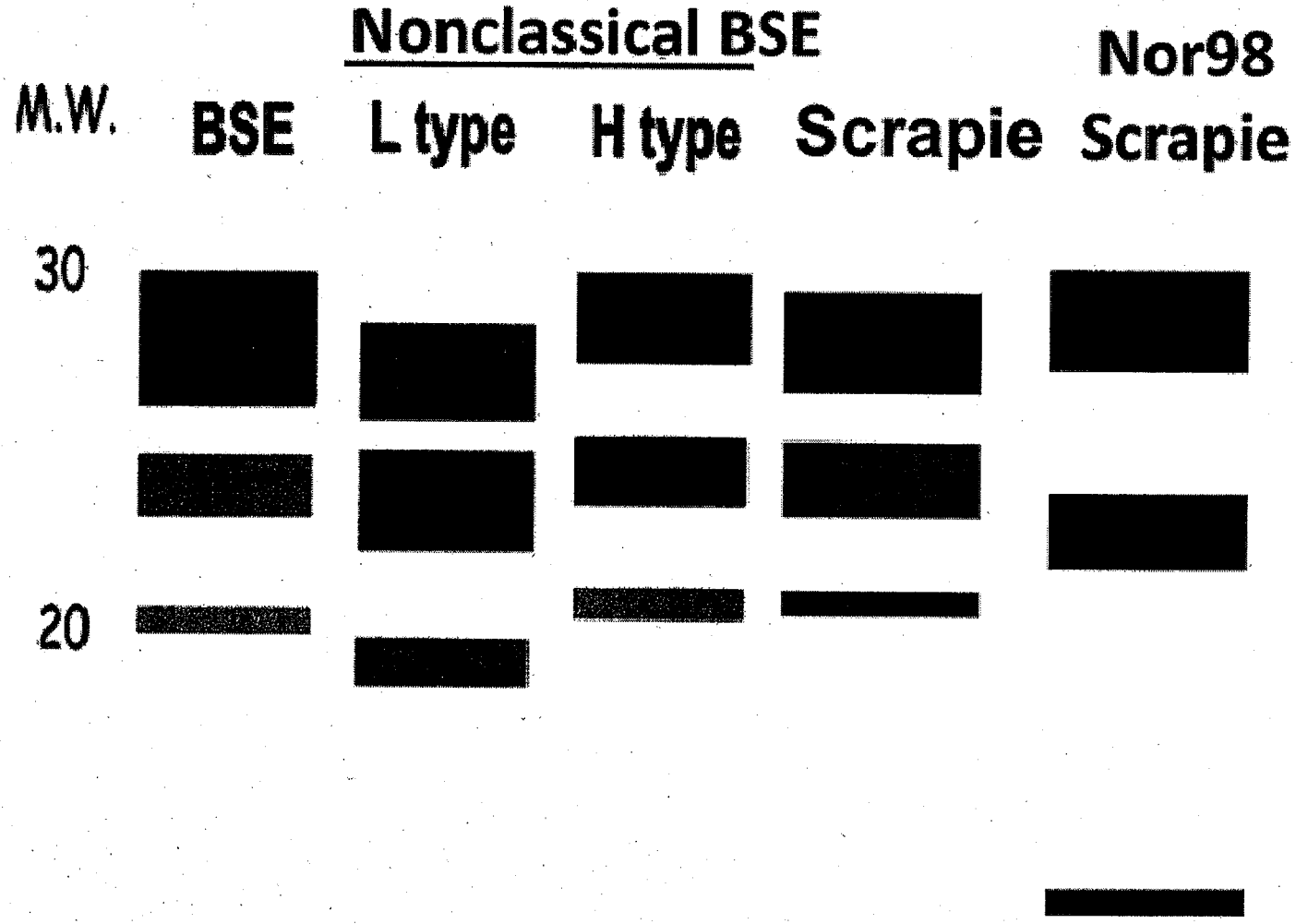
Mean 2.403 N=5

Case 4 (CA)

Mean 3.15 N=2

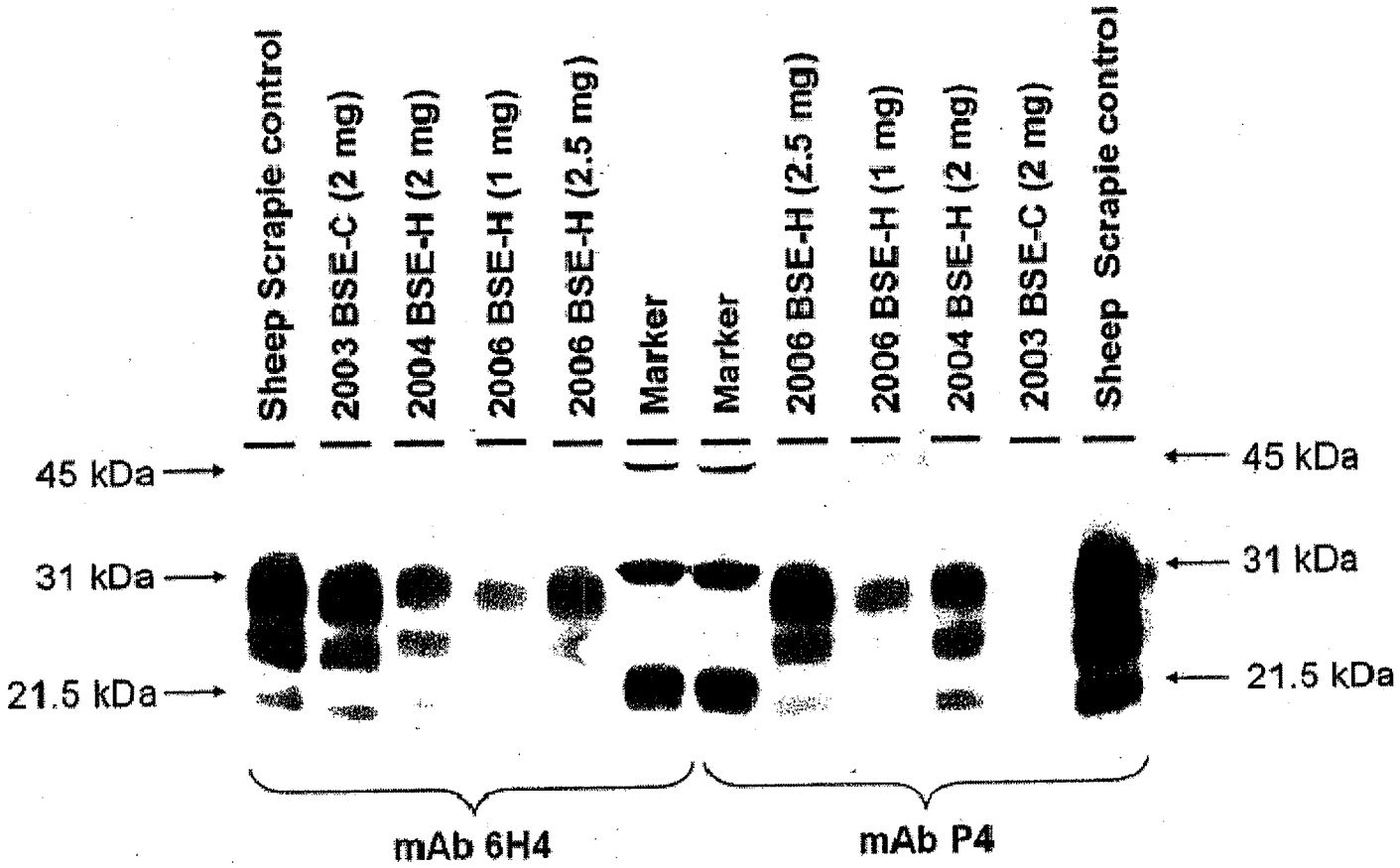


Western Blot Banding Patterns



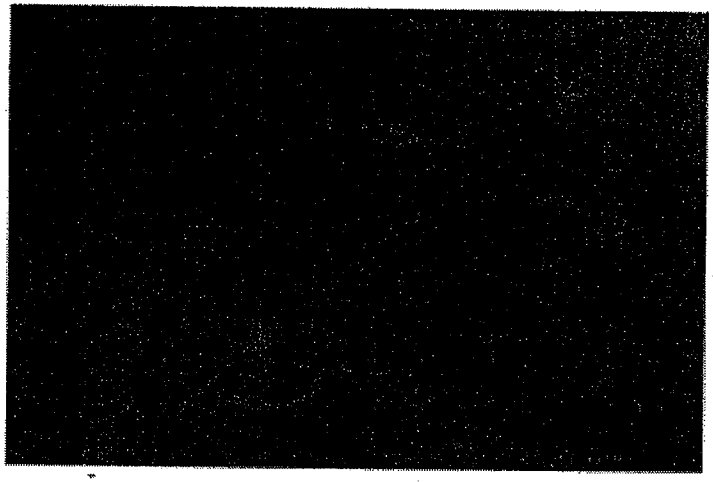
Western Blots of First Three U.S. Cases

Molecular Comparison of U.S. BSE Cases

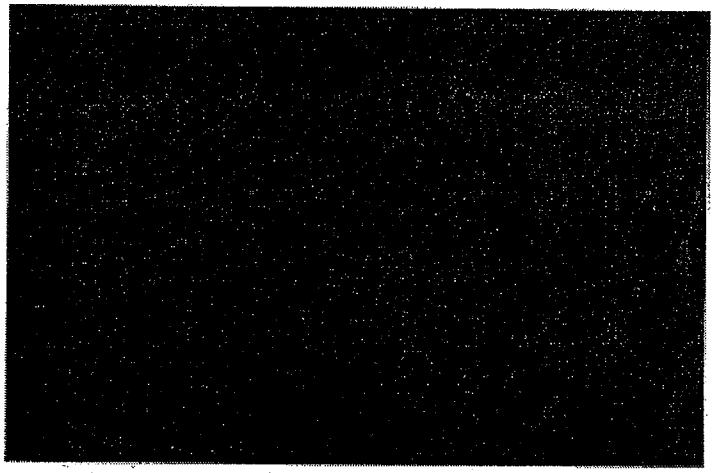


IHC Results - Case 1 vs. Cases 2 and 3

- Phenotype unusual in Cases 2 & 3
- Classical histology not seen in Cases 2 and 3
- Weaker staining by IHC in Cases 2 and 3



IHC Staining Case 1



IHC Staining Case 2

The 4th US BSE Case in Detail

179

USDA

Diagnostic Testing in California

- April 19: Obex sample delivered to the California Animal Health and Food Safety Laboratory (CAHFSL).
  - CAHFSL located in Davis, California.
- Later on April 19: CAHFSL reported an "inconclusive" test result to USDA.
  - Enzyme-linked immunosorbent assay (ELISA) BSE screening test used. Bio-rad

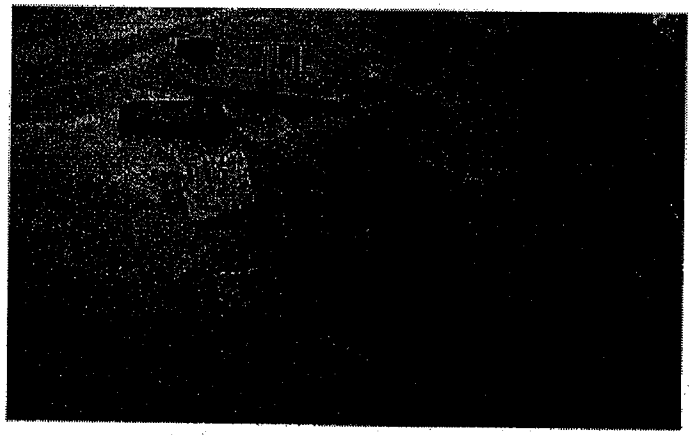
Shipment of Inconclusive Sample

- April 20: CAHFSL sent sample material to the USDA National Veterinary Services Laboratories (NVSL).
  - Located in Ames, Iowa.
- April 21: Inconclusive sample material arrived at NVSL.
  - Additional items also shipped to NVSL.
    - Ear tags (collected by the renderer).
    - Sample of hide containing a brand (registered to the Tulare County dairy) – shipped later

NVSL– Ames, Iowa

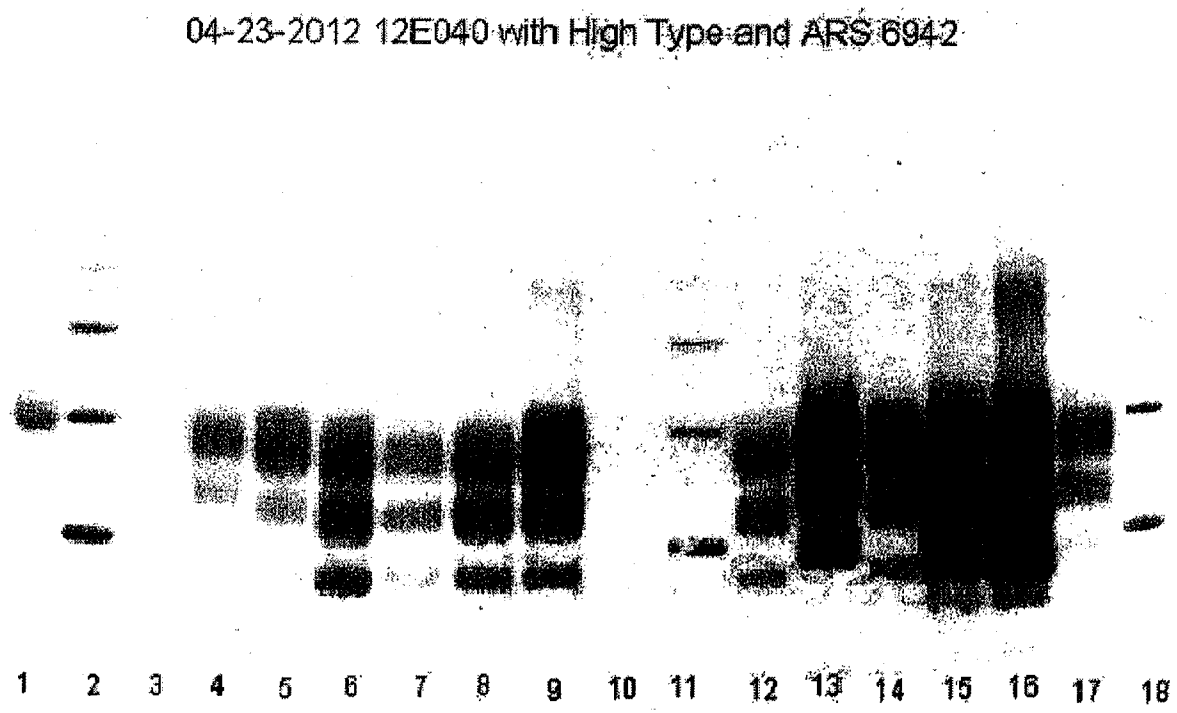
Diagnostic Testing at NVSL

- April 21: ELISA testing for BSE was positive.
- April 23: Immunohistochemistry (IHC) and Western blot (WB) testing were positive.
  - Results indicated "L-type" (low-type) BSE, known as "atypical BSE" - not "classical BSE".
- April 25: NVSL DNA genotyping completed matching branded hide, to tissue from ear tag, to positive obex sample.

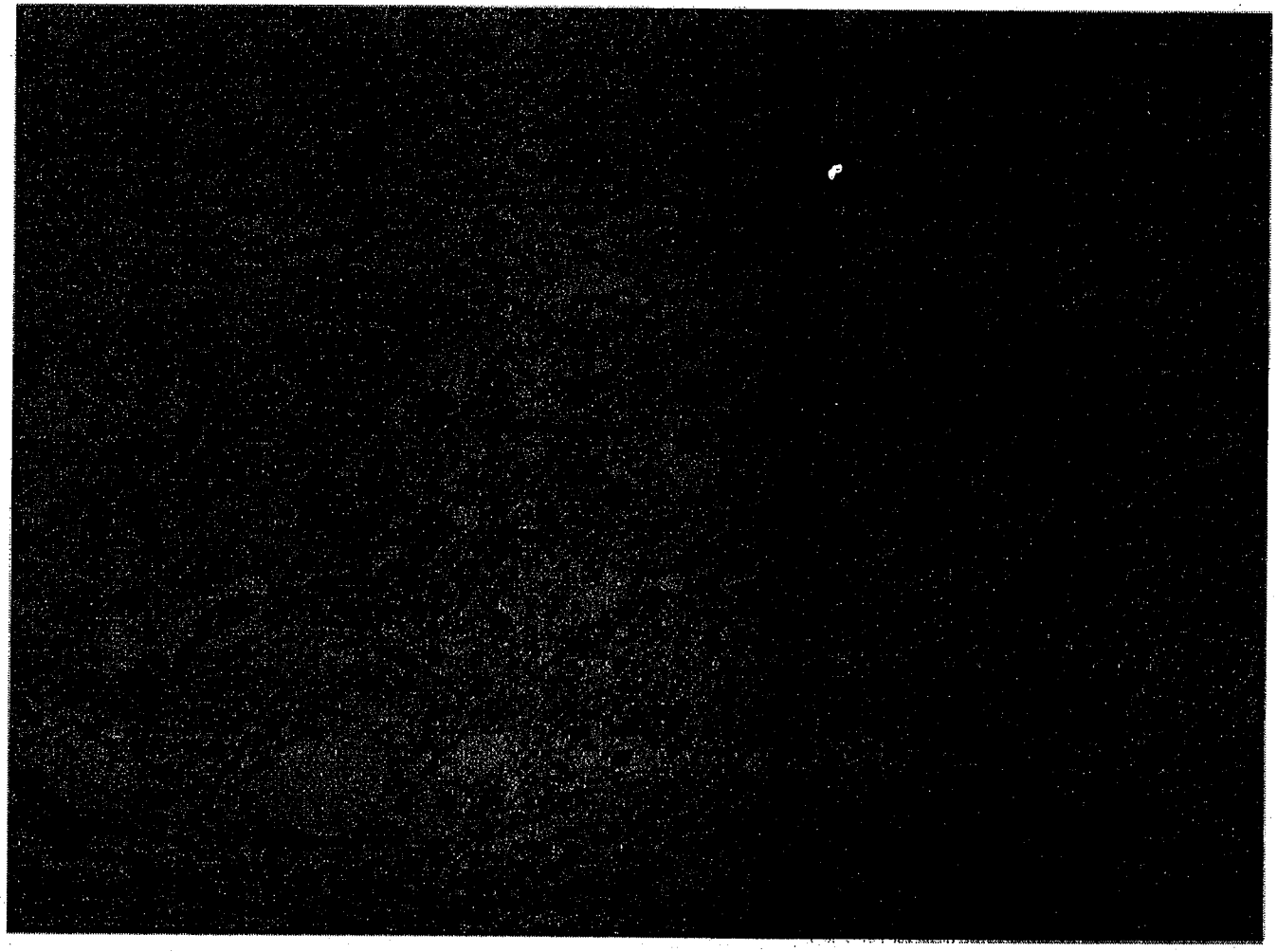


Western Blot – 4th U.S. BSE Case

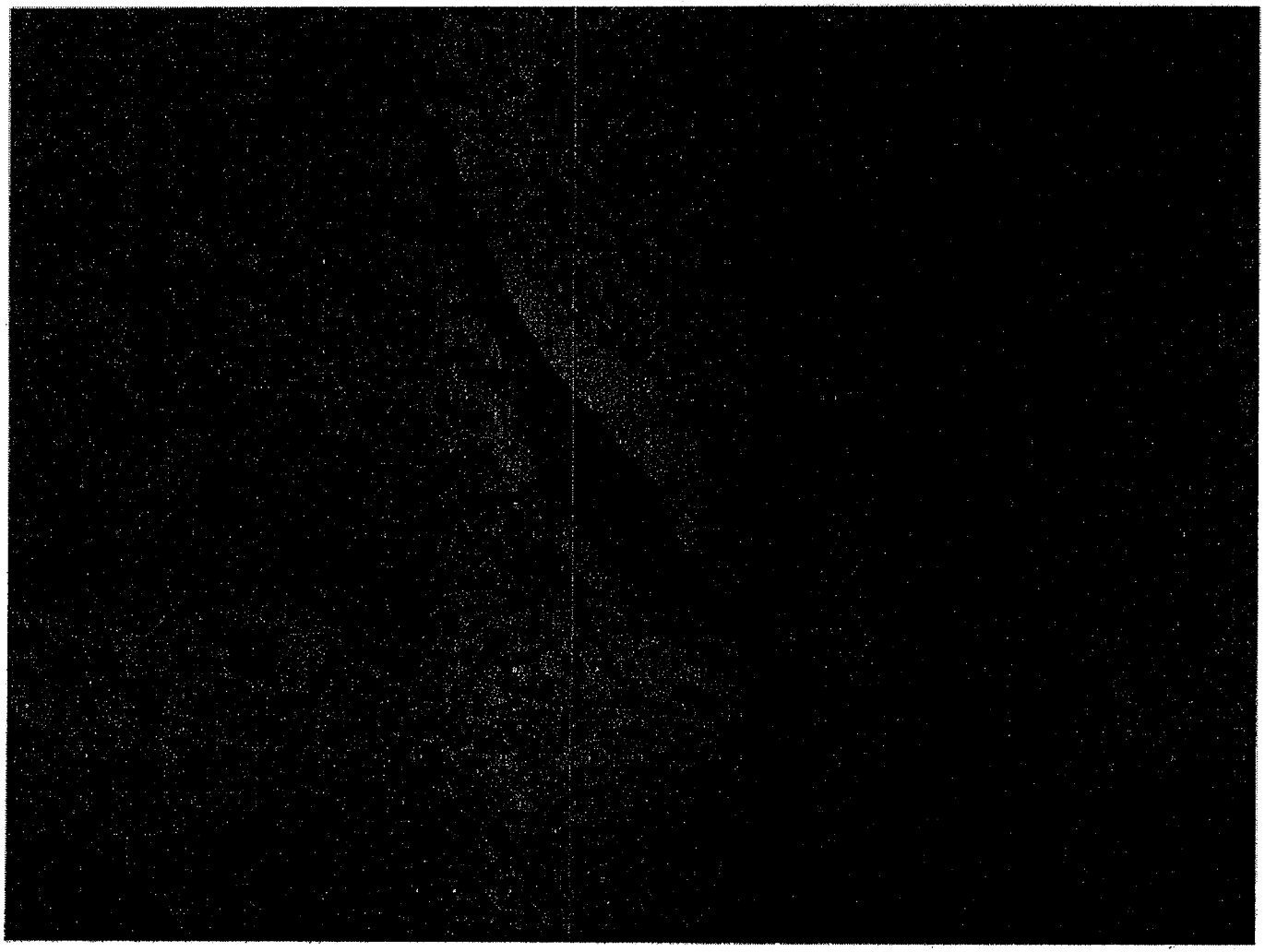
1. K
2. MM 1:10
3. neg. bovis
4. high type BSE
5. classical BSE 1:20
6. sample 1:10
7. ARS 6942
8. sample 1:25
9. classical 1:20
10. neg. scrapie
11. MM 1:10
12. sample 1:50
13. high type BSE neat
14. classical BSE 1:20
15. ARS 6942 neat
16. sample neat
17. positive scrapie
18. MM 1:20



IHC 4th U.S. BSE Case



IHC 4th U.S. BSE Case



Progeny in Last Two Years – Testing at NVSL

- Progeny heifer
  - BSE testing was negative (ELISA)
  - DNA genotyping is pending completion

981

USDA

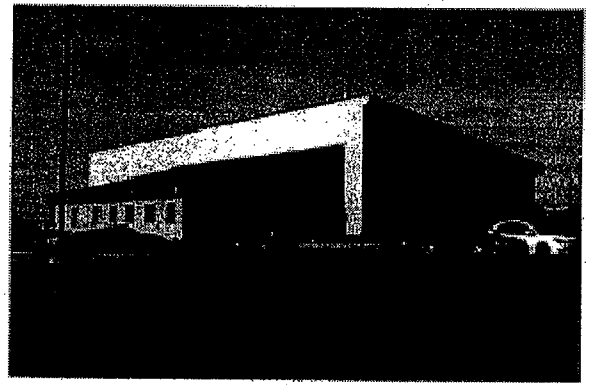
Summary

- Four Cases of BSE in US
  - First Case was Classical BSE - Imported from Canada
  - Next two cases were High-Type BSE
  - Fourth case is Low-Type BSE

- OIE BSE Labs in Canada and U.K. have received WB images and brain samples to review NVSL results.

Tissue Matching at NVSL

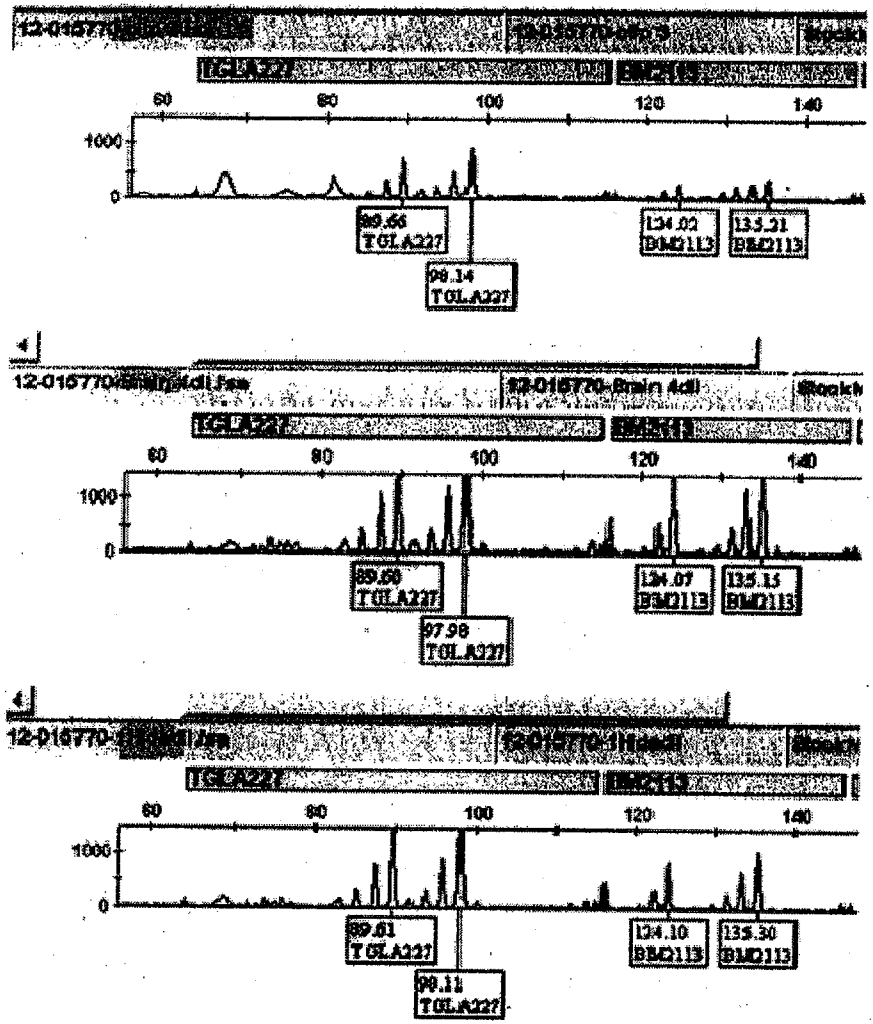
Suelee Robbe-Austerman, D.V.M., Ph.D.
Section Head, Mycobacteria Brucella
Diagnostic Bacteriology Laboratory
National Veterinary Services Laboratories



Microsatellite Genotyping (Tissue Matching)

- All newly identified cases of BSE, bovine TB, or other high consequence diseases have DNA from identification devices matched to the lesioned tissue.
- NVSL uses StockMarks™ (Life Technologies) Cattle Genotyping Kit.
  - Multiplex PCR for 11 loci that are approved by ISAG.
  - Fragment analysis on Sequencer
  - Software measures the peak location.
  - At least 7 loci must match, no mismatches
- 4th BSE case: NVSL extracted DNA from the USDA Official "Brite" ID tag, the obex tissue, and the hide.

Tissue Matching Results



	USDA Brite ID tag		Obex Tissue		Skin (Hide)	
	Peak 1	Peak 2	Peak 1	Peak 2	Peak 1	Peak 2
TGLA227	89.66	[illegible]	89.68	[illegible]	89.61	[illegible]
BM2113	124.04	135.21	124.07	135.15	124.10	135.30
TGLA53	163.58		163.78		163.65	
ETH10	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
SPS115	246.01		246.16		246.16	
TGLA126	116.01		116.05		115.97	
TGLA122	146.91	163.58	146.83	163.65	146.91	163.65
INRA23	205.07	210.71	205.27	209.82	205.20	209.83
ETH3	126.27		126.35		126.39	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
BM1824	176.32	186.80	176.38	186.93	176.37	186.86

Tissue from the Tag, Obex and Skin matched at all 11 loci, confirming they originated from the same animal.