

IDEXX Laboratories, Inc

Bovine Spongiform Encephalopathy (BSE) Antigen Test Kit

Fall 2004

Printing



Agenda

BSE Product Status

USDA-approved and successfully completed 2004 EU validation studies

Product Description

Second-generation test utilizing novel Seprion ligand technology combined with IDEXX's robust microtiter plate format

Performance

100% specificity and sensitivity

Benefits

Easy-to-use with simple sample preparation, solid performance and rapid results

Summary

IDEXX BSE test combines strong performance and ease-of-use on a trusted IDEXX platform

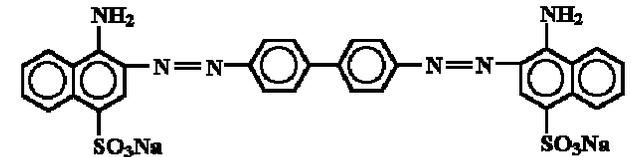
- The IDEXX BSE test is a true second-generation test based on a novel prion-capture technology, the Seprion Ligand
- This technology utilizes a chemical polymer which selectively binds PrP^{Sc} (rogue prions) in the presence of PrP^C (normal proteins) from a simple tissue and water homogenate
- This removes the need for complicated and potentially error-prone Proteinase K sample preparation
- This technology allows for a simple homogenization step combined with a straightforward EIA, revolutionizing BSE diagnostic ease-of-use and efficiency

Prions and Polyanion Interactions

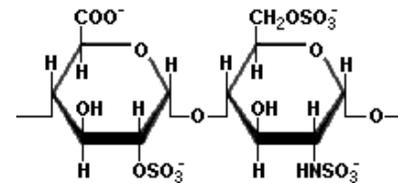
Relevant biological knowledge

- Histopathological staining of prion aggregates with dyes such as Congo Red and Serius Red
- Heparin Sulphate associates with prion protein amyloid plaques *in vivo*, and studies have shown that heparin binds to the prion protein at the same site as Congo Red and pentosan polysulphate
- Inhibition of PrP^{Sc} by Congo Red in neuroblastomas infected with PrP^{Sc}, with effectiveness relative to density of sulphation
- Treatment of mice with polyanions has been shown to delay the progression of scrapie
- Pentosan polysulphate has been used to stabilize a vCJD patient

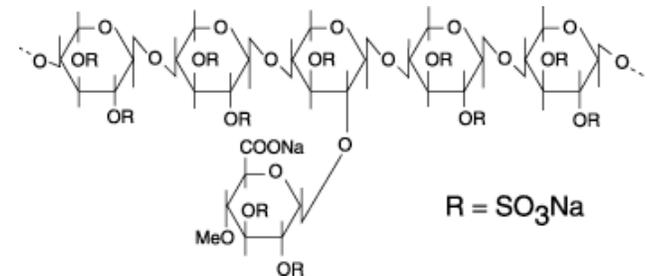
Polyanions



Congo Red



Heparin



Pentosan Polysulphate

Technology application

1. Polyionic sulphate ligand for binding PrP^{sc}

Pentosan sulphate, Dextran sulphate, etc.

2. “Matrix busters” to maximize signal

Trypsin, DNase, etc.

3. Polyanionic surfactants to optimize selectivity for PrP^{sc}

Triton X-100, N Lauryl Sarcosine, etc.



Robust assay that selectively binds PrP^{sc} (rogue prions) in the presence of PrP^c (normal prion protein) from a simple tissue and water homogenate

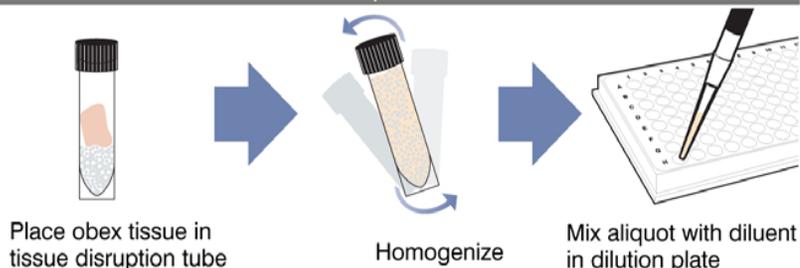
- The basis of selective PrP^{sc} capture with the Seprion ligand technology is the polyionic interaction between abnormal forms of PrP and the Seprion ligand.
- Normal PrP^c does not bind to the ligand in the presence of the competing polyanionic surfactant.

Product Description

IDEXX Production
Animal Services

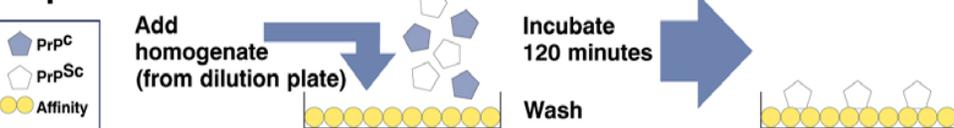
IDEXX HerdChek BSE Test—Sample Flow

Sample Preparation

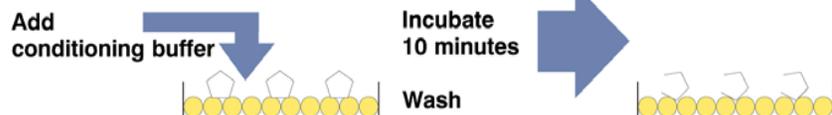


EIA Enzyme-Linked Immunoassay

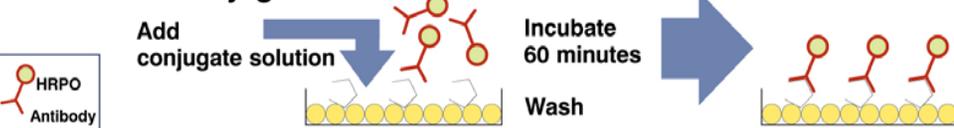
Capture



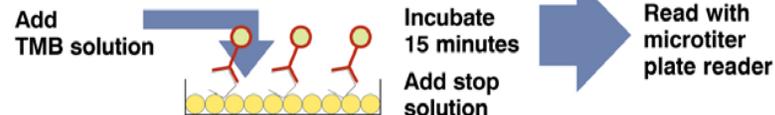
Condition



Addition of Conjugate



Read



Please refer to the package insert for complete instructions.

The IDEXX BSE test is easy to run.

- Homogenize sample
- Dilute sample aliquot
- Run EIA

It's that simple!

- No proteinase K
- No centrifuge
- No incubators
- All room temperature
- Less hands-on time
- Results in less than 4.5 hours

A half-dozen steps have been removed from sample preparation.

IDEXX
LABORATORIES

Tecan® Evo™ Automation

IDEXX Production
Animal Services



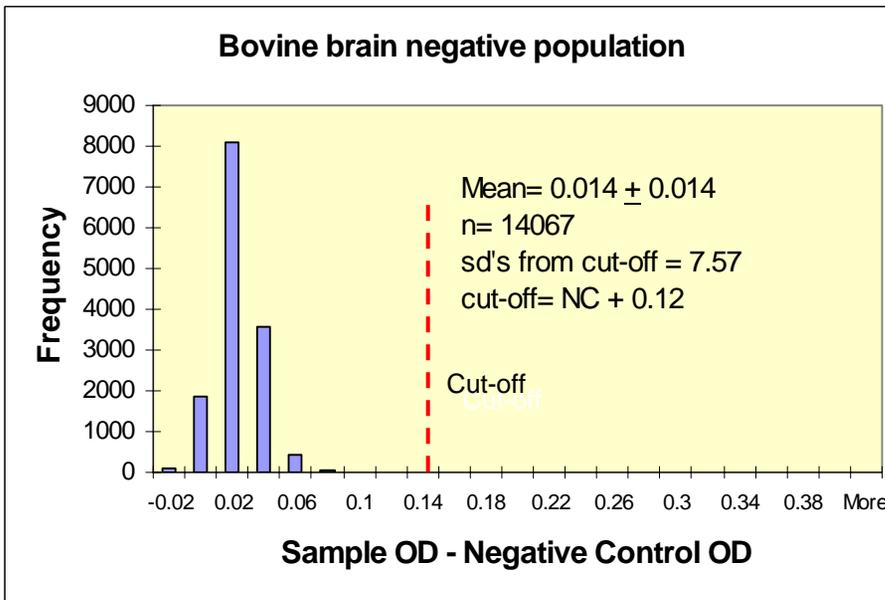
- 9 plates run in under 5 hours
- Homogenize, prepare for capture plate, place in hotel, and walk away
- Very simple application—no incubators required

Performance: 100% Specificity

US and European populations

IDEXX Production
Animal Services

Negative Population Study



Key Points

- Negative samples collected in United States and Europe
- Negative population exhibits tight distribution and good separation from cutoff
- 14067 samples, with 100% specificity

Performance: Sensitivity and Specificity

European Union- Phase One Lab Evaluation

IDEXX BSE-EIA Sensitivity and Specificity

	True positive	True negative	Totals
Test Positive	50	0	50
Test negative	0	150	150
Totals	50	150	200

	%	95% Confidence Interval one sided Poisson
Sensitivity	100	94.0 %
Specificity	100	98.0 %

Performance Summary

- 100% sensitivity and specificity as compared to immunohistochemistry

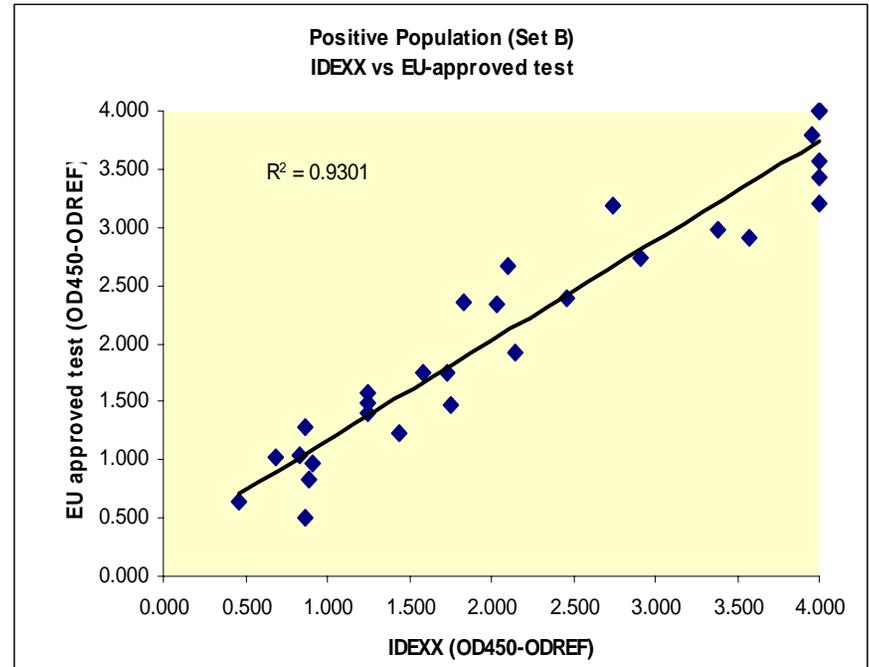
Performance:

100% Agreement with EU-approved test

IHC Positive brain samples

		Sample Set A		Sample Set B	
		IDEXX +	IDEXX -	IDEXX +	IDEXX -
EU-approved test	+	97	0	31	0
	-	0	0	0	0

Correlation 128/128 = 100%



Performance: Sensitivity—BSE dilution series

IDEXX Study

BSE Dilution Series

Sample Dilution	IDEXX $OD_{450}-OD_{Ref}$	EU-approved test $OD_{450}-OD_{Ref}$
1	3.876	4.000
4	3.750	3.896
12	3.038	2.875
36	1.861	1.704
72	1.125	0.821
144	0.677	0.541
288	0.426	0.350
576	0.264	0.182
1152	0.162	0.090
2304	0.114	0.064
negative control	0.046	0.020
cut-off	0.166	0.230

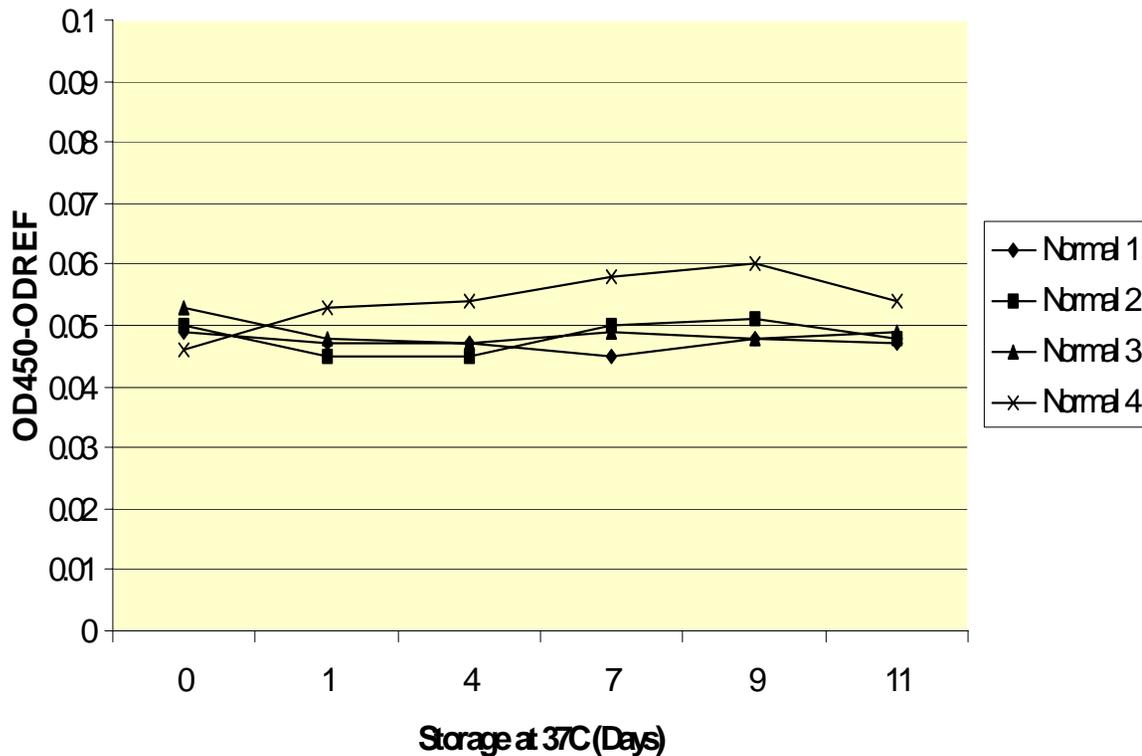
Key Points

- IDEXX detection one dilution higher than EU-approved test.
- IDEXX performance in dilution series is equal to or better than the competition.

Performance: Autolysis Stability

Tissue, 37°C

**Stability of Brain Tissue Prior to BSE-EIA Testing-
37°C Storage of Normal Bovine Brain tissue**



Key Points

- Tissue held at 37°C for 11 days
- Trial mimics EU requirement to test autolysed negative samples with no increase in signal
- Indicates test will perform well on samples collected from animals found dead in field, or samples left unrefrigerated
- Samples stay flat-negative

Summary

Product

- Strong performance—no false-positives
- 100% correlation with EU-approved product
- USDA-approved and successfully completed 2004 EU validation studies

Benefits

- Easy-to-use, fast and efficient test; less hands-on time and no extra equipment required
- Less chance for error—no PK sample preparation
- High-throughput manual or automated systems, dependent on customer needs

IDEXX Quality

- Uses proven IDEXX ELISA technology trusted and preferred by diagnosticians worldwide
- Outstanding sales and technical service when needed