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Removal of Infectious Prions from Red Cell Concentrates

Hal Baker, Senior Vice President, Pall Medical
Advisory Committee
on Blood Safety and Availability
(BSAC) Meeting
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Prions Dormancy and Disease:

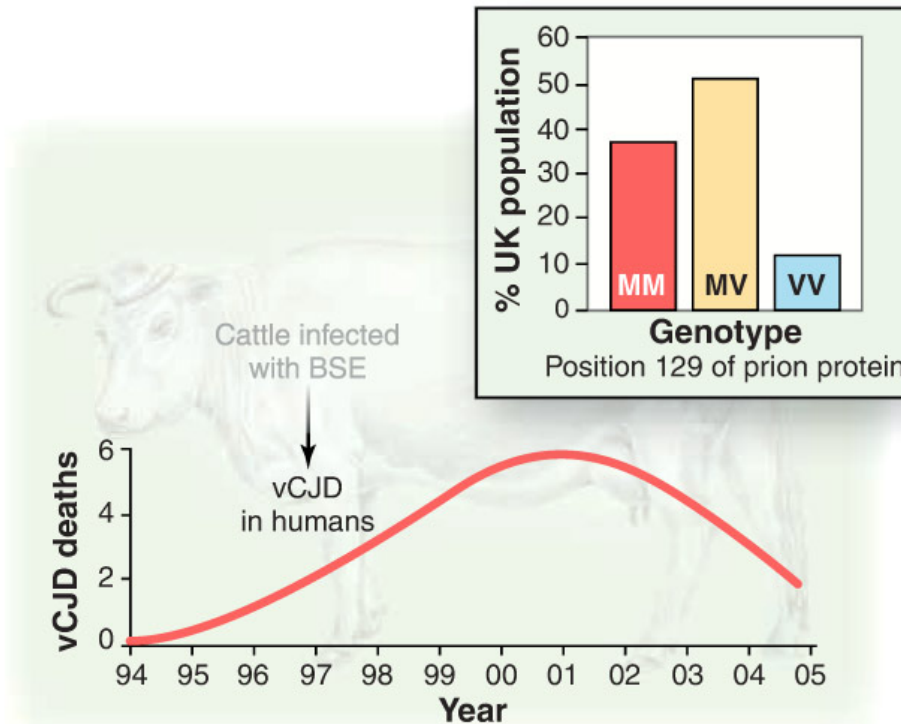
Can vCJD be Transmitted through Blood Transfusion?

- Prions can be transmitted to healthy animals through transfusion from infected animals
- Two probable cases of vCJD through blood transfusion from an asymptomatic donor
- Serious concerns of a second human-to-human wave of vCJD transmission pose a major risk to the blood supply.

A Waning Epidemic?

Two Levels of Infection: Overt (129MM) Recipient and Subclinical (129MV) Recipient

Projected Incidence in UK of vCJD Deaths



Blood Safety Tripod

A large, abstract, blue shape resembling a stylized tripod or a large arrow pointing downwards, serving as a background for the three points of the Blood Safety Tripod.

**1. Donor screening
and selection**

**2. Blood
screening
tests for
pathogens**

**3. Safety
processes**

Approach to Improving the Safety of the Blood Supply: *Prion Removal*

SMART Filter Technology

- Remove Prions Associated with Leukocytes
- Remove Prions Present in Plasma
- Removes both Prion Types (Normal + Abnormal)
- **Without** a Monoclonal Antibody
- **Without** a Ligand for Abnormal Prion
- **With** Proprietary Surface Modification (biocompatible)



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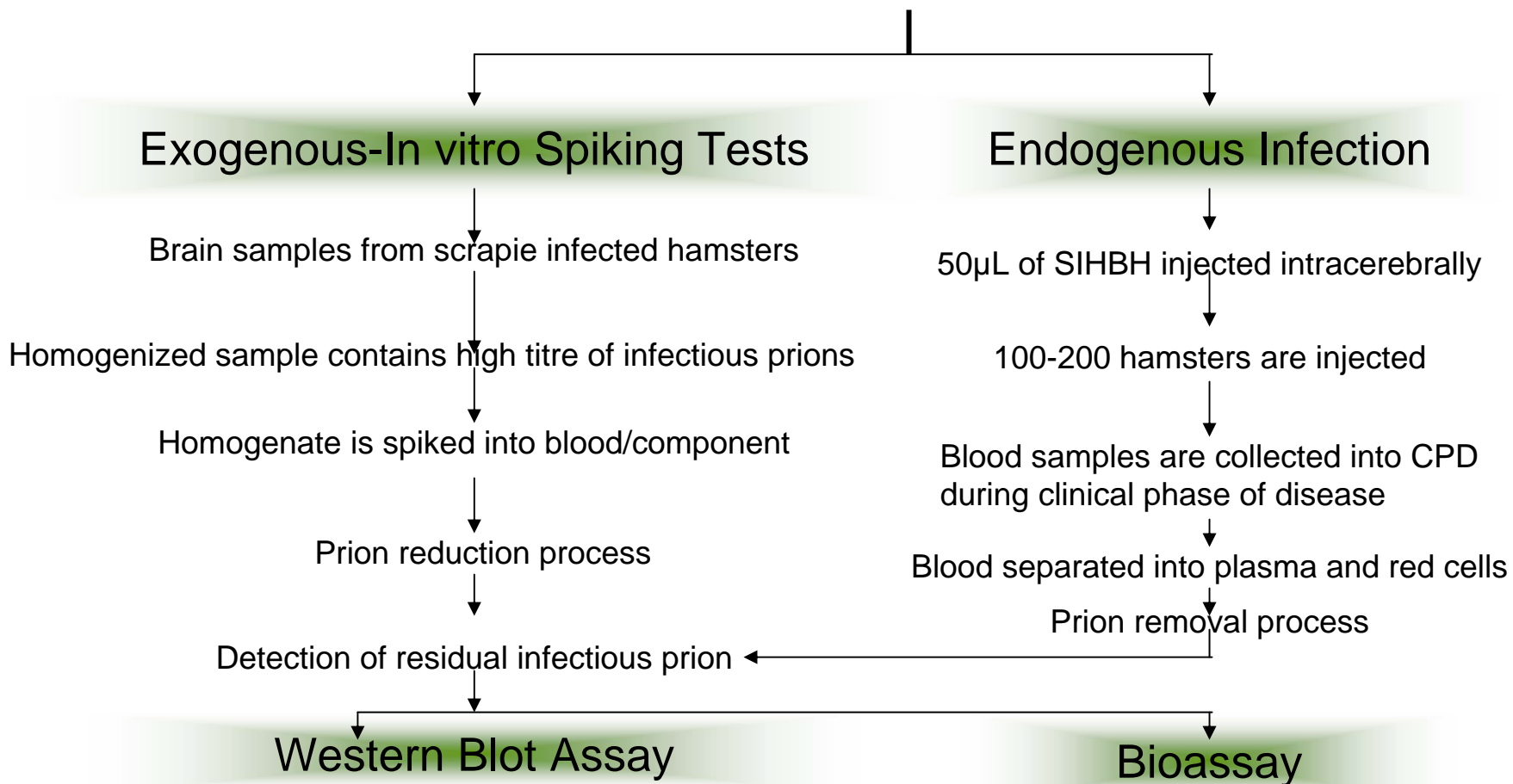
New Pall Leukotrap[®] Affinity Prion Reduction Filter

- Concurrent removal of leukocytes and infectious prions
- Removes 99.9% of vCJD infectious agent cell and non-cell associated
- Surface modification technology does not impact red cell parameters, purity or 42 day stability
- Filtration is a commonly used process, and is efficiently integrated into blood handling logistics/cGMP



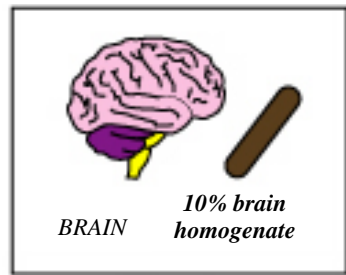
CE Mark Spring 2005

Test Methods to Validate Prion Reduction Process





Exogenous Infectivity Study: Addition of 10% (w/v) of Scrapie Infected Hamster Brain Homogenates into Red Cell Concentrate in Additive Solution



*Red Cell Concentrate
Containing
Infectious Prions*

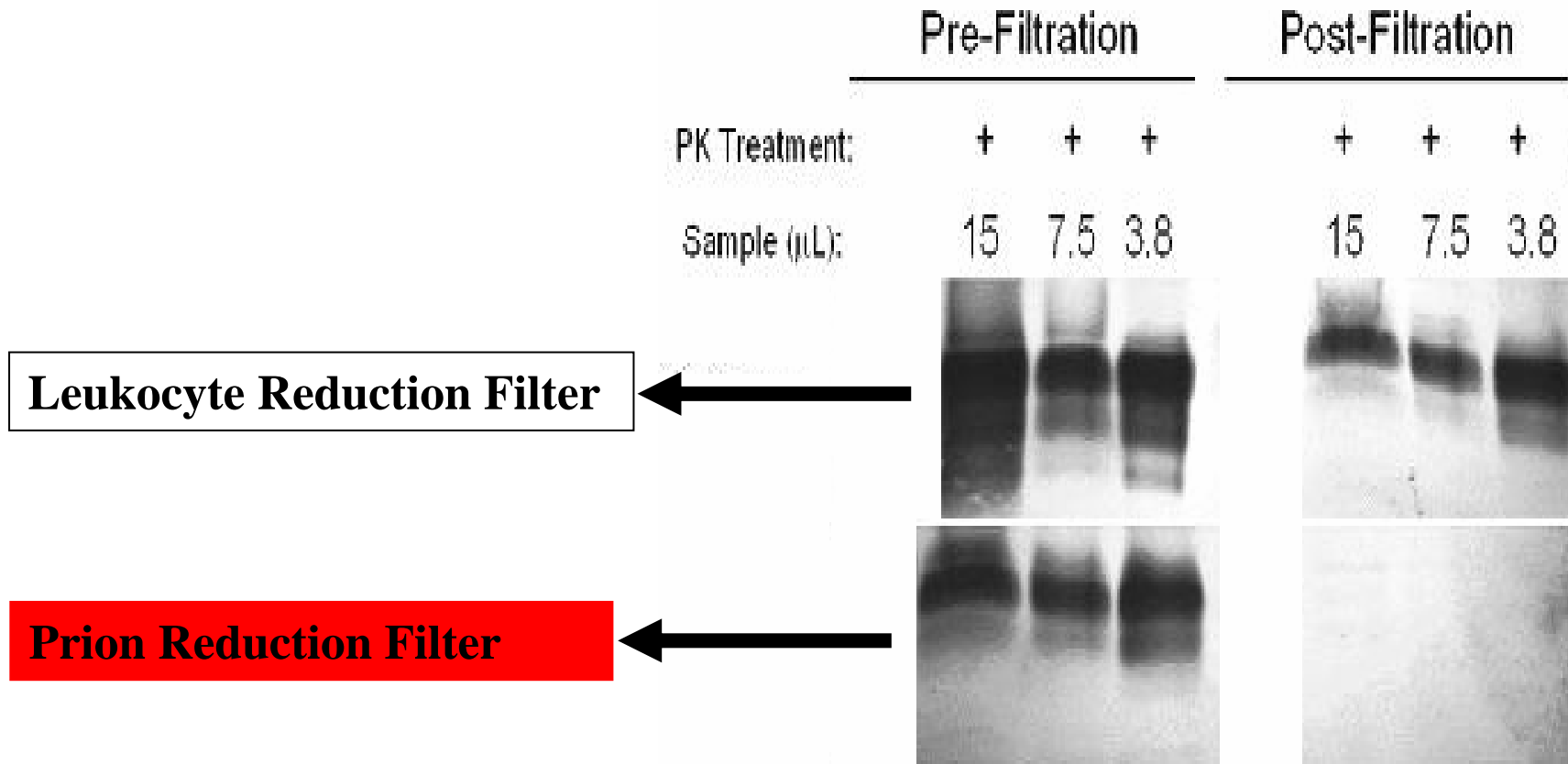
*Prion Reduction
Filter*



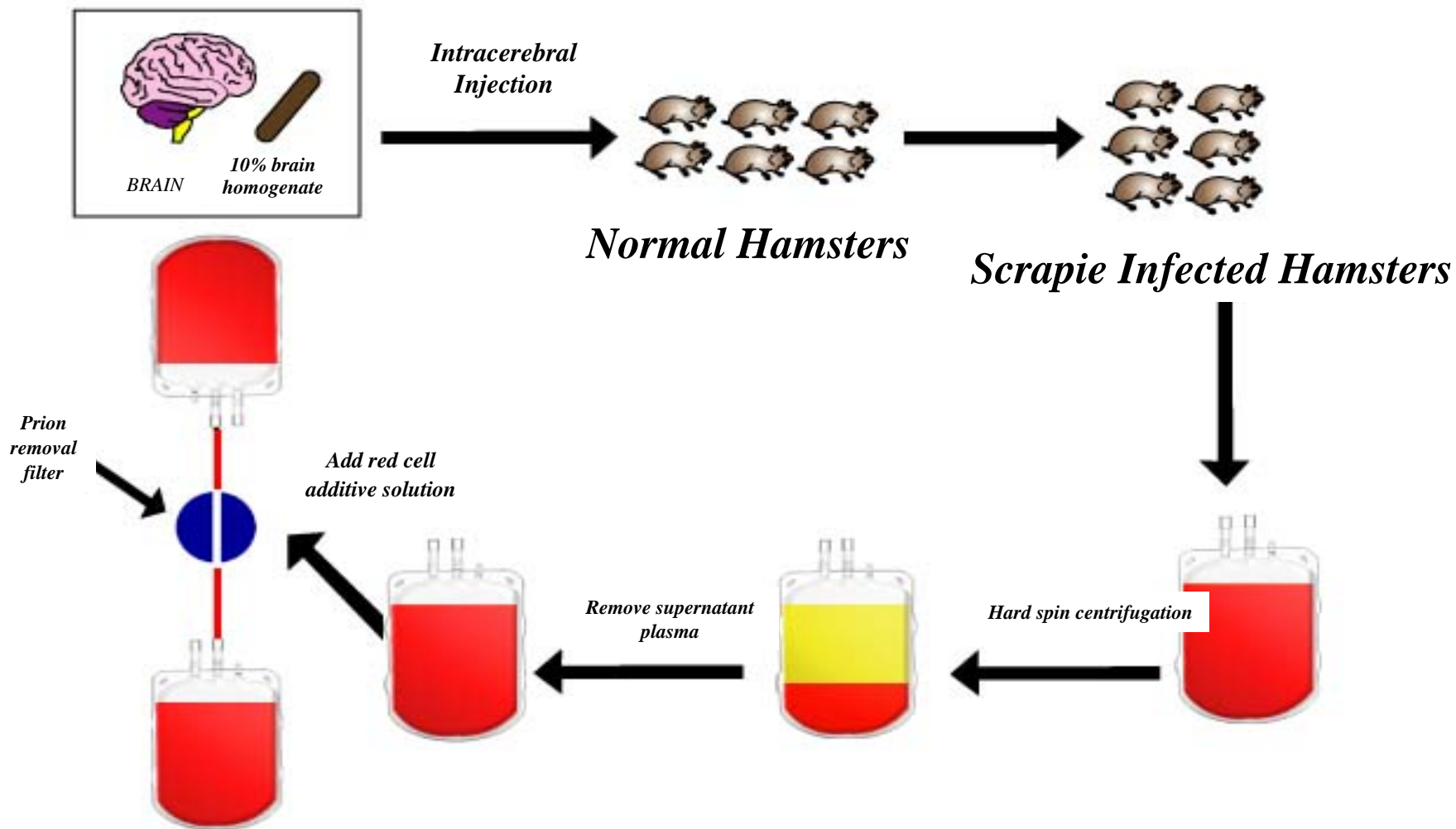
*Filtered Red
Cell Concentrate*



Western Blots - Reduction in the Levels of of Infectious Prions in Red Cell Concentrates



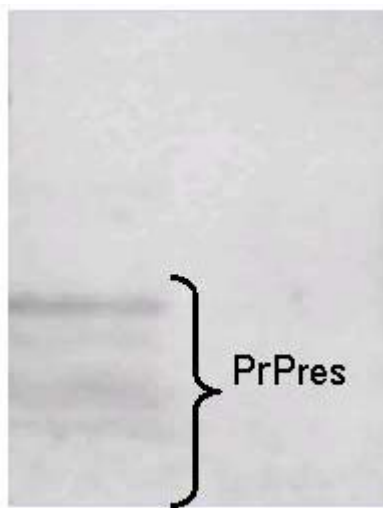
Preparation of Red Cell Concentrates from Whole Blood Obtained from Scrapie Infected Hamsters



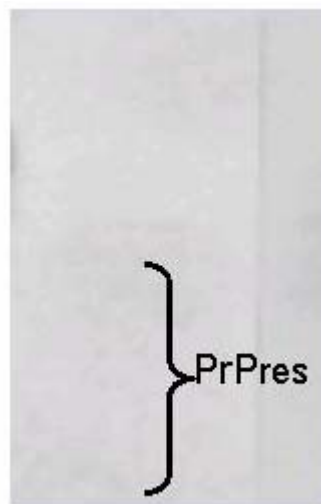


Removal of Infectious Prion from Red Cell Concentrate Endogenously Infected with Scrapie

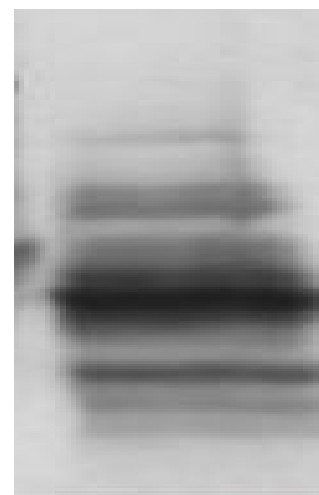
Western Blots After Proteinase K Digestion



Before Filtration



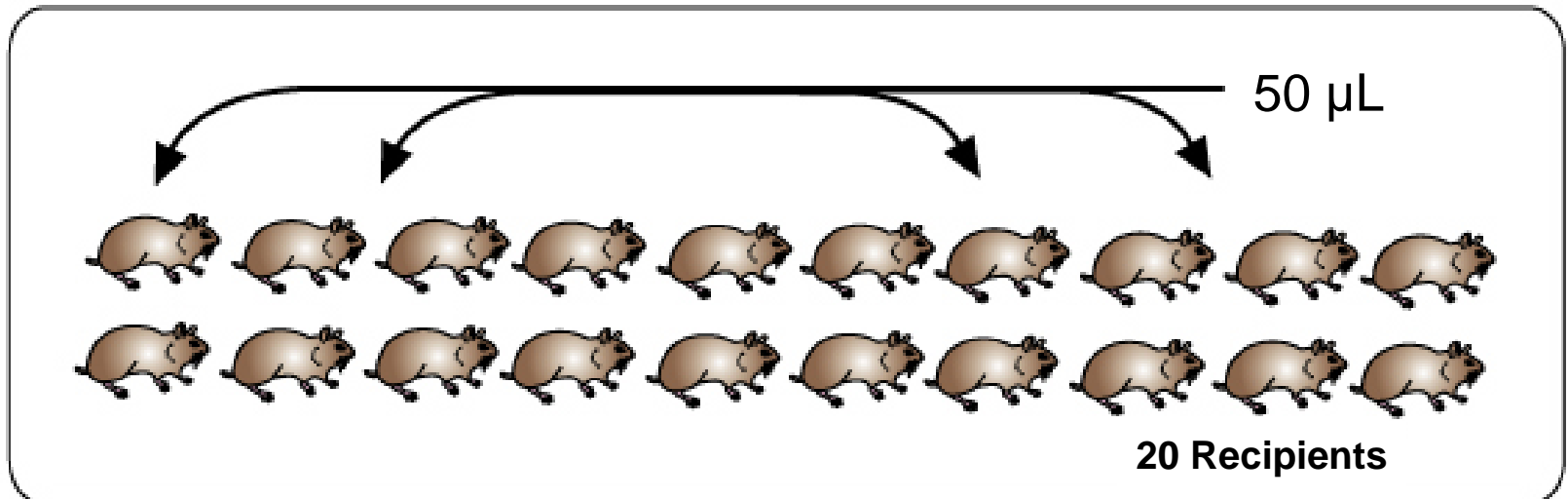
After Filtration



**Recovered from Filter
and Concentrated 500x**

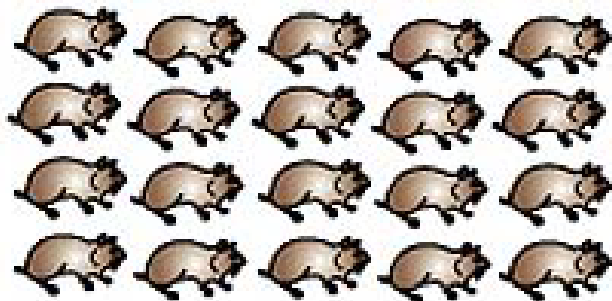
Animal Model of Blood Transfusion - Intracerebral Injection of Red Cells into Normal Healthy Hamsters

1. 50 μ L of pre and post filtration red cell concentrates were injected intracerebrally into healthy hamsters.
2. Hamsters were monitored for 300 days for any clinical signs of scrapie infection.

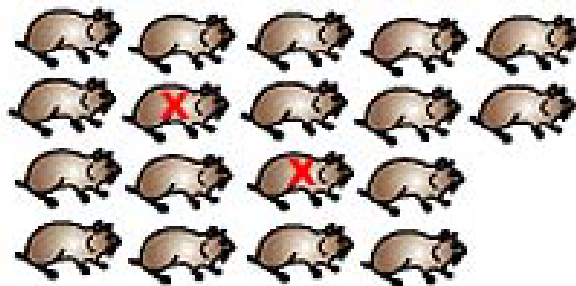


Results of Endogenous Infectivity Study

Filtered Red Cell Concentrate

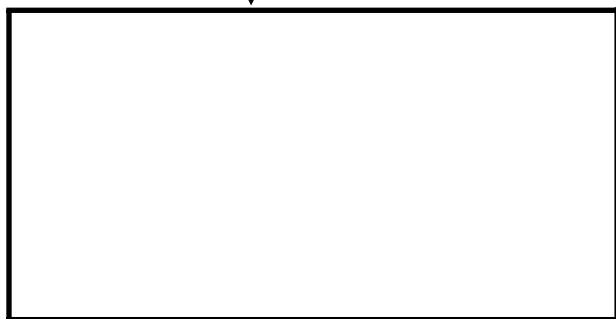


Control – UnFiltered Red Cell Concentrate

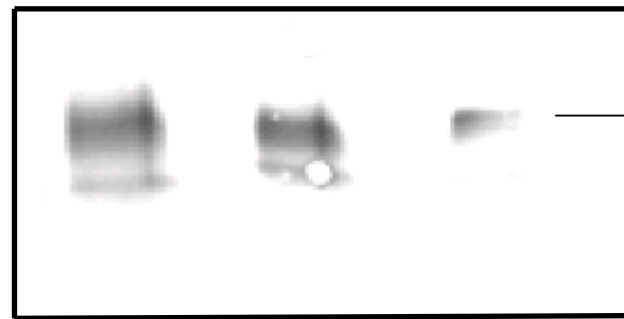


X = Clinical signs of scrapie

Western Blot of Brain Homogenates After Proteinase K Digestion



0 out of 20



3 out of 18 hamsters were infected with scrapie



SUMMARY

- **EXOGENOUS INFECTIVITY:** Prion reduction filter significantly removed different strains of infectious prion including mouse adapted model of human form of vCJD from red cell concentrates.
- **ENDOGENOUS INFECTIVITY:** Infectious prions in red cell concentrates obtained from hamsters infected endogenously with scrapie were removed below the limit of detection of our Western blot assay.

CONCLUSION

- CONCURRENT PRION AND LEUKOCYTE REDUCTION
 - ✓ Prion reduction below limit of detection
 - ✓ Leukocyte reduction below 1×10^5 per unit.

The Pall Leukotrap® Affinity Reduction Filter may help improve blood safety and availability by reducing the risk of transmission of human vCJD through blood transfusion