DRAFT

Precautionary measures to mitigate the risk of transfusion transmission of CJD by blood and blood products

1. Importation of source plasma for fractionation from the USA [a BSE ~~and vCJD-free~~ country] since 1997.

2. Deferral (exclusion) of Donors:

   (i) with family history of CJD

   (ii) who have had treatment with human growth hormone or gonadotrophin

   (iii) who have had corneal grafts

   (iv) who may have had a dura-mater graft

3. Leucodepletion of all blood components since 1999.

Under consideration:

1. Importation of FFP for clinical use from the USA

   Question: If importation for any blood component is to be considered, does the MSBT consider that this should only be imported from countries that are BSE and vCJD free.

   EMEA/MCA requirement is that:

   (i) plasma from countries with a number of cases of vCJD should not be used for the production of albumin used as an excipient for vaccines

   (ii) any plasma derivative that is subsequently shown to contain a plasma donation in the original plasma pool derived from a donor who subsequently develops vCJD must be recalled

2. Deferral (exclusion) of blood component recipients from donation

   Previous estimates from EOR MSBT paper June 2001 [MSBT 24/3].

   Based on the assumption of a long mean primary incubation period of 30 years and in the absence of any further intervention, blood components could be a significant source of secondary infections.

   In most of the scenarios explored there would be of the order of 1,500 infections to blood component recipients for each 1,000 primary infections (~~about 90 of them amongst the chronically~~ ill). The number of future infections prevented by excluding recipients from the donor pool would depend largely on the secondary incubation period.

A 12-year mean incubation period, excluding component recipients, could prevent about 120 vCJD infections per 1,000 primary infections (90 of these amongst the chronically ill).

A 3-year mean incubation period, excluding component recipients, would prevent only about 30 infections per 1,000 primaries (20 amongst the chronically ill).

NB: This potentially significant impact of a recipient ban could be eroded by other initiatives:

e.g. Sourcing clinical FFP from outside the UK

This appears to offer at least as great a risk reduction in its own right, and would also reduce the number of infections saved by a recipient ban, were this to be introduced in addition.

Balance of Risks

vCJD Risk Reduction Measures v. Continuity of Blood Supply

1. Impact on blood stocks resulting from exclusion of previously transfused donors (blood component recipients

Following a questionnaire survey of 51,000 donors in November 2000, it has been estimated that the available donor base would be reduced between 7.7% and 14.5%.

The potential loss of donations is greater than the effect on the donor base as the donors lost fall into the more regular repeat donor category.

Donor recruitment effort would need to be increased by between 50-102% to compensate for this depletion of the donor base.

A simple model of collection and supply has been constructed to qualitatively demonstrate the potential impact of implementing this donor exclusion criteria (using 8% reduction in donor numbers). Three different scenarios have been constructed:

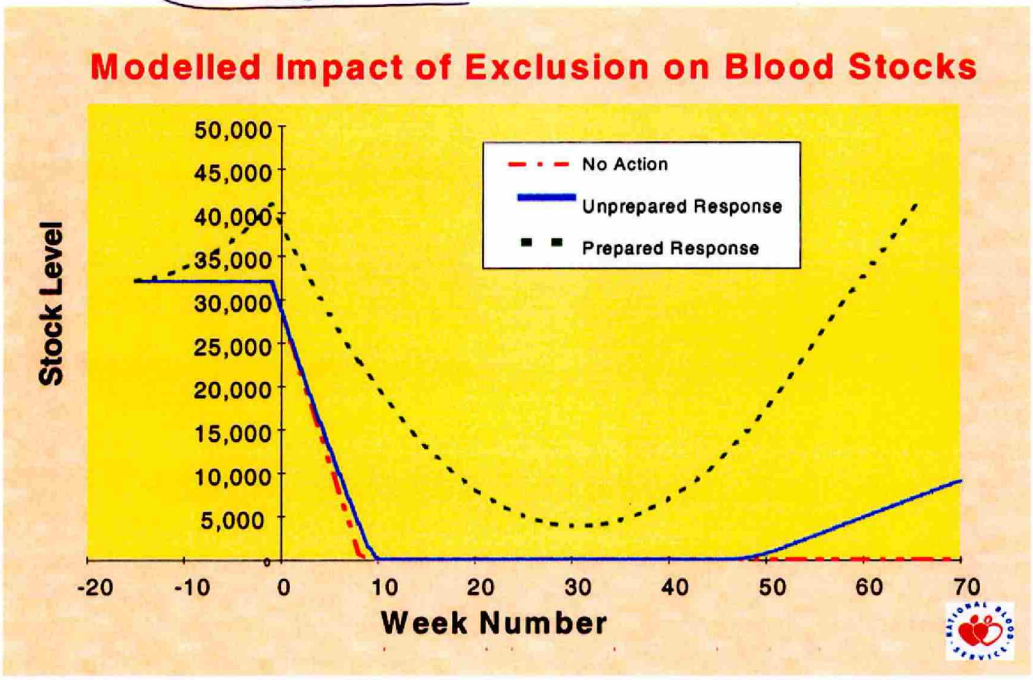
(i) No action: recruitment remains at current levels. No additional effort is made to replace the donors

(ii) Unprepared response: recruitment rates are increased by 39%. This additional recruitment is spread evenly between Week 0 and Week 52

Check this.

(iii) Prepared response: recruitment rates are increased by 39% starting in Week –15 (i.e. 15 weeks prior to the exclusion ban)

See Fig.1 Modelled impact of exclusion of transfused donor on blood stocks.



NB: The additional recruitment rate (set in the model at 39%) and the length of preparatory recruitment period have a dramatic effect on the outcome of an exclusion ban.

– UK to supply additional wording.
– etc. Explain figures.

Additional factors to consider:

A higher percentage loss of apheresis donors is predicted (9.7%). This would seriously impact on NBS ability to provide apheresis platelets, which currently form 40% of NBS platelet supply, as apheresis donors regularly donate at monthly intervals.

? Impact on special platelets.

NB: Early EOR work suggests that apheresis single donor platelets present less of a vCJD risk than buffy coat derived platelets (pool of 4 donations).

If exclusion of transfused donors is extended to include tissue donors, the impact on NBS tissue banks would be significant:

Cadaveric donors	=	28% [skin and bone donations]
Living donors	=	31% [bone donations]
Core blood donors	=	4%

? Impact on organ donors (who are heavily transfused)

Clarify. Impact (i.e. cumulative impact of apheresis) more to more apheresis

? Impact on – cancer programme – replacement programme

2. Impact of blood shortages on Hospital Transfusion Practice

A NBS/Hospital Planning Group has been developing an integrated NBS/Hospital plan based on three levels of stock, banded as green, amber and red.

		NBS Stock	Hospital Blood Stocks
Green	Current Average Stock	100%	100%
Amber	Reduced Stock	67%	67%
Red	Emergency Stock	50%	40%

Hospital blood stock levels are agreed and based on Blood Stocks Management Scheme (BSMS) information, the type of hospital, total blood usage and distance from the Blood Centre.

To assess the potential impact of this type of contingency planning on hospital transfusion practice, a 'shadow' pilot study was undertaken on two separate working days at a London DGH and Teaching Hospital. The second pilot day had twice the cross-match workload as the first pilot day.

Transfusion/Operations Cancelled/Deferred

	Day 1	Day 2
Green	0	0
Amber	4 top-ups	3 top-ups 4 CRF
Red	4 top-ups 1 CABG's 1 TAAA's	3 top-ups 4 CRF's BMT 4 CABG's 2 AAA's

All top-up transfusion requests had a pre-transfusion Hb of < 10 gm/dL and only three were above 8 gm/dL.

Should we say something about the scope this allows this particular hospital in terms of reduction in use – ie not much. May be different fo different hospitals but should we paint a worst case scenario? Was the above data derived from both hopsitals or only SMH? Also ? mention that there has been no clinical input into this as yet.

This pilot 'shadow' study will be extended to other hospitals, but key factors falling out from this preliminary work indicates that each hospital needs an emergency blood management plan and a senior hospital team to develop the plan and manage the response to reduced stock levels. ***? say that some, as in this case, may appear to have very limited scope for reduction in usage at least based on current guidelines/best practice*** It is also clear that unless hospitals develop the necessary clinical infrastructure to implement the recommendations of Better Blood Transfusion and Appropriate Use of Blood, a 10% drop in total blood stocks will have a significant impact on continuity of supply to patients and seriously disrupt hospital blood transfusion and surgical practice. ***Standards of patient management (wrt transfusion) and surgical practice need to be agreed at national level, also taking into account local hopsital variations.***

Measures which could be taken to minimise the impact of a reduction in blood supply

As a 10% reduction in blood stocks (the likely outcome of excluding transfused donors) presents a real risk to the continuity of the blood supply, potentially putting some patients at risk and/reducing their quality of care, the NBS has been considering alternative options for mitigating the vCJD risk of blood transfusion to the 'most at risk' patient groups.

1. Use of accredited donor panels for neonates and children

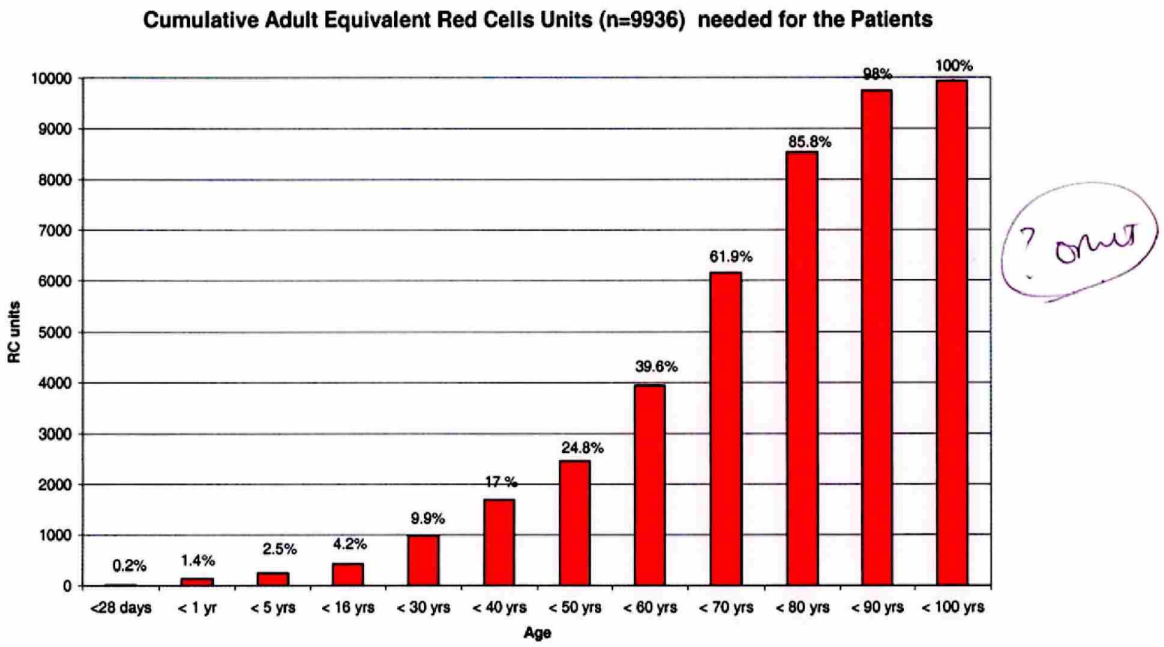
Most blood component usage is for patients who are either elderly or who have underlying conditions associated with shortening of life span such as malignancy.

It is therefore worth considering whether certain steps to mitigate against the risk of vCJD transfusion transmission could be applied to the 'most at risk' patient groups with a relatively normal life-span expectancy, i.e. neonates and children

Premature neonates and children born after the relevant food bans (i.e. after 1 January 1996) have not been exposed to the BSE agent through foodstuffs and a large percentage of these patients are likely to have a normal life expectancy post-transfusion. It could be justified therefore to provide these patients with blood components from accredited panels of non-transfused donors.

Data on component usage within the NBS are beginning to emerge from studies on the epidemiology of blood recipients. Based on this data, it has been possible to calculate the age distribution of recipients of all red cell units – see *Fig.2*.

Fig.2:



Based on an analysis of the fate of nearly 10,000 units of red cells, 4.2% are provided to children of 16 years and under.

2. Appropriate use

As discussed above

3. Other alternatives

? summarise work so far from App. Use sub-groups ie autologous/epo/ bloodless surgical units etc

Conclusions:

Although it is clear from the EOR analysis that exclusion of donors who have received transfusion of blood components in the past could have a significant impact on the occurrence of secondary vCJD infections, it is also clear that this would have a significant impact on the blood supply and management of patients requiring blood component therapy.

The balance of risks suggests that a logical and sensible approach would be to:

(1) Take precautionary measures to protect the population that has not already been exposed to the BSE food agent and/or who has a normal (long) life expectancy after their transfusion event:

i.e. all neonates, all children born on and after 1 January 1996 and children up to the age of 16

This would require establishing an accredited panel of non-transfused donors sufficient to supply the blood component requirements of this age group of patients.

(2) Take active steps to ensure that the HSC on Better Blood Transfusion (due to be published and circulated shortly) is implemented in the shortest possible timescale. This will require prioritisation of resources within hospitals recognising that this is an important risk reduction measure to prevent potential transfusion transmission of vCJD.

Need for risk analysis/EOL work to understand further
- Clinical impact
- Impact on DoH programmes
  - Cancer
  - Hips.

(3) Further groups. (ie exposed but longer life span - ? EOL work)
(ie analogous approach to FFP).

Discussion paper on progress with the risk of transfused donors + impact on hospitals

DRAFT 1.

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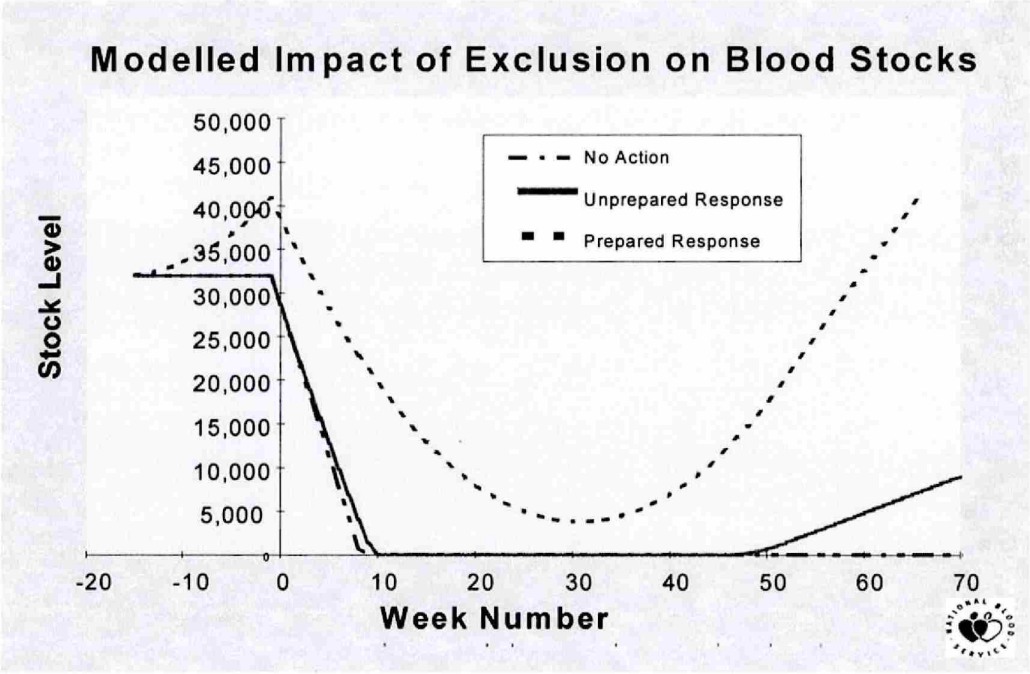

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Standards for mgt
Standards for surgical practice.

ALTERNATIVES

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2. – Appropriate use.
– As referred to above.

3. ~~Other~~ alternatives

Need exploring (papers due Jan subgps)

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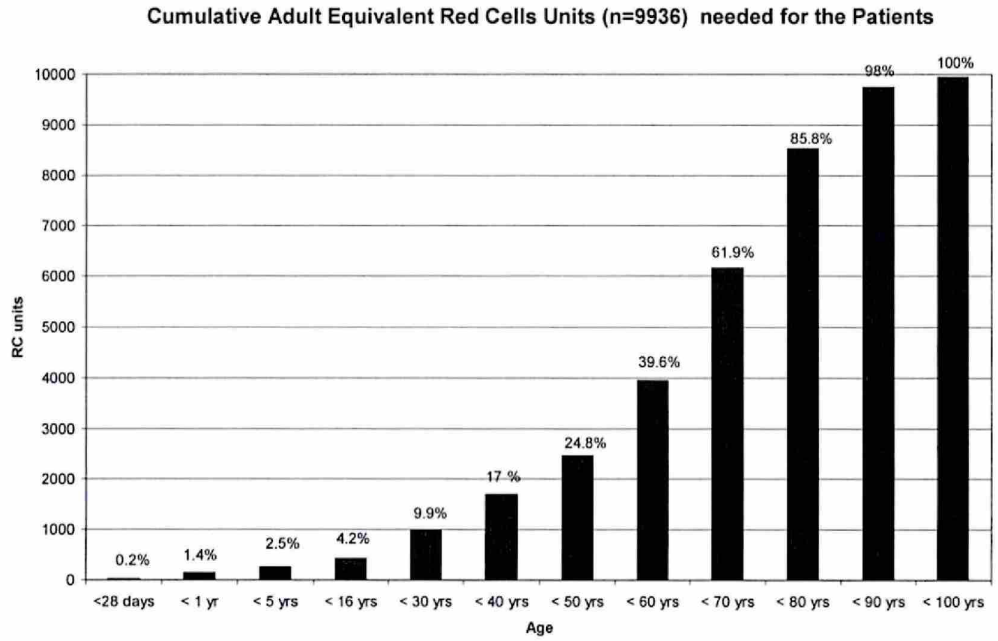

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Conclusions:

(To be updated) What does recent Sheep data do to this? BEAC??

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