

Comparing the relative risk of vCJD transmission via single unit and pooled plasma from UK and non-UK sources.

ISSUE

1. The Department of Health (DH) has asked SEAC to provide advice on a risk assessment methodology, for assessing the risks of using single unit plasma with respect to pooled plasma, from the UK or a range of non-UK source countries. The risk assessment is attached at annex 1.

RISK ASSESSMENT METHODOLOGY

2. The DH risk assessment quantifies the risks to public health of pooled plasma under a number of different scenarios. The purpose of the risk assessment is to allow the potential vCJD risks of different plasma products to be quantified and compared to inform recommendations about their use. Firstly, it presents a comparison of the risk of single unit plasma with respect to pooled plasma of various pool sizes from the *same source country*. It then compares the relative risk of single unit plasma to pooled plasma (for various pool sizes) from a *different source country*. This is done on a scenario basis, using different *assumed* values for the risk reduction from sourcing from outside the UK.
3. Due to the uncertainty of a number of key parameters associated with vCJD, the risk assessment uses a scenario-based approach for two of the main parameters: vCJD prevalence in the UK donor population and the level of infectivity of blood. Under different infectivity and prevalence scenarios, it assesses the risk of transmission of vCJD via plasma in a pooled product, compared to the baseline risk of single unit UK plasma.
4. The paper also presents a methodology for estimating the relative vCJD prevalence of a source country with respect to the UK, through comparisons of vCJD and BSE incidence, adjusted to take into account their relative degrees of active and passive surveillance.
5. Finally, the paper compares the relative risk of single unit UK plasma to pooled plasma (for various pool sizes) that has been prion filtered.

KEY ASSUMPTIONS USED IN THE DH RISK ASSESSMENT

6. The key assumptions used in the risk assessment are:
- Two scenarios for the infectivity of whole blood are used for the purposes of this model: a 'low' scenario (0.1 ID/ml i.v. transmission) and a 'high' scenario (30 ID/ml i.v. transmission).
 - 50% of the infectivity of whole blood is removed by leucodepletion and the remaining 50% of infectivity resides within the residual plasma.
 - Two scenarios for prevalence of vCJD in the UK are used: a 'low' scenario (1 in 20,000) and a 'high' scenario (1 in 4,000). In the absence of any further evidence, these will also be used for the UK donor population and applied irrespective of age or genotype.
 - The dose-response follows a Poisson distribution.
 - 100% of the population is susceptible to infection and developing clinical symptoms of vCJD.

The rationale for these assumptions is explained in the assessment.

PREVIOUS SEAC ADVICE

7. Previous SEAC advice on the pooling of blood, as well as the level, and distribution, of infectivity in blood is summarised in the risk assessment, which also includes the SEAC position statement on TSE infectivity in blood at Annex A. Other SEAC advice pertinent to consideration of the risk assessment on the geographical BSE risk categorisation and estimates of the prevalence of subclinical vCJD are given below.
8. SEAC provided advice on the sub-clinical prevalence of vCJD in its 2008 position statement on Prevalence of Subclinical variant Creutzfeldt Jakob Disease Infections². The statement concluded that it would be prudent to consider that the estimate provided by the Hilton et al study of 1 in 4,000, provides a reasonable, pragmatic and precautionary working scenario for the prevalence of subclinical infections.
9. SEAC has not previously provided advice on sourcing plasma from countries with known BSE risks. However, the committee provided advice on the Geographical BSE Risk (GBR) system for assessing sourcing risks as part of its discussion on medical implants containing bovine material, in February 2006. The committee considered that the GBR system gives a very imprecise indication of BSE risk. In relative terms, the BSE risk was likely to be lower in a GBR I country compared with a GBR III country, but the difference in risk cannot be quantified. In terms of a more robust risk analysis, the Committee considered that it is important to obtain a more reliable estimate of the prevalence of BSE in a country than simply GBR status, and to have confidence in the quality of the surveillance data. SEAC concluded that the GBR status of a country gives an imprecise indication of BSE risk and that it would be better to use an estimated prevalence of BSE in a country based on data from a robust surveillance system³.

ADVICE SOUGHT FROM SEAC

10. The Committee is asked to comment on:
- whether the assumptions used in the risk assessment are reasonable; and
 - the appropriateness of the methodology of the risk assessment to quantify and compare the potential vCJD risk that may be associated with plasma products.

Notes

1. Position Statement on TSE Infectivity in Blood, July 2006, <http://www.seac.gov.uk/statements/statement0806.htm>.
2. Position Statement on Prevalence of Subclinical variant Creutzfeldt Jakob Disease Infections, August 2008, <http://www.seac.gov.uk/statements/statement0806.htm>.
3. Medical Implants Containing Bovine Material, SEAC 91, 24 February 2006.

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