

20 June 2001

Issue 1. Summary

Deferral of Blood Donors Potentially Exposed to the Agent of Variant Creutzfeldt-Jakob Disease (vCJD)

Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC)

June 28, 2001

Issue: FDA asks the TSEAC for advice to help decide if deferral of additional blood and plasma donors potentially exposed to the agent of bovine spongiform encephalopathy (BSE) can be safely implemented to reduce further the theoretical risk of transmitting vCJD by blood, blood components and plasma derivatives while maintaining adequate national and regional supplies.

Background:

Unlike other forms of CJD, in vCJD the abnormal protease-resistant prion protein accumulates to substantial levels in lymphoid tissues. This finding raised concern that the relatively reassuring epidemiological evidence suggesting that blood was unlikely to be an important vector for classic forms of CJD might not be predictive for vCJD—a disease with which we still have only limited experience. To date, no epidemiological evidence suggests that vCJD has been transmitted by blood, blood components or plasma derivatives. However, animal models suggest that this may be possible (Taylor, 2000; Houston et al., 2000), and studies of the infectivity of blood from persons with vCJD, while negative so far, are limited (Brown P, personal communication, 2001; Baron H, presented at IBC Annual Biological Safety and Production conference, Vienna VA, April 2, 2001). Although several interesting new techniques have been proposed (Miele et al, 2001; Saborio et al, 2001 among others), there is no validated test to screen blood donors (Prusiner, 2001; Roos, 2001).

In 1999, concurrent with its issuance of guidance on donor deferral for risk of vCJD, the FDA was charged by the Surgeon General of the United States to revisit the issue of blood safety regarding possible transmission of CJD and vCJD as frequently as needed, but at least every six months. Uncertainty concerning the potential infectivity of human blood during the long asymptomatic incubation period of vCJD prompted CBER's current policy, first announced in August and in final form in November 1999. That policy recommended precautionary deferral of donors resident or traveling in the United Kingdom (UK) for any cumulative period of six months or more from the presumed start of the BSE epidemic in 1980 to the full implementation (by the end of 1996) of a series of measures to prevent human exposure to BSE-contaminated beef by protecting the food chain; those measures included—in addition to a ban on feeding ruminant materials to other ruminants, BSE surveillance and herd culling—an "age-based slaughter scheme" requiring that all cattle used for meat products be slaughtered within 30 months after birth, careful removal of "specified risk materials" from carcasses, and prohibition of mechanically recovered meat. Taken together, those measures should have substantially reduced potential contamination of products intended for human consumption. The FDA policy of November 1999 was intended to defer those donors with the greatest possible exposure to the BSE agent. FDA estimated that this deferral would remove almost 87% of the vCJD risk due to UK exposure (risk expressed as the total number of days that donors were potentially exposed to the BSE agent in the UK) and would result in a projected loss of 2.2% of the US blood supply.

In January 2001 the TSEAC reviewed information showing increasing numbers of BSE cases and the recognition of vCJD in France (three cases) and Ireland (one case in a former UK resident). TSEAC advised that the FDA recommend deferring—in addition to donors who had been in the UK for at least six months—anyone who had traveled or lived for ten years or more in France, based on evidence that during

some years of concern, a substantial part of the French Beef supply had been imported from the UK. (The number of vCJD cases in France through 2000 was approximately 5% of those in a population of similar size in the UK, and a rough estimate suggested that UK beef might have comprised about 5% of French consumption before import restrictions were imposed.) The TSEAC also advised deferring donors who had traveled or lived for ten years or more in Portugal or the Republic of Ireland from 1980 to the present, because those countries had many cases of BSE in native cattle and may have had ineffective protection of human food against BSE risk. The TSEAC further recommended deferrals for those US military personnel and dependents who had been exposed to UK beef on European bases from 1980 through 1996 for an unspecified period of time longer than six months.

The FDA acknowledges TSEAC concerns expressed in January 2001, agreeing that risk of transmission of vCJD is theoretical and that the potential loss of blood donors from increased deferrals is substantial. The FDA also understands the reluctance of the TSEAC to lump together in one deferral policy all 30 countries that, in addition to UK, are on the current USDA BSE list (USDA, 1998). However, the FDA has not been convinced that existing information is adequate to justify recommending a stratified risk-based policy for deferral of donors potentially exposed to the BSE agent in France, Ireland and Portugal while accepting the risk of exposure in other continental European countries.

The vast majority of BSE cases--more than 180,000--have been diagnosed in the UK; Britain reported 1352 cases for the year 2000 and 177 through the end of April of this year (UK MAFF, 2001). Although Ireland and Portugal indeed had the next highest numbers--613 and 568 cases to date according to recent OIE figures (June 2001)--BSE cases in Switzerland were also substantial (382), exceeding the number reported from France (296). Numbers of BSE cases in cattle born in Germany and Spain to date seem more modest--75 and 46--but it is troubling that all those cases were found within the past year. Furthermore, the recent finding of BSE in the Czech Republic casts some doubt on the ability of available risk assessments to provide reliable estimates of potential human exposure to BSE agent in various countries; the Czech Republic is a country to which the EC Scientific Steering Committee (July 2000) had previously assigned a low probability of BSE. (The USDA [1998], on which FDA has relied to determine countries with a significant risk of BSE, placed the Czech Republic--with the rest of Europe west of the Former Soviet Union--on its BSE list at the end of 1997.) On this basis, it is difficult for the FDA to be confident that a bright line can be drawn distinguishing the risk of human exposure to the BSE agent in France, Ireland and Portugal from risk elsewhere in Europe.

The American Red Cross (ARC), which collects approximately half the US blood supply, has most recently proposed a precautionary deferral policy considerably more aggressive than that offered by TSEAC. The policy of the ARC is to defer donors who lived or traveled for any aggregate period of three months or more in the UK from 1980 to the present or for six months or more in any other European country from 1980 to the present. ARC has announced that it intends to implement the new deferrals throughout its system in mid-September 2001. Concluding that the probable donor loss that might result was not justified in light of current BSE-related risk, TSEAC rejected a similar ARC proposal (deferring donors who spent ≥ 12 months in Europe from 1980 to present) at its January 2001 meeting. In light of the fact that ARC collects nearly half the US blood supply, non-ARC collectors may face legal and public relations pressures to institute deferral policies similar to that of the ARC. However, other major blood programs have publicly expressed doubts that they will be able to meet projected needs for blood if they attempt to follow the proposed ARC policy.

The FDA continues to believe that, until the results of research permit development of policies based on reliable scientific data, it is prudent to reduce the use of donors potentially exposed to the BSE agent as much as feasible. However, the USA must also maintain an adequate supply of safe blood and blood products, the lack of which would cause immediate harm to the population.

Estimation of Absolute Risk:

Several factors influence the likelihood of transfusion transmission of vCJD by blood and its components. Those include the following:

- a) Likelihood that donors have been infected by dietary or other exposures to BSE-contaminated ruminant materials
- b) Overall prevalence of the asymptomatic carrier state in the exposed population

- c) The length of the pre-clinical incubation period (mean value and range)
- d) Presence of the vCJD agent in blood of infected blood donors (during various stages of incubation) at levels sufficient to transmit disease by allogeneic transfusion
- e) Susceptibility of the recipient population to infection

Limited studies of TSE infection in sheep and rodent models support the concept that the vCJD agent may be transmissible by allogeneic transfusion. However, no data exist regarding the natural history of the infection in the human host. For that reason, it is currently impossible to estimate with any confidence the number of vCJD infections potentially transmitted by transfusion or to model how intervention strategies would affect the risk.

Estimation of Risk Reduction and Donor Loss Based on Cumulative Travel and Residence in BSE Countries:

In April 1999, a collaborative survey of donor travel was conducted among 12 blood centers. This survey was primarily targeted to collection of blood donor travel and residence data for the UK. Limited information about overall travel to other European BSE countries was also collected, but country-specific intervals could only be extrapolated using numerous assumptions. With those assumptions stated, the existing data have been applied to models that assign various risk ratios relative to the UK for BSE exposures in different European countries and for exposures on US military bases in Europe. These models have been useful to estimate the additive and cumulative reductions in vCJD risk as well as the donor losses expected to result from various deferral policies. In the absence of additional data, estimates derived from this model are dependent upon an assumption of linearity—that exposures to the BSE agent are stochastic and so are directly related to time spent in a country where beef products are contaminated with the BSE agent.

Predicted Impact of Additional Blood Donor Deferrals on Blood Supply:

Overall US supply. Maintaining adequate blood supplies across the US (the benefit) is a prime consideration for any proposed deferral option taken to reduce the theoretical risk of transmitting vCJD. While the estimated 2.2% donor loss from the initial ≥ 6 -month UK donor deferral, implemented in early 2000, was generally well tolerated across the country, the US blood supply has never experienced a one-time donor loss of more than 3.0%. (Such a loss occurred over a period of two years after donor screening for antibodies to hepatitis B virus core was introduced in 1986. The ARC estimated that it may have lost 6% of its donors—or 3% of all US donors nationwide—after it replaced ear lobe hematocrit testing with fingerstick testing last year.) Objective measures to assess adequacy of the US blood supply are currently very limited, however blood collection and utilization data gathered by the National Blood Data Resource Center indicate that whole blood collections increased 10.1% between 1997 and 1999 (at a time of extensive donor recruitment in the news media). Blood use has also increased by approximately 4.5% each year. Such data do not provide information about local availability, which is affected unevenly by differences in demand, donor demographics and other factors.

New York area blood supply. "Euroblood" comprises approximately 25% of supply in the greater metropolitan area of New York City, which imports about 145,000 units from Europe each year. None of this blood would be available after any pan-European deferral. In addition, the New York Blood Center anticipates an approximate 10% loss of donors in the NYC area who are frequent travelers, bringing the predicted total loss there to 35% or 190,000 units each year. To date, no assured alternate sources of supply for the New York area adequate to replace those losses have been identified.

Current and former US Department of Defense (DoD) personnel and dependents stationed on European bases since 1980. Up to 4.5 million DoD service personnel and dependents were exposed to UK beef supplied to US bases in Europe between 1980 and 1990 (all bases) and from 1990 through 1996 (on bases South of the Alps). Based upon DoD estimates, the maximum exposure of DoD staff and dependents to UK beef during this time might have been equivalent to 35% of the exposure of UK residents. Based upon National Center for Health Statistics data about blood donations among the US population, such individuals are likely to provide approximately 3.0% of the current US blood supply. Deferral of donors who spent six months or more cumulative on a European DoD base from 1980 through the end of 1996 would cost an estimated 2.2% of US donors. If screening questions can be designed to

eliminate from deferral those donors who were on bases North of the Alps after 1990, then the overall loss would be reduced to 1.8% of US donors.

DoD internal blood supply. DoD currently uses for transfusion 105,000 fully qualified collections per year. Under a six-month deferral policy, the predicted loss of acceptable donors is approximately 21 to 24% (from 21,725 to 25,515 donors). Using major media (newspaper) recruitment campaigns, DoD has already taken steps to increase donations by the active duty troops about 3% overall. DoD has stated that it is desirable to have a unified BSE policy and that DoD is prepared to adopt a policy compatible with the ARC proposal if necessary.

** Note that proportions of current active duty troops with potential exposure to BSE agent in Europe are less than the historical figures used to estimate impact on the civilian supply due to major reductions in size of the European DoD bases over the past ten years.

Discussion, Policy Recommendations and Additional Deferral Options:

CBER concurs with the TSEAC that an extension of the current policy to defer donors potentially exposed to the BSE agent in the UK is needed. This policy must address the additional theoretical risk of exposures to BSE in continental European countries as well as prior exposure of US military personnel and their dependents to UK beef at European bases. FDA also shares TSEAC's concern about the adverse effects that might result from anticipated losses to the US blood supply and is equally committed to maintaining adequate supplies of safe blood and blood products. In this regard, the FDA is already cooperating with the Centers for Disease Control and Prevention and other agencies in the Department of Health and Human Services to develop strategies for more effective monitoring of the US blood supply and for improved recruitment and retention of blood and plasma donors. (In the past, use of intensive campaigns to increase donor recruitment and retention as well as economic incentives attracting blood to regions with insufficient local supplies, while at least temporarily successful, have entailed substantially increased costs.) The FDA has also long encouraged adoption of clinical guidelines for appropriate use of transfusions both to reduce the occurrence of preventable transfusion-associated adverse events and to conserve blood. The potential of such strategies to increase and conserve supplies of blood over prolonged periods of time is not known.

The FDA asks the TSEAC to consider, taking account of new information about BSE and vCJD, three options for extending the current policy intended to reduce the risk of transmitting vCJD by blood and blood products. FDA has conducted an extensive assessment of the theoretical BSE risk reduction and estimated donor losses associated with three donor deferral scenarios described here; they are summarized and compared with current policy using a "risk-weighted exposure" model in the attached appendix including a table comparing the three options. The FDA would also entertain proposals for other donor deferral options consistent with its overall efforts to reduce the theoretical risk of blood-borne transmission of vCJD while maintaining adequate national and regional supplies of human blood and blood products. We anticipate that, based in part on TSEAC's advice, the FDA will issue for comment a proposed revision of its Guidance for Industry and that implementation will be requested within six months after issuance of a final revised Guidance. In addition, FDA will encourage well-designed and well-monitored pilot programs to explore the feasibility of various deferral options that exceed FDA policy.

Option #1 (policy consistent with advice offered by TSEAC in January 2001)

- Defer donors traveling or resident for any cumulative period of ten years or more in France, Portugal, or the Republic of Ireland from 1980 to the present.
- Defer donors traveling or resident for any cumulative period of six months or more in UK 1980-1996. (This would be unchanged from current FDA policy.)
- Defer donors resident for any cumulative period of six months or more on a European DoD base from 1980-1996 (or 1980-1990 if all exposure after 1990 was on DoD bases North of the Alps).

Estimated Impact: 2.2% donor loss; 44% reduction of current risk; 82% reduction of total risk.

(Note: If ARC implements its announced policy and some other blood programs follow, then both donor loss and reductions in risk would be greater than these estimates.)

Advantages:

- ❖ Limits donor loss overall: Euroblood and DoD blood supply would be only marginally affected.
- ❖ Deferral is based upon actual observations and is directly linked to observed BSE exposures in France, Portugal, and the Republic of Ireland.
- ❖ Separate DoD questions would allow distinction between exposures on Northern and Southern European DoD bases.
- ❖ Policy was previously recommended by TSEAC.
- ❖ Limitation of UK deferral to the years 1980-96 establishes precedent recognizing the protective value of effective food controls.

Disadvantages:

- ❖ Policy is based on observations that may be biased against deferring for exposure in European countries with BSE where surveillance has been inadequate.
- ❖ Policy allows continued importing of Euroblood, which (assuming a 1.5% risk compared to UK) carries a substantial level of theoretical risk of exposure. (Most Euroblood donors have lived in Europe since the beginning of the BSE epidemic.)
- ❖ Targeting of deferral policy at specific countries creates a “moving target” probably requiring rapid introduction of new deferrals as the epidemic involves new countries. The ability to define risk for individual countries will depend upon BSE and vCJD data of variable reliability reported by the country involved.
- ❖ The policy is based on surveillance and ignores the fact that BSE is probably under-reported and may already be present elsewhere in Europe.
- ❖ The option would result in non-uniform national blood donor suitability policies if ARC proceeds to implement its proposed policy as planned.
- ❖ Donor screening questions would be moderately more complex than at present.
- ❖ There is no protection against the possibility that the BSE agent has further adapted to humans who were infected by prior transfusions from donors exposed in UK
- ❖ Reduction of European risk is minimal, and most risk reduction gained by the proposed policy would result from DoD-related deferrals.

Option #2 (policy proposed by the American Red Cross)

- Defer donors for cumulative travel or residence in Europe for any period of six months or more from 1980 through the present or in the UK for three months or more from 1980 to the present.
- Defer donors who received a transfusion in the UK at any time from 1980 through the present.
- ARC plans to implement the new deferral policy throughout their system in September 2001.

Estimated Impact: 7.8 to 9.1% donor loss; 76% reduction of current risk; 92% reduction of total risk.

Advantages:

- ❖ Donor questions would be straightforward; DoD theoretical risk would be captured without the need for any separate questions.
- ❖ There would be a single national donor suitability policy, presuming that ARC proceeds with its plans.
- ❖ The policy provides the most aggressive deferral of non-DoD donors who were in continental Europe and consequently the most proactive should non-UK Europe prove to be a major contributor to overall risk of human exposure to BSE.
- ❖ The policy provides limited protection against human passage of vCJD from blood of persons who received a prior transfusion.

Disadvantages:

- ❖ The policy is comparatively inefficient if the risk of human exposure to the BSE agent in continental Europe is ~1.5% of the risk in the UK as current observations suggest.
- ❖ The impact of the predicted unprecedented 8 to 9% donor loss is unknown and probably severe, especially in the New York City metropolitan area and in other urban areas on both East and West Coasts where donors travel disproportionately more.
- ❖ The policy appears to recognize no protective effect on the human food chain by those measures that have been recommended for implementation by all countries having BSE in cattle.

Option #3 (FDA proposal)

- Defer donors for cumulative travel or residence of five years or more in any European country except UK from 1980 to the present
- Defer donors who spent any cumulative period of three months or more in UK from 1980 through the end of 1996.
- Defer donors who spent more than six months on a European DoD base from 1980 through the end of 1996 (or 1980 through 1990 if all exposure after 1990 was on DoD bases North of the Alps)
- Defer any recipient of a blood transfusion in UK from 1980 to the present.
- Implement deferrals within six months of final FDA Guidance.

Estimated Impact: 4.6 to 5.3% donor loss; 72% reduction of current risk; 91% reduction of total risk

(Note: If ARC implements its announced policy and some other blood programs follow, then donor loss would be greater and reductions in risk would be slightly greater than these estimates.)

Advantages:

- ❖ Deferral is based on current observational BSE data.
- ❖ The option allows blood establishments to institute stricter policies cautiously and with the possibility of relaxing suitability criteria if needed to maintain blood supplies adequate to meet local needs.
- ❖ Impact on blood availability is unknown but estimated to be controllable by instituting both a national recruitment campaign and a system to monitor adequate blood supply.
- ❖ The policy attempts to be proactive by assigning the current ratio of risk for BSE exposure throughout continental Europe countries as

5% of that in the UK, which is thought to represent a worst case. (Deferral is recommended for cumulative five-year residence in continental Europe, a period that is 20 times the period of three months recommended for deferral of donors resident in UK.)

- ❖ Deferral criteria will be less prone to frequent revisions than if criteria are recommended for individual countries based on current estimates of BSE.
- ❖ The policy offers limited protection against the possibility of increased adaptation of the BSE agent to humans by previous human-to-human passage via prior transfusion.

Disadvantages:

- ❖ The option will result in a non-uniform national policy if ARC proceeds with current plans.
- ❖ Donor screening questions will become more complex than they are now.
- ❖ The short-term and long-term effects of the predicted substantial donor losses (from 4% to 6%) on national and regional supplies are unknown.

Bibliography

Brown P. Bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease. *Brit Med J* 2001;322:841-844

Brown P, Will RG, Bradley R, Asher DM, Detwiler L. Bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease: background, evolution and current concerns. *Emerging Infectious Diseases* 2001;7:6-16

Donnelly CA. Likely size of the French BSE epidemic. *Nature* 2000;408:787-788

European Commission. Final opinion of the Scientific Steering Committee on the geographical risk of bovine spongiform encephalopathy (GBR). July 6, 2000; available at <http://europa.eu.int/comm/food/fs/sc/ssc/out113_en.pdf>

Houston F, Foster JD, Chong A, Hunter N, Bostock CJ. Transmission of BSE by blood transfusion in sheep. *Lancet* 2000;356:999-1000

Miele G, Manson J, Clinton M. A novel erythroid-specific marker of transmissible spongiform encephalopathies. *Nature Medicine* 2001;7:361-364

Office International des Epizooties. Number of reported cases of BSE worldwide (excluding the United Kingdom). OIE Webpage 2001; available at <www.oie.int/eng/info/en_esbmonde.htm>

Prusiner SB. Shattuck Lecture. Neurodegenerative diseases and prions. *New Engl J Med* 2001;344:1516-1526

Roos RP. Controlling new prion diseases. *New Engl J Med* 2001;344:1548-1551

Saborio GP, Permanne B, Soto C. Sensitive detection of pathological prion protein by cyclic amplification of protein misfolding. *Nature* 2001;411:810-813

Taylor DM, Fernie K, Reichl HE, Somerville RA. Infectivity in the blood of mice with a BSE-derived agent. *J Hosp Infect* 2000;46:78-79

UK Ministry of Agriculture, Fisheries and Food. BSE status report. MAFF BSE Enforcement Bulletin 2001;58:2

US Department of Agriculture, Animal and Plant Health Inspection Service. Restrictions on the importation of ruminants, meat and meat products for ruminants, and certain other ruminant products. Interim rule and request for comments (6 Jan 1998). Federal Register 1998;63:406-408

US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research. Guidance for Industry. Revised precautionary measures to reduce the possible risk of transmission of Creutzfeldt-Jakob disease (CJD) and new variant Creutzfeldt-Jakob disease (nvCJD) by blood and blood products. (November) 1999. CBER Guidance Documents available at <www.fda.gov/cber/guidelines.htm>

Questions for the TSEAC

1. Do TSEAC members concur with the FDA proposal (Option #3) to defer additional blood and plasma donors based on potential exposure to the agent of BSE?
2. If not, do TSEAC members advise the FDA to recommend the blood and plasma donor deferral policy recently proposed by the American Red Cross (Option #2)?
3. If not, do TSEAC members advise the FDA to recommend the blood and plasma donor deferral policy proposed by the TSEAC on 18 January 2001 (Option #1)?
4. If not, do TSEAC members advise FDA to recommend some other revised policy to reduce further the risk of blood-borne transmission of vCJD while maintaining adequate regional and national supplies of blood and blood products? Please specify.
5. Please comment on steps that should be taken to monitor and ensure adequate national and regional supplies of blood, blood components and plasma derivatives if additional donors are deferred based on possible exposures to BSE agent.

Issue 1 Summary: Appendix

TSEAC June 28, 2001

Deferral of Blood Donors Potentially Exposed to the Agent of vCJD:

**BSE RISK REDUCTION AND DONOR LOSS ESTIMATES
BASED UPON A FDA/CDC-PROPOSED
RISK-WEIGHTED EXPOSURE DAY MODEL****

Policy	Reduction of Total Risk^a	Reduction of Current Risk^b	Donor loss^c	Efficiency^d
Current	68%	0	(2.2%)	31
TSEAC ^e	82%	44%	2.2%	20
ARC ^f	92%	76%	7.8 - 9.1%	9.7 - 8.4
FDA proposed ^g	91%	72%	4.6 - 5.3%	15.7 - 13.6

^a Total risk is defined as total estimated BSE risk burden to the US blood supply prior to any intervention. (See model explanation below.)

^b Current risk is defined as total estimated BSE risk minus the component of UK risk removed by the November 1999 deferral for ≥ 6 months travel/residence in UK.

^c Donor loss is the additive loss for a modified deferral policy (i.e. not including the previous 2.2% donor loss). Projected loss includes Euroblood loss (1.2%) for all proposed pan-European deferrals

^d Efficiency is defined as % current risk reduction / % donor loss

^e January 2001 TSEAC-recommended deferral for ≥ 10 yr France or Portugal or Republic of Ireland 1980-present; ≥ 6 mo time spent on DoD European base 1980-1996

^f ARC plans to implement deferral for all donors who have spent ≥ 3 mo in UK 1980-present and/or 6 mo in Europe 1980-present

^gFDA proposes deferral for ≥ 6 mo time spent on DoD European base 1980-1996; ≥ 3 mo. travel/residence in the UK 1980-1996; ≥ 5 yr travel/residence in Europe 1980-present, and deferral for any transfusion in the UK 1980-present

**** Notes: FDA/CDC proposed risk model:**

UK = 1.0; France = 0.05; Other Europe = 0.015; DoD = 0.35

1. The UK has experienced the greatest impact from both BSE and vCJD and is the reference value for other geographic exposures. There were an estimated 998,064 person-years (P-Y) exposure to the current US blood supply, based on travel/residence patterns measured by the 1999 blood donor travel survey. A total of 868,316 P-Y (87%) were removed by the 1999 ≥ 6 mo UK travel/residence deferral.

2. A 5% risk of BSE is estimated for France (compared to UK) based upon reports of extensive shipments of UK beef to France during the years 1980-1996 and the recognition of two known (and one probable) vCJD cases. (35,580 P-Y)

3. UK beef shipments to other parts of Europe are less well documented, and BSE exposures for other European countries are estimated primarily by observed BSE in indigenous herds. Switzerland has experienced high rates of BSE, and surveillance in Switzerland has been intensive. The herd size-adjusted BSE rate in Switzerland is 1.5% that of the UK. As a worst-case scenario, all European countries other than France have been assigned a 1.5% risk level. (19,155 P-Y European travel/residence estimated from 1999 donor travel survey + 45,150 P-Y estimated for annual imports of Euroblood).

4. Department of Defense European-base risk (35%) is estimated from DoD-supplied data regarding UK beef shipped to European bases (North of Alps 1980-1990; South of Alps 1980-1996 yielding Total: 172,625 P-Y)