APPENDIX 1

TABLE A1. Table of contents and legend

PRIORITY DEFINITIONS

- **Red** = Agents with low to high scientific/epidemiologic evidence of risk regarding blood safety with the potential for severe clinical outcomes. This prioritization also may be influenced by the committee's estimate of the risk of emergence of these agents in the US and Canada as well as public and/or regulatory concern.
- **Orange** = Agents with scientific/epidemiologic evidence of risk regarding blood safety that might support their elevation to a higher priority at some time in the future.
- **Yellow** = Agents with absent to low scientific/epidemiologic evidence of risk regarding blood safety for which there is public and/or regulatory concern.
- **White** = Agents evaluated but for which no higher prioritization appears warranted at this time.

TABLE A2. Priority assessment of prion agents

Categories	Chronic wasting disease	Classical CJD	vCJD*
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	THEORETICAL†	LOW‡
Public perception and/or regulatory concern regarding blood safety	VERY LOW	VERY LOW	HIGH
Public concern regarding disease agent	LOW/MODERATE	ABSENT	MODERATE

* Agent causes transfusion-transmitted infection in humans.
† After extensive studies, transfusion transmission to humans has not been demonstrated despite proven risk from human tissue (e.g., dura mater, pituitary growth hormone).
‡ Due to the absence of endogenous human infection in North America and the possible impact of stringent donor deferral policy. There is strong evidence for transfusion transmission in the UK.

TABLE A3. Priority assessment of viral agents (A-En)

Categories	Borna disease virus	Chikungunya virus	Colorado tick fever virus*	Crimean-Congo hemorrhagic fever virus	Dengue viruses*	Eastern equine encephalitis virus	Ebola virus	Enteroviruses
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	THEORETICAL†	VERY LOW	THEORETICAL‡	LOW in US§	THEORETICAL	THEORETICAL‡	THEORETICAL
Public perception and/or regulatory concern regarding blood safety	ABSENT	VERY LOW/ABSENT in US; MODERATE/ HIGH in non-US endemic and threatened areas	ABSENT	ABSENT	VERY LOW/ABSENT in US; MODERATE/ HIGH in non-US endemic areas	ABSENT	VERY LOW/ ABSENT	ABSENT
Public concern regarding disease agent	ABSENT	VERY LOW/ABSENT in US; MODERATE/ HIGH in non-US endemic and threatened areas	ABSENT, but VERY LOW in endemic areas	VERY LOW, but MODERATE in endemic areas	VERY LOW/ABSENT in US; MODERATE/ HIGH in non-US endemic areas	VERY LOW	MODERATE	ABSENT

* Agent causes transfusion-transmitted infection in humans.
† Although no transfusion transmission has been documented, rapid reemergence, increased pathogenicity, and asymptomatic viremia suggest that transfusion transmission is possible.
‡ There are reasonable scientific grounds to confirm or suggest that viremia is a feature of infection with these agents. Asymptomatic viremia has been neither well studied nor sought aggressively, so there are few or no data to make a critical assessment of risk.
§ Overall priority is related to asymptomatic viremia that may result in transfusion transmission and substantial potential for emergence in the US. This risk is mitigated by the low prevalence of autochthonous transmission in the continental US, and deferrals for malaria that would exclude most travelers coming from endemic areas.

TABLE A4. Priority assessment of viral agents (Ep-Hep)

Categories	Epstein-Barr virus*	GB/Hepatitis G viruses*	Hantavirus New World	Hantavirus Old World	Hepatitis A virus*	Hepatitis B virus variants*	Hepatitis E virus*
Scientific/Epidemiologic evidence regarding blood safety	VERY LOW	ABSENT†	THEORETICAL	THEORETICAL	LOW	VERY LOW‡	VERY LOW§
Public perception and/or regulatory concern regarding blood safety	ABSENT	ABSENT	VERY LOW/ABSENT	VERY LOW/ABSENT	VERY LOW/ABSENT	ABSENT	ABSENT
Public concern regarding disease agent	ABSENT	ABSENT	LOW, but MODERATE in endemic areas	LOW, but MODERATE in endemic areas	LOW/MODERATE	ABSENT	ABSENT

* Agent causes transfusion-transmitted infection in humans.
† Transmission documented but no disease associated despite extensive studies.
‡ In US and other countries where testing for antibody to the hepatitis B core antigen (anti-HBc) is performed.
§ Probably higher in countries where transfusion-transmitted cases have been reported.

TABLE A5. Priority assessment of viral agents (Her-J)

Categories	Herpes viruses (other than CMV, EBV, and HHV-8)	HHV-8*	HIV variants*	HTLV variants	Human parvovirus B19*	Influenza A and B viruses (other than H5N1)	Influenza A virus (H5N1)	Japanese encephalitis virus
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	VERY LOW†	THEORETICAL‡	THEORETICAL‡	VERY LOW/LOW‖	THEORETICAL	THEORETICAL	THEORETICAL††
Public perception and/or regulatory concern regarding blood safety	ABSENT	LOW	LOW/MODERATE§	ABSENT	VERY LOW¶	VERY LOW	VERY LOW	ABSENT
Public concern regarding disease agent	ABSENT	VERY LOW	LOW/MODERATE§	ABSENT	LOW	MODERATE	HIGH	ABSENT

* Agent causes transfusion-transmitted infection in humans.
† No disease has been documented although transfusion transmission occurs in the absence of leukoreduction.
‡ Although the wild-type agents are transfusion transmitted, transfusion transmission of the variants has not been documented. If variants are transmissible, the risk would be very low in the US due to cross-reactivity of screening tests, use of donor screening questions, and limited global distribution of variants.
§ Based on transmission of HIV in general, rather than HIV variants.
‖ In the US, there is a higher level of concern for immunocompromised individuals, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients. A Low to Moderate rating is reasonable for pooled plasma and fractionated products based on variable implementation of NAT.
¶ In the US, there is an exception for this priority for patients with hemophilia; concern exists for immunocompromised individuals, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients. Priority level is considered to be LOW to MODERATE in several European countries with screening programs.
†† Because of similarity to West Nile virus, transfusion risk during JEV outbreaks may occur.

TABLE A6. Priority assessment of viral agents (L-Pa)

Categories	La Crosse virus	Lassa virus	Lymphocytic choriomeningitis virus	Marburg virus	Monkeypox virus	Mumps virus	Papillomaviruses
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	THEORETICAL†	THEORETICAL‡	THEORETICAL†	THEORETICAL	THEORETICAL	THEORETICAL
Public perception and/or regulatory concern regarding blood safety	ABSENT	ABSENT	ABSENT	VERY LOW/ABSENT	ABSENT but VERY LOW at time of 2003 outbreak	VERY LOW	ABSENT
Public concern regarding disease agent	VERY LOW but LOW in endemic areas	VERY LOW	ABSENT	LOW	ABSENT but VERY LOW at time of 2003 outbreak	VERY LOW but MODERATE in areas affected by an epidemic	LOW/MODERATE

† There are reasonable scientific grounds to confirm that viremia is a feature of infection with these agents. Asymptomatic viremia has been neither well studied nor sought aggressively, so there are few or no data to make a critical assessment of risk.
‡ Due to documented transmission via transplants but not transfusion.

TABLE A7. Priority assessment of viral agents (Po-S)

Categories	Polyomaviruses	Porcine endogenous retrovirus (PERV)	Porcine parvovirus	Rhabdovirus	St Louis encephalitis virus	SARS coronavirus	Spumavirus (simian foamy virus)
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	THEORETICAL	THEORETICAL	ABSENT‡	THEORETICAL§	THEORETICAL	THEORETICAL¶
Public perception and/or regulatory concern regarding blood safety	ABSENT	ABSENT†	ABSENT	VERY LOW	LOW	VERY LOW‖	ABSENT††
Public concern regarding disease agent	ABSENT	ABSENT	ABSENT	MODERATE	LOW, but MODERATE in some regions of US where outbreaks have occurred	MODERATE‖	ABSENT

† This is an issue for public health and regulatory agencies based on perception that xenotransplant recipients or their contacts will become blood donors and may transmit this agent. There is a current moratorium on xenotransplantation in the US.
‡ Rare cases of transmission in organ/tissue transplants probably associated with infection of neurologic tissue; no known viremic phase.
§ Because of similarity to West Nile virus, transfusion risk during SLEV outbreaks may occur.
‖ No natural infections recognized since 2004. Reemergence of agent would alter public perception.
¶ Transmission from transfusion has not been documented in humans but has been demonstrated in nonhuman primates. No known disease in infected humans.
†† Public policy makers in US have discussed agent in open public forums without concern expressed by stakeholder groups or other members of the public. However, Health Canada has enacted a permanent deferral for donors who handle monkeys or their body fluids as part of job-related duties (effective January 1, 2007).

TABLE A8. Priority assessment of viral agents (T-Z)

Categories	Tick-borne encephalitis virus complex*	Torque teno virus (TTV complex)*	Vaccinia virus	Variola virus	Western equine encephalitis virus
Scientific/Epidemiologic evidence regarding blood safety	VERY LOW	ABSENT†	THEORETICAL	THEORETICAL	THEORETICAL
Public perception and/or regulatory concern regarding blood safety	ABSENT	ABSENT	VERY LOW‡	ABSENT§	ABSENT
Public concern regarding disease agent	ABSENT	ABSENT	ABSENT	VERY LOW‖	ABSENT

* Agent causes transfusion-transmitted infection in humans.
† Transmission documented but no disease associated despite extensive studies.
‡ The existence of any small threat of vaccinia to blood safety is dependent on the occurrence of an accidental or intentional release of variola or a threat of bioterrorism sufficient to require a significant and widespread reintroduction of smallpox immunization.
§ There is no risk to the blood supply in the absence of accidental or intentional release of this virus.
‖ Natural variola has been eradicated and risk remains low, but not absent, due to the risks of a bioterrorism event or accidental release of the virus.

TABLE A9. Priority assessment of rickettsial agents

Categories	*Anaplasma phagocytophilum**	*Coxiella burnetii**	*Ehrlichia chaffeensis*	*Orientia tsutsugamushi*	*Rickettisa prowazekii*	*Rickettsia rickettsii**
Scientific/Epidemiologic evidence regarding blood safety	VERY LOW	VERY LOW	THEORETICAL	THEORETICAL	THEORETICAL	VERY LOW
Public perception and/or regulatory concern regarding blood safety	ABSENT	ABSENT	ABSENT, but LOW in selected populations (e.g., military)	LOW, but ABSENT in US	ABSENT	VERY LOW
Public concern regarding disease agent	ABSENT, but LOW in focal endemic areas	ABSENT	ABSENT, but LOW in selected populations (e.g., military)	ABSENT	ABSENT	ABSENT/LOW, but higher in selected areas

* Agent causes transfusion-transmitted infection in humans.

TABLE A10. Priority assessment of bacterial agents

Categories	*Bacillus anthracis*	*Bartonella henselae*	*Borrelia burgdorferi*	*Borrelia* species*	*Brucella* species*	*Chlamydia pneumoniae*	*Francisella tularensis*	*Listeria monocytogenes*	*Yersinia enterocolitica**	*Yersinia pestis*
Scientific/ Epidemiologic evidence regarding blood safety	THEORETICAL	THEORETICAL	THEORETICAL	VERY LOW	VERY LOW in North America; LOW in endemic areas	THEORETICAL	THEORETICAL	THEORETICAL	LOW/MODERATE†	THEORETICAL
Public perception and/or regulatory concern regarding blood safety	VERY LOW	ABSENT	VERY LOW	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	VERY LOW	ABSENT
Public concern regarding disease agent	HIGH	VERY LOW	MODERATE	VERY LOW	LOW	VERY LOW	VERY LOW, but LOW in regions where outbreaks have occurred	LOW	ABSENT	HIGH

* Agent causes transfusion-transmitted infection in humans.
† There has been a decreased frequency of reported transfusion-associated cases over the past 10 years.

TABLE A11. Priority assessment of protozoan and nematode agents

Categories	*Babesia* species*	Filariae	*Leishmania* species*	*Plasmodium* species*	*Toxoplasma gondii**	*Trypanosoma brucei*	*Trypanosoma cruzi**
Scientific/Epidemiologic evidence regarding blood safety	MODERATE/HIGH	ABSENT†	LOW	LOW in most nonendemic countries, but HIGH in hyperendemic countries‡	VERY LOW	THEORETICAL	LOW§
Public perception and/or regulatory concern regarding blood safety	VERY LOW, but MODERATE in endemic regions	ABSENT	LOW	MODERATE‡	VERY LOW	ABSENT	MODERATE
Public concern regarding disease agent	VERY LOW, but MODERATE regionally‖	ABSENT	LOW, but MODERATE among military personnel	MODERATE	LOW, but MODERATE among pregnant women	VERY LOW	LOW

* Agent causes transfusion-transmitted infection in humans.
† Allergic reactions to transfused microfilaria may occur.
‡ Risk and concern with regard to blood safety may be moderate to high in some nonendemic countries based on donor demographics and travel patterns of the donor population.
§ Since the implementation of blood donor screening
‖ Regulatory concern is increasing.

TABLE A12. Red priority agents

Categories	vCJD*	Dengue viruses*	*Babesia* species*
Scientific/Epidemiologic evidence regarding blood safety	LOW†	LOW in US‡	MODERATE/HIGH
Public perception and/or regulatory concern regarding blood safety	HIGH	VERY LOW/ABSENT in US; MODERATE/HIGH in non-US endemic areas	VERY LOW, but MODERATE in endemic regions
Public concern regarding disease agent	MODERATE	VERY LOW/ABSENT in US; MODERATE/HIGH in non-US endemic areas	VERY LOW, but MODERATE regionally

Red = Agents with low to high scientific/epidemiologic evidence of risk regarding blood safety with the potential for severe clinical outcomes. This prioritization also may be influenced by the committee's estimate of the risk of emergence of these agents in the US and Canada as well as public and/or regulatory concern.

* Agent causes transfusion-transmitted infection in humans.
† Due to the absence of endogenous human infection in North America and the possible impact of stringent donor deferral policy. There is strong evidence for transfusion transmission in UK.
‡ Priority is related to asymptomatic viremia that may result in transfusion transmission and substantial potential for emergence in the US. This risk is mitigated by the low prevalence of autochthonous transmission in the continental US and deferrals for malaria that would exclude most travelers coming from endemic areas.

TABLE A13. Orange priority agents

Categories	Chikungunya virus	St. Louis encephalitis virus	*Leishmania* species*	*Plasmodium* species*	*Trypanosoma cruzi**
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL†	THEORETICAL‡	LOW	LOW in most nonendemic countries, but HIGH in hyperendemic countries§	LOW‖
Public perception and/or regulatory concern regarding blood safety	VERY LOW/ABSENT in US; MODERATE/HIGH in non-US endemic and threatened areas	LOW	LOW	MODERATE§	MODERATE
Public concern regarding disease agent	VERY LOW/ABSENT in US; MODERATE/HIGH in non-US endemic and threatened areas	LOW, but MODERATE in some regions of US where outbreaks have occurred	LOW, but MODERATE among military personnel	MODERATE	LOW

Orange = Agents with sufficient scientific/epidemiologic evidence of risk regarding blood safety that might support their elevation to a higher priority at some time in the future.

* Agent causes transfusion-transmitted infection in humans.
† Although no transfusion transmission has been documented, rapid reemergence, increased pathogenicity, and asymptomatic viremia suggest that transfusion transmission is possible.
‡ Because of similarity to West Nile virus, transfusion risk during SLEV outbreaks may occur.
§ Risk and concern with regard to blood safety may be moderate to high in some nonendemic countries based on donor demographics and travel patterns of the donor population.
‖ Since the implementation of blood donor screening.

TABLE A14. Yellow priority agents

Categories	Chronic wasting disease	Hepatitis A virus*	HHV-8*	HIV variants*	Human parvovirus B19*	Influenza A virus (H5N1)	Spumavirus (simian foamy virus)	*Borrelia burgdorferi*
Scientific/Epidemiologic evidence regarding blood safety	THEORETICAL	LOW	VERY LOW†	THEORETICAL‡	VERY LOW/LOW‖	THEORETICAL	THEORETICAL††	THEORETICAL
Public perception and/or regulatory concern regarding blood safety	VERY LOW	VERY LOW/ ABSENT	LOW	LOW/MODERATE§	VERY LOW¶	VERY LOW	ABSENT‡‡	VERY LOW
Public concern regarding disease agent	LOW/ MODERATE	LOW/ MODERATE	VERY LOW	LOW/MODERATE§	LOW	HIGH	ABSENT	MODERATE

Yellow = Agents with absent to low scientific/epidemiologic evidence of risk regarding blood safety for which there is public and/or regulatory concern.

* Agent causes transfusion-transmitted infection in humans.
† No disease has been documented although transfusion transmission occurs in the absence of leukoreduction.
‡ Although the wild-type agents are transfusion transmitted, transfusion transmission of the variants has not been documented. If variants are transmissible, the risk would be very low in the US due to cross-reactivity of screening tests, use of donor screening questions, and limited global distribution of variants.
§ Based on transmission of HIV in general, rather than HIV variants.
‖ In the US, there is a higher level of concern for immunocompromised individuals, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients. A LOW to MODERATE rating is reasonable for pooled plasma and fractionated products based on variable implementation of NAT.
¶ In the US, there is an exception for this priority for patients with hemophilia; concern exists for immunocompromised individuals, patients with chronic anemia (sickle cell, thalassemia), and bone marrow transplant patients. Priority level is considered to be LOW to MODERATE in several European countries with screening programs.
†† Transmission from transfusion has not been documented in humans but has been demonstrated in nonhuman primates. No known disease in infected humans.
‡‡ Public policy makers in US have discussed agent in open public forums without concern expressed by stakeholder groups or other members of the public. However, Health Canada has enacted a permanent deferral for donors who handle monkeys or their body fluids as part of job-related duties (effective January 1, 2007).

TABLE A15. Transfusion-transmissible EID agents

Category	Agent	Evidence of transmission by blood transfusion
Prion agents	vCJD	• Documented experimentally in sheep for BSE (36% of exposed recipients). Transmissions occurred from donor animals at 50% of the estimated incubation period. Also documented for scrapie (43%) in the same experimental system. • Relatively high rates of transmission by blood transfusion in humans: ◦ Documented transfusion transmission to four recipients of nonleukoreduced red cells. Three had disease while one had prions in tissue, but no disease. These were part of an ongoing study of 66 recipients followed after receiving labile blood components from 18 donors who subsequently developed vCJD. The four recipients represent 12.5% of the recipients surviving longer than 5 years. ◦ The three recipients who developed vCJD showed symptoms at 6.3-8.5 years. ◦ These four cases arose from three asymptomatic donors who subsequently developed clinical vCJD between 17 and 42 months after donation. • The first case of vCJD from Factor VIII containing plasma from a donor who later developed vCJD is being investigated in the UK. The recipient died of unrelated causes but did have vCJD prion in his spleen.
Viral agents	Dengue viruses	• The first documented transfusion-associated case of dengue occurred during a local outbreak in Ma Wan, Hong Kong, in 2002, an area that is not endemic for dengue. The index recipient was a 76-year-old seronegative woman who developed fever without rash 2 days after receiving a unit of packed red blood cells collected from a 17-year-old donor who was diagnosed with dengue (generalized rash) 7 days postdonation. The blood had been stored at 4-8°C for 38 days prior to transfusion. RT-PCR testing of the recovered donor plasma and archived specimens from the donor and recipient were found to be positive for dengue virus type 1. IgM-specific antibody also developed in the recipient posttransfusion. • The second documentation of transfusion transmission was a transmission cluster reported from Singapore, an area endemic for dengue. The donor was a 52-year-old male whose components were transfused to three recipients. The donor reported fever the day following donation and a stored serum sample was positive for dengue virus type 2. Both the red cell and FFP recipients reported fever 1-2 days posttransfusion and also tested positive by PCR for dengue virus type 2; the donor's and the two recipients' virus were confirmed by sequencing to be dengue type 2. The platelet recipient was asymptomatic for dengue. All three recipients tested antibody positive for IgM and/or IgG with documented seroconversion in the red cell recipient 11 days posttransfusion. • Transmission also has been observed after needle-stick exposure and in bone marrow and kidney transplant recipients.
	Hepatitis A virus	• HAV transmission through blood is rare, but well documented. It can be amplified in neonatal intensive care units where multiple infants develop infection after receiving aliquots of blood components from an infected donor. • The rarity of transmission in adults is attributed to the short infectious viremic stage, low incidence of HAV in the US, absence of a carrier state, prevalence of immunity in many recipients, and neutralization of virus from a concurrent blood product that may contain specific antibody.

TABLE A15. *Continued*

Category	Agent	Evidence of transmission by blood transfusion
Viral agents		
	HHV-8	• A study of transfusion recipients in Uganda provides strong evidence of transfusion transmission by relatively fresh (≤4 days old) nonleukoreduced whole blood from seropositive donors compared with that from seronegative donors. • Other studies in highly endemic populations of African children strongly suggest transfusion transmission with nonleukoreduced products. • Two postsurgical seroconversions in cardiac surgery patients receiving nonleukoreduced components have been described in the US; transfusion transmission was suspected but not proven. • Two previous small studies in the US and Jamaica showed lack of transmission in 32 recipients receiving components from HHV-8 seropositive units. • Evaluation of linked donor-recipient blood samples from the US TTVS study during the 1970's showed no difference in seroconversion rates between transfused patients and untransfused surgical control patients.
	HIV variants	• Well documented for all HIV-1 group M clades and several HIV-2 clades. • Likely occurs with HIV-1 group N and O and with circulating recombinant strains.
	Human parvovirus B19	• Rarely from blood components (four clinical cases documented in literature); actual frequency of transmission not assessed prospectively. • Solvent-detergent (SD) treated plasma lots in the US with B19V DNA titers of $>10^7$ IU per mL transmitted to patients and to seronegative volunteers; units with $<10^4$ IU per mL of virus did not transmit. • Commonly transmitted from Factor VIII and Factor IX concentrates prior to B19V DNA testing. • Very rarely transmitted from intravenous immunoglobulin (IVIG).
	Colorado tick fever virus	• One documented case transmitted by transfusion
	Epstein-Barr virus	• Documented through seroconversion in seronegative recipients and in case reports using molecular methods.
	GB/Hepatitis G viruses	• Well documented in prospective studies
	Hepatitis B virus variants	• HBV variants have been demonstrated to be transmitted similar to wild-type HBV.
	Hepatitis E virus	• Documented in endemic areas (e.g., Saudi Arabia and Hokkaido in Japan) and rarely in nonendemic areas (UK and France).
	Tick-borne encephalitis virus complex	• Two recipients in Finland developed symptoms after receiving components from a donor who became symptomatic (febrile) hours after donating blood. A serological diagnosis of TBE was made in the donor and both recipients, and no other risk factors were identified in the recipients.
	Torque teno virus (TTV complex)	• Well documented in prospective studies.
Rickettsial agents		
	Anaplasma phagocytophilium	• Two cases from asymptomatic donors reported in US. In neither were the blood components leukoreduced. In the one fully published case, the implicated donor unit was retrospectively identified as PCR positive for *A. phagocytophilum*; in this case, *A. phagocytophilum* was also isolated from the recipient by PCR and antibody titers of 1:512 and 1:256 were detected by IFA at 50 and 81 days after donation. • A cluster of cases of human-to-human transmission of *Anaplasma phagocytophilium* infection (and the first report of human granulocytic anaplasmosis [HGA] in China) associated with blood contact was reported in 2008. The infection was not confirmed by blood smear or culture in the index patient, but *A. phagocytophilium* DNA was amplified from and sequenced from the index patient, who had been bitten by a tick, and nine family members or healthcare workers who had been in close contact. All nine reported contact with the patient's blood; seven had contact with respiratory secretions. The index patient died before seroconversion but all nine contacts seroconverted.

TABLE A15. *Continued*

Category	Agent	Evidence of transmission by blood transfusion
Bacterial agents		
	Coxiella burnetii	• A single case of transmission from blood transfusion has been described. The donor and the recipient both showed serological evidence of *C. burnetti* infection and the clinical symptoms and their time courses were compatible with the diagnosis of Q fever. • Also reported to have been transmitted by bone marrow transplantation. • Increased antibody prevalence in drug users HIV-infected and dialysis patients further supports the possibility of transmission by blood.
	Rickettsia rickettsii	• The only known case was from a donor who donated blood 3 days before the clinical onset of RMSF. The donor reported tick removal 18 hours after a whole blood donation and subsequently died after 7 days. *Rickettsia rickettsii* was identified in several tissues (indirect fluorescent antibody). The recipient became mildly ill 6 days after transfusion and fully recovered after appropriate antibiotic treatment (starting at the fourth day of illness). • In 1997, an investigation of 377 National Guard blood donors at Fort Chaffee, AR, identified 10 recipients of units from donors later identified as probable RMSF cases. No recipient was infected, although the infection status of the donors at the time they were bled is unknown.
	Borrelia species	• Louse- and tick-borne relapsing fevers have been transmitted by laboratory exposure to clinical samples in over 40 cases. • In the 1930s, six cases of transfusion transmission of relapsing fever borreliosis (unknown types) were reported from China with documentation of spirochetes in blood of donors and recipients. Transmission by blood has been alleged in Africa.
	Brucella species	• A few probable cases of transmission by blood transfusion have been reported worldwide. • A case report from Turkey strongly suggests transmission of brucellosis by bone marrow transplantation.
	Yersinia enterocolitica	• Multiple case reports (>30) of transfusion transmission of *Y. enterocolitica* from asymptomatic donors have occurred since 1975 (lack of reports prior to that may have been due to shorter storage times in use), including from autologous transfusion. *Y. enterocolitica* accounts for more than half the cases of sepsis arising from transfusion of RBCs. At least one case of a transfusion reaction due to *Y. enterocolitica* contaminating a pooled platelet concentrate has been reported. • Clinical disease symptoms in transfusion recipients may be due to endotoxemia and/or subsequent growth of the organism.
Protozoan and nematode agents		
	Babesia species (Continued on next page)	• *B. microti* documented in over 70 cases; all cases have occurred in the US, except for one case in Canada (donor was exposed in the US) and one case in Japan; potentially one case in Europe. • *B. duncani*: 2 cases reported in the literature • Travelers from non-endemic areas infected while visiting endemic areas, donors from babesiosis-endemic areas who donate elsewhere, and exportation of blood products are increasingly implicated in transfusion cases

TABLE A15. *Continued*

Category	Agent	Evidence of transmission by blood transfusion
Protozoan and nematode agents	*Babesia* species (Continued)	• Since fiscal year 1998, an increasing number of fatalities and Blood Product Deviations (BPDs) have been reported to the FDA. A total of 272 BPDs related to possible *Babesia* infection in donors were reported from FY 1998-2007 of which 52 were investigated as possible transfusion-transmitted *Babesia* infections. Twelve fatalities were reported since 1998, with 9 of 12 reported in the last 3-year period. Five of these patients received their transfusions in states where *Babesia* was not endemic. All recipients who died were infected with *B. microti*. Red blood cells were implicated in each case, including one frozen deglycerolized product. Each infection was diagnosed by thin peripheral blood smear; associated donors had antibody titers ≥1:128 by IFA. • The American Red Cross reported 18 definite or probable cases of transfusion-transmitted *B. microti* from 2005-2007, including five fatalities. Seventeen antibody-positive donors were implicated including the donor of one split red cell unit that infected a 1-day old infant and a 32-year old sickle cell patient. Of the 17 antibody-positive donors, 11 were residents of *Babesia*-endemic areas, while 4 residents of nonendemic areas had a history of travel to endemic areas.
	Leishmania species	• Transfusion transmission has been documented in at least three cases in nonendemic areas in which the transfused recipients were either infants or immunocompromised patients. One probable case of *L. donovani* transmission by platelet transfusion has been reported. • No transfusion cases reported in US. • *Leishmania* species have been transmitted via clinical transfusions from seropositive donor dogs to recipient dogs.
	Plasmodium species	• Multiple cases worldwide ◦ Common in endemic countries ◦ Only three cases in US from 1998-2007 ◦ Overall, US case rate has dramatically decreased during the last 40 years. • The large majority of transmissions are from red cells, but platelet components have been implicated, probably due to presence of red cells. • Four of five *Plasmodium* species transmitted, but a large majority of recent US cases have been due to *P. falciparum* and, to a lesser extent, *P. vivax*.
	Trypanosoma cruzi	• Seven documented cases in US and Canada, but more are likely to have occurred and been undetected. • In Latin America, 12-25% of recipients of seropositive units were infected following the transfusion of fresh, whole blood. • Infection leading to detectable clinical disease more common in immunocompromised recipients. • Components with greatest risk of transmission are whole blood and platelets. In four of the US cases where an implicated donor was identified (based on history of having resided in a Chagas endemic area), the component responsible for transmission was a platelet unit. In a fifth case, transmission from a platelet unit was also likely. The transmitting component in the other two North American cases was not identified in the case reports.
	Toxoplasma gondii	• Rare; four cases of transmission associated with granulocyte concentrates from CML donors have been identified. • There are no known transmissions from red cells and FFP. One possible case from a platelet transfusion has been reported.

TABLE A16. Vector-borne EID agents

Category	Agent	Vector and reservoir involved
Viral agents		
	Dengue viruses*	• *Aedes* species mosquitoes • Both urban (human-mosquito) and sylvatic (monkey-mosquito) cycles are observed, but the relative importance of the sylvatic cycle to human infection is uncertain.
	Chikungunya virus	• Mosquitoes, mainly of the Aedes family: *A. aegypti, A. albopictus, A. polynesiens*, as well as: C*ulex, Anopheles, Mansonia, Eretmapodites*, and *Coquillettidia* • Infected species: Birds, humans, chimpanzees, some domestic animals, reptiles • Human-to-mosquito-to-human infection occurs without the need for an intermediate amplifying host.
	St Louis encephalitis virus	• Mosquitoes (*Culex* species) associated with wild migratory passeriform (e.g., sparrows) and columbiform (e.g., pigeons) birds
	Colorado tick fever virus*	• Adult wood ticks of the species *Dermacentor andersoni* • Other tick species may carry the virus, but their roles in transmission are uncertain.
	Crimean-Congo hemorrhagic fever virus	• Transmitted by ixodid ticks, especially from the genus *Hyalomma* that can also serve as a reservoir • Documented transovarial transmission among ticks • Vertebrate hosts include livestock (e.g., sheep, goats, cattle, ostriches), large wild herbivores, hares, and hedgehogs.
	Eastern equine encephalitis virus	• Mosquitoes: *Culiseta melanura, Culex* species; associated with wading birds, pheasants, passerine songbirds, and starlings
	Japanese encephalitis virus	• Main epidemic vector is mosquitoes of the *Culex* species, especially *Culex tritaeniorhynchus*. • In temperate regions, pigs and birds (principally ardeid species, such as egrets and black-crowned night herons, and possibly ducks) are effective amplifying hosts.
	La Crosse virus	• Transmitted by female *Aedes triseriatus*, a "tree-hole mosquito," the reservoir and vector for La Crosse virus. • Although their main breeding site is in holes in hardwood trees, the mosquitoes can also breed in artificial containers that hold rainwater, including discarded tires. • Persistence in endemic areas is a result of vertical transmission of La Crosse virus from *Aedes triseriatus* females to their offspring, venereal transmission among adult mosquitoes, and horizontal transmission to small mammals (e.g. chipmunks, squirrels, woodchucks and foxes) that serve as amplifying hosts. • Humans do not maintain prolonged viremias and therefore are "dead-end" hosts unable to amplify the virus and reinfect the vector. • The introduction and spread in the US of another potentially efficient vector, *Aedes albopictus*, has raised concern about further geographic spread of La Crosse virus infections.
	Tick-borne encephalitis virus complex*	• *Ixodes ricinus* (Western Europe); *I. persulcatus* (eastern Eurasia); *I. ovatus* (China and Japan) • *Dermacentor* species and *Haemaphysalis* species also implicated vectors in *Ixodes*-free areas. • Maintained in nature in small wild vertebrate hosts (rodents and insectivores); large mammals, such as goats, sheep, and cattle are a less important source of infection.
	Western equine encephalitis virus	• Principal vector: mosquitoes, primarily *Culex tarsalis* • Reservoir: associated with domestic and passerine birds
Rickettsial agents		
	Anaplasma phagocytophilum	• Ticks of genus *Ixodes* (*I. scapularis*, *I. pacificus*, *I. ricinus*) • The tick nymph is primarily responsible for transmission of Lyme disease, babesiosis and HGA; because of its small size, the bite may not be noticed and consequently the tick not be removed before disease transmission occurs. • White-footed mice (*Peromyscus leucopus)* and white-tailed deer (*Odocoileus virginianus*) serve as reservoir hosts.

* Agent causes transfusion-transmitted infection in humans.

TABLE A16. *Continued*

Category	Agent	Vector and reservoir involved
Rickettsial agents		
	Erlichia chaffeensis	• Lone star tick, *Amblyomma americanum* distributed throughout southeastern and south central US. • Cases in the western US suggest additional vectors that are thought to be *Dermacentor variabilis* and *Ixodes pacificus*. • White-tailed deer are thought to be the major reservoir.
	Orientia tsutsugamushi	• *O. tsutsugamushi* is maintained in nature by highly efficient transovarial transmission in larval trombiculid mites (chiggers). • Rodent reservoirs can also harbor the bacterium.
	Rickettsia prowazekii	• The body louse, *Pediculus humanus corporis*, is the vector and chronically infected humans the most important reservoir. • Lice live in clothing, take multiple blood meals per day, acquire infection from their blood meal, excrete *R. prowazekii* in feces, and abandon febrile hosts for other hosts. Infected body lice eventually succumb to their *R. prowazekii* infections so do not function as a major reservoir. • Other reservoirs for *R. prowazekii* include Southern flying squirrels (*Glaucomys volans*) in the Americas and ticks feeding on livestock in Africa.
	*Rickettsia rickettsii**	• Ticks (primarily *Dermacentor* species) are the main vectors in the US. • Ticks also are the agent reservoir, given that there are tick-to-tick mechanisms of transmission, allowing infection to all four tick life-cycle stages (eggs, larvae, nymphs, and adults). • Usually, only 1-5% of ticks are infected by Rickettsia rickettsii, even in high incidence areas. • The main tick species involved in transmission are: ◦ *Dermacenter variabilis* (American dog tick)—Eastern and far west US. Dogs and medium sized mammals are preferred hosts ◦ *Dermacenter andersoni* (Rocky mountain wood tick)—Western US states and southwestern Canada. Small rodents and large mammals are preferred hosts. ◦ *Rhipicephalus sanguineus* (Brown dog tick)—Mexico, US (Arizona) and Europe. This is a newly recognized vector in the US. • Other reservoirs include wild rodents (e.g., capybaras), dogs, horses and donkeys. • Humans are not considered as reservoirs, only accidental hosts.
Bacterial agents		
	Borrelia burgdorferi	• *Ixodes* (hard) ticks, referred to as black-legged or deer ticks, including *I. scapularis* and *I. pacificus*—Same tick also can be infected with *B. microti* and *A. phagocytophilum*. • White-footed mice (*Peromyscus leucopus*) and white-tailed deer (*Odocoileus virginianus*) serve as reservoir hosts; unlike mice, deer do not become infected but serve to transport and maintain the tick population. • Birds and other animals may contribute to the spread of infected ticks.
	Borrelia species*	• Argasid (soft) ticks: Tick-borne (endemic) relapsing fever. Rodents are the reservoir. • Human body louse: Louse-borne (epidemic) relapsing fever. No nonhuman reservoir.
	Yersinia pestis	• Fleas, most commonly *Xenopsylla cheopis*, the oriental rat flea, but other fleas can be competent vectors. • Reservoir is various species of mammal depending on the locale.
Protozoan and nematodes agents		
	Babesia species*	• *Ixodes* ticks for *B. microti*; *I. scapularis* (also referred to as *I. dammini*) in the eastern United States is the most common; however, other tick species may be involved. • White-footed mice serve as amplifying hosts for *B. microti*. • Although white-tailed deer (*Odocoileus virginianus*) are not infected with *B. microti*, they serve as the transport and reproduction hosts for adult ticks. • *I. ricinus* is one tick species identified as a vector for *B. divergens* in Europe • For some of the *Babesia* species, the tick vector and reservoir host have not been identified.
	Leishmania species*	• Phlebotomine sandflies: *Phlebotomus* genus (Old World) and *Lutzomyia* genus (New World).

* Agent causes transfusion-transmitted infection in humans.

TABLE A16. *Continued*

Category	Agent	Vector and reservoir involved
Protozoan and nematodes agents	*Plasmodium* species*	• Female mosquitoes of the genus *Anopheles.*
	*Trypanosoma cruzi**	• Triatomine or reduviid bugs, particularly those from the Genus *Triatoma*, *Rhodnius*, and *Panstrogylus*; 11 species reported in the US. • Large sylvatic reservoir populations exist in endemic countries. In the US, *T. cruzi* is found in 18 mammal species including opossums, raccoons, and other sylvatic animals.
	Trypanosoma brucei	• Tsetse flies of the genus *Glossina* • Primarily infects humans

* Agent causes transfusion-transmitted infection in humans.

TABLE A17. CDC categorization of those EID bioterrorism agents included in the fact sheets

Category A agents†	Category B agents†
Bacillus anthracis	Brucella species
Yersinia pestis	*Rickettsia rickettsii*
Variola virus	*Rickettsia prowazekii*
Francisella tularensis	*Coxiella burnetii*
Ebola virus	Eastern equine encephalitis virus
Marburg virus	Western equine encephalitis virus
Lassa virus	
Crimean-Congo hemorrhagic fever virus	

† The agents listed are classified as bioterrorism agents according to the US Centers for Disease Control and Prevention. Information on these agents is included in the agent Fact Sheets.

TABLE A18. Characteristics and potential actions in the event of an attack with a category A agent and donor deferral guidelines

Agent (type)	Anthrax (Bacterium)	Botulism (Toxin)	Plague (Bacterium)	Smallpox (Virus)	Tularemia (Bacterium)	VHF† (Viruses)
Incubation (days)	1-7	0-8	1-7	7-17	1-14	2-21
Blood phase (asymptomatic)	Yes?	NA‡	Yes	Yes	Probable§	Probable§
Blood phase (disease)	Yes	NA‡	Yes	Yes	Yes	Yes
Secondary transmission‖	No	No	Yes	Yes	No	Yes
Donor deferral (exposed)¶	No	No	Yes††	Yes	Yes††	Yes
Donor deferral (cases)‡‡	Yes††	No	Yes††	Yes	Yes††	Yes
Donor deferral (contacts)§§	No	No	Yes††	Yes	Selected‖‖	Selected‖‖
Product retrieval	Yes	Cases only	Yes	Yes	Yes	Yes
Facility remediation¶¶	Yes	No	No	No	Advisable	No

† VHF, Viral hemorrhagic fevers
‡ NA, not applicable
§ Although there are no definitive data, a presymptomatic blood phase is highly likely.
‖ Secondary transmission means that an infected person can transmit the infection to other people, resulting in second and perhaps subsequent waves of disease.
¶ The extent to which it would be appropriate to defer individuals exposed to the attack
†† Deferred until a course of antibiotic treatment has been completed and infection has been shown to have been eliminated
‡‡ The extent to which it would be necessary to defer individuals who developed disease as a result of the attack
§§ The extent to which it would be necessary to defer individuals who have been in contact with persons with disease resulting from the attack
‖‖ Deferral probably necessary only for those involved in direct care of, and contact with, symptomatic cases
¶¶ Remediation is special clean-up measures for a facility that has been directly exposed to the attack