

# Transfusion-Transmitted Infection (TTI)

# 19

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## Summary

This year, there is no data summary table in this chapter, because cases will now be identified by the year of transfusion, rather than the year in which the report was made to SHOT or in which the investigation was completed. Table 19.1 includes the number of confirmed TTI incidents, by year of transfusion with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2013 (Scotland included from October 1998).

The risks of a component potentially infectious for HBV, HCV or HIV being released for use in the UK are very low, however haemovigilance is maintained and investigations performed if a recipient is suspected to have been infected via transfusion.

Bacterial contamination of a component remains possible despite screening of platelets and the Blood Service should be informed immediately of all adverse reactions and events including those suspected of being the result of bacterial contamination of a component.

This chapter describes the possible transfusion-transmitted infection incidents investigated by the United Kingdom (UK) Blood Services and reported to the National Health Service Blood and Transplant (NHSBT)/Public Health England (PHE) Epidemiology Unit in 2013.

UK Blood Service investigations in 2013 have confirmed:

- One probable transfusion-transmitted hepatitis B virus (HBV) incident investigated in 2013 following a transfusion in 2012
- One hepatitis E virus (HEV) transfusion-transmitted incident pending from a 2012 investigation
- No proven bacterial transfusion-transmissions were reported in 2013
- One near miss bacterial incident (this was not reported to SHOT as a near miss incident, so is not included in the overall near miss figures in Chapter 7 Near Miss Reporting (NM))

A retrospective study has detected HEV ribonucleic acid (RNA) in 0.03% of 225,000 donors in England at the time of donation.

## Definition of a TTI:

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection following transfusion with blood components and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection

**and, either:**

- At least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

**or:**

- At least one component received by the infected recipient was shown to contain the agent of infection

## Requesting and reporting a suspected TTI investigation

The data in the TTI chapter are mostly based on UK Blood Service investigations into suspected transfusion-transmitted infections (TTI) which are reported to the NHSBT/PHE Epidemiology Unit. The investigation reports are reconciled with reports by hospitals to the SHOT online reporting system which, in most cases, will also have been reported to the Medicines and Healthcare products Regulatory Agency (MHRA).

Guidance on reporting an incident, and the required supporting information, for suspected transfusion-transmitted infections (TTIs) for hospitals served by NHSBT can be found on the Requests for Investigation of Adverse Events & Reactions page at [http://hospital.blood.co.uk/library/request\\_forms/aer/](http://hospital.blood.co.uk/library/request_forms/aer/).

For other UK Blood Services please contact the local Blood Centre.

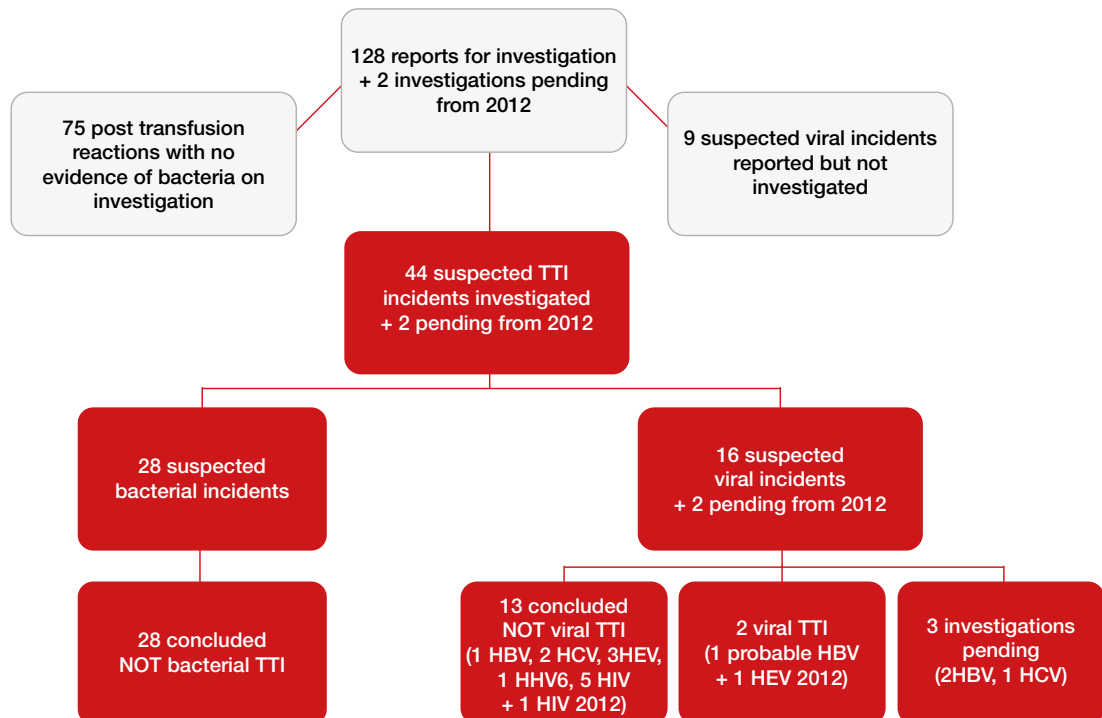
### Learning point

- Cases should be reported to both SABRE and SHOT as soon as practical once the TTI investigation is requested, and reports should be updated once the outcome of the Blood Service investigation is received. This advice applies to all cases, whether or not infections are currently screened for by the UK Blood Services. Where reports are made initially by sources outside the transfusion team, a report to SHOT/SABRE will need to be completed as soon as the transfusion team become aware of the case

## Summary of reports made to the NHSBT/PHE Epidemiology Unit in 2013

During 2013, the UK Blood Services were asked to investigate 128 suspected TTI incidents (see Figure 19.1), a similar number to recent years, consisting of 103 possible bacterial cases and 25 suspected viral incidents. A further 2 pending investigations from 2012 were finalised in 2013.

Figure 19.1:  
Outcome of reports  
of suspected  
TTIs made to  
the NHSBT/PHE  
Epidemiology Unit  
in 2013



HBV = hepatitis B virus; HCV = hepatitis C virus; HEV = hepatitis E virus; HIV = human immunodeficiency virus; HHV6 = Human herpes virus 6

## Bacterial reports 2013

Similar to previous years, 75/103 packs returned to the Blood Service with a request for bacterial culture following a patient reaction had no bacteria detected in the pack, and no positive patient blood culture reported by the hospital. These were reclassified as possible transfusion reactions. Sixteen of these were known to have been reported to SHOT as acute transfusion reactions (ATR). Others may have been deemed too mild to report, reported to other categories or not reported.

In the remaining 28 possible bacterial cases, the recipient's transfusion reaction was probably not caused by bacteria from a transfusion of a blood component from the UK Blood Services. Reconciliation with the MHRA showed that these cases included two of the three cases reported to SABRE in 2013 as a possible bacterial TTI (see Chapter 6 Medicines and Healthcare products Regulatory Agency (MHRA) Report on Blood Safety and Quality Regulation in 2013). The third possible case reported to SABRE was not reported to the Blood Service for bacterial investigation and is included in Chapter 15 Acute Transfusion Reactions (ATR). Seven of the 28 cases were known to have been reported to SHOT as ATR.

### Learning points

- If a transfusion reaction is suspected to have been caused by bacterial contamination of the pack the Blood Service should be informed immediately so that any associated packs can be recalled
- Reports of UK Blood Services investigations into possible transfusion-transmitted infections (TTI) may not align with the Serious Adverse Blood Reactions and Events (SABRE) reporting year or category

### Bacterial TTIs 2013

There were no proven bacterial incidents in 2013 but one near miss described below.

#### Bacterial contamination noticed before transfusion 2013

In September 2013 hospital staff noted clumping in an apheresis platelet pack 'A' and contacted the Blood Service prompting a recall of an associated pack 'B' which had been issued to another hospital. Both packs were returned to the Blood Service for testing. Clumps were no longer visible in pack 'A' but were beginning to form in pack 'B' on return. Figure 19.2 shows an example of clumping in a contaminated pack. Gram-positive cocci were observed from samples taken from both platelet packs and on culture identified as *Staphylococcus aureus*. The isolates from the two packs were indistinguishable on molecular typing. Growth had not been detected in the original BacT Alert screening by day 7, however, the bottles were not available for further testing. There was no evidence of any failure in the screening process - all protocols were followed and it could be shown that both platelet packs were sampled. The donor was shown to be a carrier of *Staphylococcus aureus* and permanently suspended from the donor pool. The most likely reason for the failure of detection was due to a lack of organisms being present in the original samples either due to 1) low bacterial numbers in the packs at the time of sampling or 2) the microorganisms growing in clumps or as a biofilm and not spread evenly through the packs at the time of sampling.



Note: the white clumping seen in the top left hand corner is similar to that seen in the incident described above, illustrating that vigilance is still required despite screening

**Figure 19.2:**  
Example of a platelet pack contaminated with *Staphylococcus aureus*

### Bacterial TTIs 1996-2013

The last documented confirmed bacterial TTI was in 2009, but this predated universal bacterial screening of platelets throughout the UK Blood Services and the lack of cases may not, therefore, be totally explained by the introduction of screening. Conversely screening of platelet components cannot guarantee freedom from bacterial contamination. Packs are released for issue as 'negative-to-date' which may be before bacteria have multiplied sufficiently to trigger an initial screening reaction. On the other hand, an initial screen reactive result may be a false positive result, or related to bacteria which are of low pathogenicity and unlikely to cause any noticeable reaction in the recipient. A total of 36/43 bacterial transfusion-transmissions to individual recipients (33 incidents) have been caused by the transfusion of platelets (Table 19.1) since reporting began.

#### Learning points

- Screening will not prevent all contaminated units entering the supply
- Visual inspection of packs before use can alert staff to signs of bacterial growth
- Swift reporting of a suspected contaminated pack allows recall to occur before any associated packs are used
- Bacterial contamination is a factor to be considered if a transfusion reaction occurs
- Be aware that bacterial transmissions also have the potential to occur via red cells

Advice on clinical management and investigation of serious adverse reactions can be obtained from the hospital consultant responsible for blood transfusion and the British Committee for Standards in Haematology (BCSH) guideline on investigation and management of acute transfusion reactions [50]. See Chapter 15 Acute Transfusion Reactions (ATR), for comment on bacterial investigations following an acute transfusion reaction.

### Viral TTI reports 2013

In 2013 nine suspected viral incidents reported to the Blood Service were not investigated for the following reasons: positive antibody results were due to passive transfer during intravenous immunoglobulin therapy (1 HBV); infection was not confirmed (2 HCV); infection was not proven to be absent prior to transfusion (2 cytomegalovirus (CMV)); infection was more likely to have been acquired by another route e.g. recipient born in and/or transfused or operated on in an endemic country (3 HBV, 1 HCV).

#### Learning points

- A post-transfusion investigation will not commence until the infection status of the recipient has been clarified:
  - Requests for investigation of possible hepatitis C (HCV) transmission in individuals who are HCV polymerase chain reaction (PCR) negative, HCV antibody reactive, will not be investigated unless HCV antibody reactivity has been confirmed using two different assays, because of the possibility of non-specific antibody reactivity. If not locally available, the Blood Service can perform the required testing
  - Cytomegalovirus (CMV) seroconversion should be demonstrated by testing pre- and post-transfusion samples in parallel by the same laboratory
  - Immunoglobulin therapy can lead to passive transfer of antibodies which may be confused with infection. Careful review of the markers and timing can rule out infection before a report is made to the UK Blood Services

### **Viral investigations 2013**

Sixteen reports of suspected viral TTIs made in 2013 were investigated. One suspected HBV incident was confirmed as a probable TTI according to the above definition, Case 1 below.

### **Viral investigations pending in 2012**

Two investigation outcomes were pending at the end of 2012 and finalised in 2013. One suspected HEV TTI incident has been confirmed as proven, Case 2 below. One HIV TTI investigation was concluded as not TTI.

#### **Case 1: Report of probable HBV transmission investigated in 2013**

*An elderly female on immunosuppressive therapy received 7 units of red cells in summer 2012 during surgery for a bowel problem. The recipient was first tested in April 2013 because of mildly abnormal liver function tests (LFT) and found to be hepatitis B surface antigen (HBsAg) positive, low level IgM antibodies to hepatitis B core (anti-HBc IgM), hepatitis B e antigen (HBeAg) positive, avidity results inconclusive. The virus was identified as belonging to genotype A. Another sample taken from the patient in June 2013 suggested that this was a HBeAg-positive chronic hepatitis B infection. There was no obvious source of this hepatitis B infection and due to the possibility of recent acquisition the case was reported for investigation. Of the seven donors investigated, six were negative for evidence of hepatitis B infection but one was found to be HBV deoxyribonucleic acid (DNA) reactive on the index archive sample, tested retrospectively by individual sample testing having tested negative by routine pooled triplex nucleic acid test (NAT) screening at the time of donation. The donor was found to be anti-HBc positive on a subsequent sample. An archive sample from 2011 was also antibody to hepatitis B core (anti-HBc) positive, but HBV DNA negative. A follow-up sample from the donor has been found to be antibody to hepatitis B surface antigen (anti-HBs) positive and HBV DNA positive. These test results could reflect a resolving HBV infection or reactivation of an occult chronic HBV infection. Both donor and recipient are of non-UK, European heritage. Tattooing was reported by the donor but not in the timeframe that would be thought to correspond to active infection at the time of the index donation or that would require deferral (within 4 months of donation) or additional testing for anti-HBc (between 4 to 12 months prior to donation). This is a case of probable HBV transmission. Genotyping of the donor virus could not be undertaken due to insufficient HBV DNA in the donor's samples.*

#### **Case 2: Report of HEV transmission investigated 2012/13**

*A male recipient with multiple medical problems on immunosuppressive therapy received 129 donor exposures during a period of intensive plasma exchange and blood transfusion in May 2012. He became HEV RNA positive in July 2012 and seroconverted in August 2012. The vast majority of donors were cleared on the basis of subsequent negative serology and all tested index samples were RNA negative except for one. This donor was HEV RNA positive, anti-HEV negative at the time of the index donation and had cleared the HEV virus and seroconverted at the time of the next donation 5 months later. Sequencing confirmed this donation to be the source of infection in the recipient. The donor was a male repeat donor over 60 years old who reported no pre- or post-donation illness.*

### **Viral TTIs 1996-2013**

The year of transfusion may be many years prior to the year in which the case is investigated and reported to SHOT because of the chronic nature, and therefore late recognition, of some viral infections. Since 1996, 25 confirmed incidents of transfusion-transmitted viral infections have been reported, involving a total of 30 recipients. HBV is the most commonly reported proven viral TTI in the UK. This is partly because the 'window period' where an infectious donation from a recently infected donor is not able to be detected by the screening tests is longer than for HCV or HIV, despite NAT testing.

### **Risks of HBV, HCV or HIV being transmitted by transfusion**

The risks of a component potentially infectious for HBV, HCV or HIV being released for use in the UK are very low. It is currently estimated that, of 2.4 million donations made in the UK each year, testing will NOT identify approximately two potentially infectious HBV window period donations every year, one potentially

infectious HCV window period donation every 12 years and one potentially infectious HIV window period donation every three years [62]. Far fewer TTIs are observed in practice, partly because the estimates have wide uncertainty and the model is based on the risk in all packs released. The model does not incorporate pack non-use, recipient susceptibility to infection, or underascertainment/underreporting, for example due to recipients dying from an underlying medical condition before a chronic asymptomatic viral condition is identified, or, in the case of HBV, an asymptomatic acute infection.

### HEV commentary

The UK Blood Services' Standing Advisory Committee on Transfusion Transmitted Infection (SACTTI) is alerted to any new infectious threats to the UK blood supply through a wide range of reporting mechanisms, and will commission risk assessments where necessary to inform decisions on whether action should be taken to protect the safety of the blood supply [63]. There has been a recent increase in the number of cases of HEV reported to the UK Blood Services for investigation as suspected TTI incidents, probably due to increased awareness [64]. In 2012 and 2013 seven cases were reported for investigation with two proven to be HEV TTI. An HEV study has been conducted jointly by NHSBT and PHE to address the growing concern about HEV and blood safety.

The study aimed to define:

- The incidence of HEV in donors
- The extent of HEV transmission from virus-containing components
- The outcome of acquiring HEV from transfused components

The following study results are extra to cases reported to SHOT. Retrospective HEV RNA testing on a total of 225,000 donations given in 2013 indicated that 0.03% of tested donations were viraemic. A total of 62 HEV-containing components were transfused into 60 recipients, of whom 42 were available for follow-up; testing for HEV markers indicated infection in 19, giving a 43% overall transmission rate. Red cells were less likely to be linked to transmission than platelets or FFP. Antibody titres were more likely to be lower, and HEV RNA viral loads to be higher, in donations that resulted in transmission. Infected immunocompetent recipients cleared the virus very quickly, usually in the absence of any signs or symptoms of hepatitis. Immunosuppressed recipients exhibited a more prolonged viraemia, as reported elsewhere [65], but eventual clearance has been confirmed in those cases where prolonged follow-up was possible. This study indicates a high HEV incidence in donors, with an associated high transmission rate to recipients. Understanding the outcome of receiving HEV-containing components was an essential and complex part of this study, with the underlying medical condition and its management in the recipient playing a significant role [66].

### Learning points

- The risk of transfusion-transmitted hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV) is very low in the UK and this is one reason the UK Blood Services will require evidence of confirmed infection and/or seroconversion prior to commencing an investigation
- The large number of donors to investigate in some cases, and the retrospective nature of some investigations, emphasises the importance of UK Blood Services maintaining an easily accessible system for archive samples

### Parasitic TTIs

There were no reported parasitic infections for investigation in 2013. There have been two proven malaria TTIs reported to SHOT, the last in 2003 (Table 19.1). Malaria antibody testing was not applicable at the time according to information supplied at donation, and the donor selection guidelines were updated after these incidents to minimise the risk of further malaria TTIs [67]. The current selection guidelines on deferral and additional testing for malaria can be accessed at the UK transfusion guidelines web pages at <http://www.transfusionguidelines.org.uk>.

## **Variant Creutzfeld-Jakob Disease (vCJD) 2013**

There were no vCJD investigations in 2013.

### **vCJD 1996-2013**

The three vCJD incidents (Table 19.1) took place prior to the introduction of leucodepletion and other measures taken by the UK Blood Services to reduce the risk of vCJD transmission by blood, plasma and tissue products [68].

### **vCJD control measures**

Despite international research efforts there is currently no suitable blood test available for screening blood donations for vCJD. The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) has been reviewing the measures in place to prevent transmission through blood transfusion [69]. This included considering the potential uses of donations from people in the UK at lower risk of vCJD i.e. those born since January 1996 and not thought to be exposed via the food chain. These young adults became old enough to donate in the UK from January 2013. New data published in 2013 suggests 1 in 2000 people in the UK may be carriers of vCJD [70] and a House of Commons Select Committee inquiry is currently underway to determine if the control measures in place are sufficient to minimise transfusion-transmitted infection in light of the potential for large numbers of carriers.

## Cumulative data

Table 19.1: Number of confirmed TTI incidents\*, by year of transfusion\*\* with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2013 (Scotland included from October 1998)

Year of transfusion*	Number of incidents (recipients) by infection											Implicated component			
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV I	Parvovirus (B19)	Malaria	vCJD/prion	Total	RBC	Pooled platelet	Apheresis platelet	FFP
Pre 1996	0	0	1 (1)	0	0	0	2 (2)	0	0	0	<b>3 (3)</b>	3	0	0	0
1996	0	1(1)	1 (1)	1 (1)	0	1 (3)	0	0	0	1 (1)	<b>5 (7)</b>	5	1	0	1
1997	3 (3)	0	1 (1)	1 (1)	0	0	0	0	1 (1)	2 (2)	<b>8 (8)</b>	6	1	1	0
1998	4 (4)	0	1 (1)	0	0	0	0	0	0	0	<b>5 (5)</b>	2	1	2	0
1999	4 (4)	0	2 (3)	0	0	0	0	0	0	‡ (1)	<b>6 (8)</b>	5	3	0	0
2000	7 (7)	1 (1)	1 (1)	0	0	0	0	0	0	0	<b>9 (9)</b>	1	5	3	0
2001	5 (5)	0	0	0	0	0	0	0	0	0	<b>5 (5)</b>	0	4	1	0
2002	1 (1)	0	1 (1)	0	0	1 (1)†	0	0	0	0	<b>3 (3)</b>	2	1	0	0
2003	3 (3)	0	1 (1)	0	0	0	0	0	1 (1)	0	<b>5 (5)</b>	1	1	3	0
2004	††	0	0	0	1 (1)	0	0	0	0	0	<b>1 (1)</b>	1	0	0	0
2005	2 (2)	1 (1)	1 (1)	0	0	0	0	0	0	0	<b>4 (4)</b>	1	3	0	0
2006	2 (2)	0	0	0	0	0	0	0	0	0	<b>2 (2)</b>	0	1	1	0
2007	3 (3)	0	0	0	0	0	0	0	0	0	<b>3 (3)</b>	2	1	0	0
2008	4 (6)	0	0	0	0	0	0	0	0	0	<b>4 (6)</b>	0	2	4	0
2009	2 (3)	0	0	0	0	0	0	0	0	0	<b>2 (3)</b>	1	0	2	0
2010	0	0	0	0	0	0	0	0	0	0	<b>0</b>	0	0	0	0
2011	0	0	1 (2)	0	1 (2)	0	0	0	0	0	<b>2 (4)</b>	2	0	0	2
2012	0	0	1 (1)	0	1 (1)	0	0	1(1)	0	0	<b>3 (3)</b>	2	0	0	1
2013	0	0	0	0	0	0	0	0	0	0	<b>0</b>	0	0	0	0
<b>Number of incidents</b>	<b>40</b>	<b>3</b>	<b>12</b>	<b>2</b>	<b>3</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>70</b>				
Number of infected recipients	43	3	14	2	4	4	2	1	2	4	<b>79</b>	<b>34</b>	<b>24</b>	<b>17</b>	<b>4</b>
Death due to, or contributed to, by TTI	11	0	0	0	0	0	0	0	1	3	<b>15</b>				
Major morbidity	28	2	14	2	2	4	2	1	1	1§	<b>57</b>				
Minor morbidity	4	1	0	0	2	0	0	0	0	0	<b>7</b>				
<b>Implicated component</b>															
RBC	7	1	11	2	2	2	2	1	2	4	<b>34</b>				
Pooled platelet	20	2	1	0	0	1	0	0	0	0	<b>24</b>				
Apheresis platelet	16	0	1	0	0	0	0	0	0	0	<b>17</b>				
FFP	0	0	1	0	2	1	0	0	0	0	<b>4</b>				

\*No screening was in place for vCJD, human T cell lymphotropic virus (HTLV), HAV, HEV or parvovirus B19 at the time of the documented transmissions. In both malaria transmissions, malaria antibody testing was not applicable at the time according to information supplied at donation

\*\* Year of transfusion may be prior to year of report to SHOT due to delay in recognition of chronic infection

† The two HIV incidents were associated with window period donations (anti-HIV negative/HIV RNA positive) before HIV NAT screening was in place. A third window period donation in 2002 was transfused to an elderly patient, who died soon after surgery. The recipient's HIV status was therefore not determined and not included

†† In 2004 there was an incident involving contamination of a pooled platelet pack with *Staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely. This case was classified as 'not transfusion-transmitted'

‡ Same blood donor as one of the 1997 transmissions so counted as the same incident; note: counted as two separate incidents in previous reports

§ A further prion case died but transfusion was not implicated as the cause of death. The outcome was assigned to major morbidity instead because although there was post-mortem evidence of abnormal prion proteins in the spleen the patient had died of a condition unrelated to vCJD and had shown no symptoms of vCJD prior to death



Please contact the National Coordinator for Transfusion Transmitted Infections (see page 2, inside front cover) for further information or alternative breakdown of data.

## Recommendations

- Clinical staff requesting investigation of a possible transfusion-transmitted infection (TTI) by the UK Blood Services are reminded to report as soon as practical to Serious Adverse Blood Reactions and Events (SABRE) and SHOT. The reporter should remember to tick the SHOT box to prompt SHOT reporting. Reporters should update their report once the outcome of the UK Blood Services investigation is known. These should be reported even if not currently screened for by the Blood Service

**Action: Hospital Transfusion Teams (HTT), Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff**

### 2012 Recommendations still active

- Retain suspected bacterially contaminated packs, even if near empty, for return to the Blood Service as the residue can be washed out and cultured. Report a suspected bacterial transfusion-transmitted infection (TTI) promptly to the Blood Service to allow recall of any associated packs for testing. If sampling packs locally for bacterial testing, use ports rather than breaching the pack to minimise environmental contamination of the pack

**Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff, Transfusion and Microbiology Laboratory Managers (see Chapter 15, previous recommendation on recall)**

- Hospitals and Blood Centres investigating a possible viral TTI are reminded of the importance of locating any archived recipient samples (transfusion-related or not) for testing. It is important that laboratories facilitate access to those samples (with due consent of appropriate parties including the patient)

**Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff, Transfusion Laboratory Managers, HTTs**

### 2010 Recommendations still active

- Even if TTI is excluded in a case of ATR, the case should still be reported to SHOT as an ATR if necessary

**Action: HTTs, Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff**

- Clinicians investigating suspected viral TTIs should explore all possible risk exposures in parallel with the Blood Service investigations, in order to determine the patient's most likely source of infection. This includes checking records and testing samples taken prior to the implicated transfusion(s) to check that the recipient was not infected prior to transfusion

**Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff, UK Blood Services**

Recommendations still active from previous years are available in the 2013 Annual SHOT Report Supplement located on the SHOT website, [www.shotuk.org](http://www.shotuk.org) under SHOT Annual Reports and Summaries, Report, Summary and Supplement 2013.