ADVISORY COMMITTEE ON THE SAFETY OF BLOOD, TISSUES AND ORGANS

FINAL MINUTES OF THE EIGHTEENTH MEETING, 10TH DECEMBER 2012

WELLINGTON HOUSE, LONDON SE1 8UG

Present:			
Professor	John	Forsythe	Chair
Members			**Area of expertise**
Professor	John	Cairns	Health Economist
Dr	Paul	De Sousa	Regenerative Medicine
Dr	George	Galea	Blood/Transplant Service Manager
Professor	Kate	Gould	Microbiologist/Bacteriologist/Virologist
Mrs	Gill	Hollis	Patient Representative
Professor	Richard	Knight	Prion Disease
Dr	Harpreet	Kohli	Epidemiology/Public Health
Professor	Joanne	Martin	NHS Management
Professor	Alison	Murdoch	IVF/Fertility/Stem Cells
Professor	Tom	Solomon	Microbiologist/Bacteriologist/Virologist
Professor	Richard	Tedder	Microbiologist/Bacteriologist/Virologist
Professor	Marc	Turner	Haematologist
Professor	Anthony	Warrens	Immunologist
Dr	Lorna	Williamson	Medical Director, Blood Services
Observers			
Mr	Nigel	Goulding	Medicines and Healthcare products Regulatory Agency (MHRA)
Dr	Aileen	Keel	Scotland
Dr	Sheila	MacLennan	UK Forum
Dr	Elizabeth	Reaney	Northern Ireland
Mrs	Jenny	Thorne	Wales (via telephone link)
Secretariat			
Dr	Rowena	Jecock	Department of Health (DH)
Mr	Mark	Noterman	DH
Dr	Stephen	Thomas	DH/NHS Blood and Transplant (NHSBT)
Mrs	Tina	Lee	DH
Others			
Dr	Peter	Bennett	DH Health Protection Analytical Team
Dr	Steve	Field	Welsh Blood Service (via telephone link)
Mr	Gary	Hughes	Deputising for Ms Léonie Austin, NHSBT Communications
Mr	Andrew	Parker	DH Health Protection Analytical Team
Mr	Andrew	Broderick	Prospective member of Secretariat

Item 1: Welcome, introductions and apologies

1.1 Apologies had been received from Professor John Dark, Mrs Catherine Howell, Dr Eithne MacMahon and Dr Mallika Sekhar (SaBTO members); and Professor Adrian Newland (National Blood Transfusion Committee), Ms Victoria Gauden (Human Tissue Authority) and Ms Triona Norman (DH, Transplantation Policy Lead) (Observers).

1.2 Mrs Jenny Thorne joined the meeting via a telephone link, as did Dr Steve Field, Medical Director, Welsh Blood Service.

1.3 The Chair warmly welcomed the new members who were present: Dr Paul De Sousa, Professor Kate Gould, Mrs Gill Hollis, Professor Alison Murdoch and Professor Tom Solomon. Dr Mallika Sekhar, the other new member, was unfortunately not able to attend. All attendees introduced themselves briefly.

1.4 The Chair congratulated Dr Sheila MacLennan on her recent election as Chair of the CD-P-TS, the Steering Committee on Blood Transfusion of the Council of Europe's European Directorate for the Quality of Medicines and HealthCare (EDQM).

Item 2: Minutes of the meeting held on 11th September 2012

2.1 The Chair reminded members that, as was usual, the minutes of the meeting on 11th September had been approved by members via email, and had been published on the SaBTO website.

2.2 Clarification of point 4.2.4 was requested, concerning the qualifications in points 4.2.1 and 4.2.2 to SaBTO's endorsement of the continuation of the study to test deceased donors for abnormal prions using splenic/ocular tissue. It was agreed that:

2.2.1 4.2.1: SaBTO had noted the opportunity to explore also the utility of blood tests in this group of donors, and asked that it should be considered when the next study was designed: its inclusion was not an absolute requirement;

2.2.2 4.2.2: it was agreed it would be sensible to take post-mortem blood samples and store them, for testing in future.

2.2.3 It was noted that SaBTO members were to have been updated on the outcome of a joint meeting of the Blood Services' Prion Working Group and the Advisory Committee on Dangerous Pathogens (ACDP) TSE Risk Assessment Sub Group on 25th October, when blood tests for vCJD in development were reviewed. It was reported that four tests had been reviewed, and concerns had been expressed about specificity, sensitivity and confirmatory algorithms. The question of how blood samples used in test evaluations should be managed to ensure complete donor anonymity and unlinking would need very careful consideration. The minutes of the joint meeting would be shared with SaBTO when they had been finalised, following the next joint meeting of the Prion Working Group and ACDP TSE RA Sub Group in around three months' time.

Item 3: Action points and matters arising from the meeting on 11th September 2012

3.1 *Action 17/01: Dr Lorna Williamson to share the data on blood testing for West Nile Virus (WNV) with the organ donation and transplantation directorate of NHSBT.* This had been completed.

3.2 *Action 17/02: Professor Anthony Warrens to circulate the data to the British Transplantation Society.*
On consideration, Professor Warrens had considered circulation by NHSBT would be more appropriate. The Chair noted that the link between WNV and transplantation would be further considered at agenda item 9.

3.3 *Matters arising*: There were no further matters arising.

Item 4: Use of a prion filter for red cells as a vCJD risk reduction measure: recommendations of the SaBTO Prion Sub Group

4.1 SaBTO considered the evidence currently available and expert advice from the SaBTO Prion Sub Group. The Sub Group had worked closely with other relevant groups and specialists including the UK Blood Services Prion Working Group and the Advisory Committee on Dangerous Pathogens Transmissible Spongiform Encephalopathies Risk Assessment Sub Group.

4.2 Following this consideration, SaBTO concluded that the evidence did not currently support the introduction of this filter, and the provisional recommendation it made in 2009 should be rescinded. SaBTO would consider re-evaluation of this conclusion if further evidence became available about this filter.

4.3 SaBTO agreed to consider other filter technologies if evidence should become available.

NOTE: Some material has been redacted for legal reasons. SaBTO may be in a position to publish this at a later date.

Item 5: "Club 96" as blood donors

5.1 A paper was provided. The UK Blood Services "Club 96" Working Group had developed a model of demand for and supply of blood components donated by those born on or after 1st January 1996 ("Club 96"), and so presumed to not have been exposed to BSE through diet. The group expected to report to SaBTO in 2013, but requested advice on the prioritisation of recipients and the use of first time donations, to allow modelling to proceed.

5.2 **Prioritisation of recipients**

5.2.1 Three options were presented which, it was noted, were not mutually exclusive. These were:
a) to supply the youngest patients first, as they generally had the greatest life expectancy. This would maximise the benefit from these donations in terms of QALYs
b) to supply patients who had not previously been exposed to a blood borne risk of vCJD, such as those not previously transfused
c) to supply those at greatest risk, such as haemoglobinopathy patients who were exposed to multiple transfusions.

5.2.2 It was noted that practical considerations were relevant. Certain components were currently manufactured to particular specifications and labelled specifically for groups such as intrauterine transfusion, neonates or infants. "Club 96" donations could relatively easily be streamed into these products.

5.2.3 Ensuring some patients received "Club 96" products when being treated on wards alongside similar patients not receiving such products would be difficult to arrange in practice and also might potentially give rise to confusion amongst both clinicians and patients.

5.2.4 SaBTO was asked:

Question 1: Is SaBTO content for the modelling work to be based upon a quantifiable benefit, such as quality adjusted life years? If not, which approach should be taken?

5.2.5 The following points were raised in discussion:

5.2.5.1 It was agreed that SaBTO would not want to make value judgements about the needs of the different patient groups.

5.2.5.2 It was clarified that directing "Club 96" donations to intrauterine transfusions, neonates and infants would be relatively easy in practice. Targeting children under 16 years old would be possible but problems would arise when, for example, children were on specialist rather than paediatric wards. More problematic would be patients born on/after 1 January 1996 but over 16 years old, and so being treated on adult wards alongside older patients. It would be particularly challenging to target patients in option c), eg haemoglobinopathy patients, which would require a separate supply stream for patients with particular diagnoses rather than an age-group; they also have more specific antigenic requirements.

5.2.5.3 The long term aim of the Blood Services was to generate a section of the population presumed not exposed to BSE through diet, and also protected from other risks (eg by receiving "Club 96" donations); they could donate blood which could potentially be presumed to be 'safer'. This was the best way to maximise benefit to the greatest number of patients in the shortest possible time.

5.2.5.4 Currently, because of the potential risk of a transfusion, transfusion recipients were not allowed to donate blood. The Blood Services could not consider reversing this policy to maximise the pool of 'safer' donors if they had been exposed to blood-borne risk of vCJD through transfusions.

5.2.5.5 On this basis, as well as for practical reasons, it made sense to prioritise the youngest patients first (intrauterine transfusions, neonates and infants); then, when the supply allowed, those not yet exposed through diet or transfusion; then those most at risk. Modelling showed that if the second group alone were prioritised, the supply may not be sufficient until 2018; if the first group were prioritised, components may be available for intrauterine and neonatal exchange transfusions by 2015.

5.2.5.6 Other routes of infection by which "Club 96" might be put at risk of vCJD were raised. It was noted that evidence was lacking for transmission of human prion diseases from parent to child; there was a theoretical risk of transmission via surgery and dental treatment, but recently published data showed no evidence of any transmissions by those routes.

5.2.5.7 It was noted that SaBTO would not want to lose the opportunity of gaining a potential long term benefit by failing to protect young people now. However, interpretation of the results of the appendix study, and resulting assumptions about prevalence, were uncertain in the absence of such information as might be gained from examining appendices extracted before BSE, and from those not exposed to BSE through diet.

5.2.5.8 Such uncertainty reinforced the value of being pragmatic and supplying the youngest first, as was easiest in practice. As the 'safer' pool of donors grew, donation could be encouraged to make the potential benefit available more widely.

5.2.6 SaBTO concluded that the Working Group should proceed on the basis of prioritising the youngest patients first, then those not yet exposed, then those most at risk, though noting these are not mutually exclusive. The Group's report should state the arguments clearly for prioritisation of each group, including assumptions, practical problems with adoption etc.

5.3 **The use of first time donors**

5.3.1 Currently components for neonates and infants were not manufactured from a donor's first donation, as evidence showed first time donors were more likely to have a blood borne infection, which could be in the 'window period' at the time of donation and so not detected. This measure was introduced in 1997, before the introduction of NAT (Nucleic Acid Amplification Technology) testing, which reduced the window period.

5.3.2 Until components from "Club 96" donors became available, this group would receive components carrying a very small risk of vCJD. If first donations from "Club 96" donors were used, modelling showed the supply might be sufficient to supply components two or three years earlier.

5.3.3 SaBTO was asked:

Question 2: Is SaBTO content for a risk assessment to be performed, comparing the risk of viral transmission from first time "Club 96" donations with the risk of vCJD transmission from UK repeat donors?

5.3.4 In discussion, it was mentioned that:

5.3.4.1 First time donors were a fairly small proportion, and many never returned.

5.3.4.2 The risk assessment should include infections that were common in late childhood, such as cytomegalovirus and Epstein Barr Virus.

5.3.5 SaBTO was content for the risk assessment to be performed, as long as that concern was taken into account.

5.3.6 SaBTO was asked:

Question 3: Is SaBTO content for the UK blood services to take samples from donors before their 17th birthday?

5.3.7 The following points were raised in discussion:

5.3.7.1 This would provide an opportunity to promote the benefits of transfusion to that population.

5.3.7.2 It made sense to make 'special donors' feel special: that could be done here.

5.3.7.3 If such a donor tested positive for an infection, special care would need to be taken in feeding that back to such a young donor.

5.3.8 SaBTO agreed that potential donors could be tested before their 17th birthday, to detect infections and ensure the residual risk from window period infections was minimised.

5.3.9 It was noted that "Club 96" was a working title only, and suggestions were invited for an alternative.

5.4 **Appendix studies:** SaBTO reiterated its strong support for the commissioning by DH of the two proposed studies of appendices, collected before 1980 (ie pre-BSE) and from those born on/after 1 January 1996 (presumed not exposed to BSE through diet).

Item 6: Update on the Cell Based Advanced Therapies Working Group

6.1 An update was provided. The Group's focus would be donor-related risks, arising for example from infection, genetics or procurement, rather than exogenous risks, which fell within the remit of the MHRA. It was expected most of the work would be completed by autumn 2013.

Item 7: Update on the MSM Tissues & Cells Donor Selection Working Group

7.1 An update was provided. The Group planned to group products for the purposes of their Report and recommendations. They aimed to report to SaBTO in March or June 2013.

Item 8: Hepatitis E infections and blood safety

8.1 A paper was provided. It was reported that there were four genotypes (g1 – 4) of hepatitis E virus (HEV). Genotype 1 and g2 infected humans only, whilst g3 and g4 infected humans and animals. Genotypes 1 and 2, found predominantly in developing countries, could cause extensive mortality in pregnant women, and accounted for imported cases of HEV in the UK, whilst g3 accounted for the majority of HEV cases but did not adversely affect pregnancy. Seroprevalence of antibody to HEV (anti-HEV) in England was 10-15%, with an annual attack rate of 0.1-0.2%. A new phylogenetic variant of g3 had recently appeared, however, which might be more pathogenic and more transmissible. There would have been around 6,000 cases in the UK in 2012. HEV g3 was primarily transmitted zoonotically in the UK, and pig meat was the main dietary source, especially pork sausages and processed ham. Older men in their 60s and 70s were more likely to present with clinical HEV than women; however these clinical cases only occurred in a very small proportion of people who became infected with g3 in the UK. Severe HEV occurred, but rarely. Chronic infection with progressive liver disease was seen in immunosuppressed patients but responded to anti-viral therapy.

8.2 The first UK case of transfusion transmitted HEV was identified in 2004 and confirmed as g3. Infection generally caused no symptoms, or mild jaundice. In immunosuppressed patients, however, it could lead to chronic infection, which could lead to liver disease and even death.

8.3 NHSBT and HPA were carrying out a joint study to find out more about the potential problems HEV might give rise to for blood transfusion. Early results

indicated that a small number of donors were currently viraemic at the time of donation. While it was too early to say if disease would be seen in recipients, it might be that certain groups of recipients would require protection.

8.4 The following points were raised in discussion:

8.4.1 In lookback exercises, it had to be established when the recipient patient first became viraemic in order to identify the donors who might be implicated.

8.4.2 Longitudinal studies of transplant recipients were being undertaken in France. Genomic methods had to be used, as the persistently infected immunosuppressed patients did not produce antibodies until viral clearance.

8.4.3 It was noted that it was important to understand the implications of HEV, both to maintain confidence in the blood supply and because, since blood was ruled to be a consumer product, the Blood Services were liable for its safety. It was reported that only a small number of cases had arisen and been investigated fully; transfusion had been ruled out of several. There had been one incident of transfusion-associated transmission in 2012, with one donor infecting two recipients, and other potential cases were under investigation.

8.4.4 Tissue transplants were more usually life enhancing than life saving, and recipients were seldom immunosuppressed. Nevertheless a precautionary approach was advisable as HEV was not tested for in donors.

8.4.5 Transplantation of an infected organ would be unusual, given the short viral turnover period, but the risk might need to be considered for liver transplant recipients. Infection of transplant recipients was sometimes acquired post transfusion through the dietary route.

8.5 In summary, more information was needed, especially on the implications of screening blood and also tissues, less so for organs. Information was also needed on the pathogenicity of the new variant form of HEV when delivered by transfusion. The Chair undertook to discuss the question with Professor Tedder and report back to SaBTO on what action, if any, was needed.

8.6 **Action point 18/01: The Chair and Professor Tedder to consider the implications of hepatitis E, and report back to SaBTO on what action, if any, was needed.**

Item 9: West Nile Virus

9.1 A paper was provided on NHSBT's 2012 move to testing the donations of those returning from areas affected by West Nile Virus (WNV) rather than deferring them. Data was provided on the predicted number of deferrals from affected areas, based on the viral areas in 2011; 'worst case' predicted deferrals if WNV spread to France, Spain and Portugal; and the number of donations tested. The number of tests exceeded the 'worst case' expectation by October, with 23,651 tests at the end of October 2012, but no confirmed positive results had been recorded. This data would be useful for planning for the 2013 season.

9.2 A letter from the Veterinary Record of 15 September 2012 reported surveillance in the UK by the Health Protection Agency had identified the species of mosquito responsible for transmitting the virus from birds to humans, *Culex modestus,* at several sites in Kent and Cambridgeshire.

9.3 The Blood Services in Wales, Scotland and Northern Ireland would decide whether to change from deferral to testing on the basis of epidemiological evidence.

9.4 The following points were made in discussion:

9.4.1 Tissue donors were tested for WNV if they would have been deferred from blood donation because of a relevant history of WNV risk, such as travel to a WNV circulating area.

9.4.2 Regarding organ donation, a donor history was taken but it was reported that, on the ground, the teams were not clear which were the WNV affected areas. Information on the Geographical Disease Risk Index is available on the website of the UK Blood Transfusion and Tissue Transplantation Services at http://www.transfusionguidelines.org.uk/index.aspx?Publication=GDRI&Section=66

9.4.3 **WNV and organ transplantation**

9.4.4 The Chair outlined a possible scenario whereby a donor of organs and tissues was found to be infected with WNV (when tested as a tissue donor), but the test result was not available until after the organs had been transplanted. Transplant units might find it helpful to have clear advice on how to proceed in these circumstances. NHSBT did not currently have a management policy in place.

9.4.5 The following points were made in discussion:

9.4.5.1 There was no point removing the organ as the infection probably would have been transmitted. There was no treatment for WNV.

9.4.5.2 It was suggested it might be possible to have a panel of WNV immune plasma donors to make products to treat the recipient of an organ from a donor who had returned from a WNV-affected area.

9.4.5.3 WNV was just one of a number of extremely rare infections that may cause encephalitis, rabies being another. Information on some of these was included in *Guidance on the microbiological safety of human organs, tissues and cells used in transplantation,* published by SaBTO in February 2011. Undiagnosed encephalitis was also a matter of concern, but fell within the scope of the Working Group developing the Organ / Donor Risk Index.

9.4.6 It was concluded that SaBTO should provide some advice for the WNV scenario outlined by the Chair.

9.4.7 **Action point 18/02: SaBTO to develop advice on management of an organ recipient when tissue from the same donor tested positive for West Nile Virus.**

Item 10: Council of Europe deliberations on donor deferral / MSM

10 SaBTO received an update on work undertaken by the CD-P-TS, the Steering Committee on Blood Transfusion of the Council of Europe. The draft resolution from the CD-P-TS supports an approach based on risk assessment, as used by the UK. It was amended in light of concern raised by the European Union about

policies being potentially discriminatory. The policies in England, Wales and Scotland of deferral for 12 months following the last risk activity, which are based on SaBTO's review and recommendation, are compliant with the EU position.

Item 11: Any other business

11.1 It was reported that a case of transfusion transmitted hepatitis B had occurred in 2011, the first since 2005. Investigation had shown the donor was a long-term male donor who was in the window period of acute infection when he donated. The donation took place before the change in policy for MSM donors was implemented, but this was not a risk factor in the case. The infection was not identified on routine screening (minipools of 24 donations by NAT testing), and when the archive sample was tested (singleton NAT), the result was again negative. The infection was only identified by use of a reference assay, and further investigation for markers of a cleared infection in the subsequent donation three months later. The recipient of the red cells seroconverted and became a chronic carrier, but had no symptoms. The recipient of plasma developed disease. The NHSBT Board considered whether donations should be tested in pools of 6 rather than 24, or individually, but decided no change was warranted. It would have made no difference in this instance, and the additional cost would have been £11.7 million (for pools of six) or £18.5 milion (for individual testing) per extra infectious donation detected.

11.2 Professor Peter Braude had drawn to SaBTO's attention a change in the EU Tissues and Cells Directive 2006/17/EC whereby partner donors of reproductive cells would be tested within 3 months of first donation, and at fixed intervals of up to 2 years thereafter, rather than at the time of each donation, as currently. This would come into force by June 2014 at the latest, but the HFEA had not yet issued instructions.

11.3 SaBTO was informed of two clusters of coronavirus infection in the last few months. One was in Saudi Arabia, the other in healthcare workers attending a patient with severe respiratory disease. There was a 50% mortality rate. It was a very rare infection, and would not be looked for in the UK without epidemiological evidence of exposure, relevant symptoms and the exclusion of other respiratory infections. No action by SaBTO was currently required.

11.4 The Chair noted that Dr Stephen Thomas's secondment to the SaBTO secretariat was to end in January, though he was expected to see through to completion the work he was currently supporting, and would attend the meeting in March 2013. The Chair thanked Dr Thomas for his superb assistance to the Committee, in helping to drive through several pieces of work.

Dates of 2013 SaBTO meetings

Tuesday 5 March 2013
Monday 24 June 2013
Tuesday 25 June 2013 – Open meeting
Tuesday 17 September 2013
Tuesday 3 December 2013