ADVISORY COMMITTEE ON THE SAFETY OF BLOOD, TISSUES AND ORGANS

FINAL MINUTES OF THE SEVENTEENTH MEETING, 11TH SEPTEMBER 2012

WELLINGTON HOUSE, LONDON SE1 8UG

Present:			
Professor	John	Forsythe	Chair
Members			**Area of expertise**
Professor	Peter	Braude	IVF/Fertility/Stem Cell Specialist
Professor	John	Cairns	Health Economist
Professor	John	Dark	Solid Organ Transplant Surgeon
Dr	George	Galea	Blood/Transplant Service Manager
Mrs	Catherine	Howell	Nurse
Professor	Deirdre	Kelly	Physician
Dr	Harpreet	Kohli	Epidemiology/Public Health
Dr	Eithne	MacMahon	Microbiologist/Bacteriologist/Virologist
Professor	Joanne	Martin	NHS Management
Mr	Elwyn	Nichol	Patient Representative
Professor	Hamish	Simpson	Orthopaedic Surgeon
Dr	Lorna	Williamson	Medical Director, Blood Services
Observers			
Mrs	Jenny	Thorne	Wales
Dr	Sheila	MacLennan	UK Forum
Dr	Victoria	Gauden	Human Tissue Authority (HTA)
Secretariat			
Mr	Mark	Noterman	Department of Health (DH)
Dr	Stephen	Thomas	DH/NHS Blood and Transplant (NHSBT)
Mrs	Tina	Lee	DH
Others			
Dr	Jill	Shepherd	HTA
Ms	Samantha	Fletcher	NHSBT Communications
Dr	Peter	Bennett	DH
Mr	Andrew	Parker	DH

Item 1: Welcome, introductions and apologies

1.1 The Chair welcomed members to the meeting. Apologies had been received from Professor Richard Knight, Professor Marc Turner and Professor Richard Tedder (SaBTO members); Dr Aileen Keel, Dr Elizabeth Reaney, Mr Nigel Goulding, Professor Adrian Newland and Ms Triona Norman (Observers); and Dr Rowena Jecock (Secretariat).

1.2 The Chair welcomed Dr Jill Shepherd of the Human Tissue Authority (HTA), who was to speak to agenda item 6(c).

Item 2: Minutes of the meeting held on 9th March 2011

2.1 The Chair reminded members that, to facilitate early publication, the minutes of the meeting on 9th March had been approved by members in April via email. This would be the routine process for approving minutes in future.

2.2 As the meeting of 29th May had been cancelled, this was the first opportunity to update members on the action points from the March meeting.

Item 3: Action points and matters arising from the meeting on 9th March 2012

3.1 *Action 16/03: Secretariat to seek clarification of the remit of the Welsh Government's Clinical Advisory Group (CAG).*
Completed. A written update had been provided to SaBTO, and was noted.

3.2 The Chair also reported that he had visited Wales, and had helpful and cordial meetings with the Minister and with officials. The Welsh Government was satisfied that communications with SaBTO were good; and that the role of the National Specialist Advisory Group for Haematology services (which would replace the Clinical Advisory Group) would not cut across SaBTO's work.

3.3 *Action 16/04: Secretariat to inform DH of SaBTO's recommendation that a communication should be issued clarifying that those born after 1st Jan 1996 (and adults with TTP) should continue to be treated with imported FFP.*
Completed. The Chair reported that notifications had been published in the Department of Health (DH) Medical Directors' and Chief Nursing Officer's Bulletins, and letters had been sent out by DH to the Medical Directors of the Blood Services and to NHS Blood and Transplant (NHSBT), the National Blood Transfusion Committee and the British Committee for Standards in Haematology asking them to use their contacts to ensure all services were aware of SaBTO's recommendation.

3.4 *Action 16/05: Professor John Dark to make enquiries about organ donation and West Nile virus (WNV).*
Completed. There had been a report of WNV transmission via a kidney transplant in Italy in 2011, and Professor Dark had made enquiries to establish whether WNV was causing a problem in transplantation. He had spoken to SNOD (specialist nurse - organ donation) managers and to contacts within NHSBT, and reported that it did not appear that donors were being lost because of their travel history / risk of WNV.

NHSBT had been testing blood donations from travellers returning from WNV affected areas this year. Around 4,000 per month had been tested, and all had proved negative.

Action 17/01: Dr Lorna Williamson to share the data on blood testing for WNV with the organ donation and transplantation directorate of NHSBT

Action 17/02: Prof Anthony Warrens to circulate the data to the British Transplantation Society

3.5 *Action 16/06: The Chair to write and thank Dr Mike Potter.*
Completed. The Chair had written to Dr Potter in March.

3.6 *Matters arising*: There were no matters arising.

Item 4: Relating to vCJD risk reduction measures

(a) Studies relating to vCJD and tissue donation

4.1 The Committee received an update on three studies relating to tissues / cells and prion disease.

4.2 **Operational / Feasibility study to test deceased donors for abnormal prions using splenic/ocular tissue**: this study had been undertaken at a time when there was no possibility of a blood test for prion disease, in order to test the feasibility of this alternative testing approach. The first phase (tissue only donors consented by blood transfusion services staff) had involved limited numbers, and much had been learned; the second, still ongoing, was larger (tissue and ocular donors consented by blood transfusion services staff) with more than 800 analyte samples tested, and the third phase (to extend the study to tissue and ocular donors consented by SNODs) would depend on the success of the earlier phases. All results to date had been negative.

4.2.1 It was suggested that a comparative study could be included in the next phase, comparing tissue testing with blood testing. It might be easier to obtain post-mortem blood samples than spleen samples, and the turnaround time for a blood test might be quicker than the current three days for a tissue test.

4.2.2 Blood tests currently in development were being assessed for sensitivity and specificity. It was noted that a joint meeting of the Blood Services' Prion Working Group and the Advisory Committee on Dangerous Pathogens (ACDP) TSE Risk Assessment Sub Group, scheduled for 25th October, would review some tests in development. Following this, SaBTO members would be updated at the meeting on 10th December.

4.2.3 Any blood test would need to be validated for both pre-mortem and post-mortem testing.

4.2.4 With the caveat set out in 4.2.1 above, and subject to further advice following the meeting noted in 4.2.2 above, SaBTO endorsed the continuation of the study.

4.3 **Study to assess the feasibility of tracing donors / recipients of organs and tissues to / from people who subsequently developed vCJD**: this was required because of the complexity of tracing tissues and organs in comparison to blood. The study involved a 'lookback' exercise to trace donors/recipients of organs or tissues to/from the 176 UK cases of vCJD. The report was expected to be published shortly.

4.4 **Processing of femoral heads to remove residual marrow and blood**: in 2010 SaBTO decided it could not recommend adoption of the new washing method without considering clinical data. It was reported that a group in Aberdeen had obtained a grant for a study with 25 patients in each of two arms, followed up over 18 – 24 months, to compare the conventional and new methods.

4.4.1 It was agreed SaBTO could review the subject when the study's findings were available.

(b) Methylene blue (MB) treated fresh frozen plasma (FFP)

4.5 An update was provided on the use of MB FFP in the UK. This had been reviewed by JPAC (the Joint UK Blood Services / Health Protection Agency Professional Advisory Committee) following the decision in France in 2011 to withdraw MB FFP because of concerns that it caused more allergic reactions. The UK haemovigilance data showed the level of allergic reactions to MB FFP was similar to, or lower than, to standard FFP, so did not support its withdrawal from use. One factor may be that in the UK, MB FFP was used for children, while in France it was used more widely. It was noted that as MB FFP would now be used for increasing numbers of patients born after 1st January 1996, monitoring would be needed for longer.

4.6 There was also concern in France about variation in fibrinogen concentrate levels in MB FFP, but JPAC found them to be within acceptable levels in the UK.

4.7 JPAC recommended that SHOT (Serious Hazards of Transfusion) should undertake proactive monitoring of future FFP reaction rates: JPAC would review these data and amend its recommendations if appropriate. JPAC also recommended that anaphylactic reactions should be referred to an immunologist.

4.8 SaBTO endorsed JPAC's view that no action was currently required, but that increased haemovigilance should be undertaken.

(c) ACDP Position Statement and HPA Health Protection Report

4.9 These documents related to the prevalence of the abnormal prion protein associated with vCJD in the UK, according to the findings of the study of archived appendix samples from people born between 1941 and 1985. It was now proposed to study appendix samples collected before 1980 (ie pre-BSE), and from people born after 1996 (when meat controls were in place). Funding had not yet been confirmed, but SaBTO would be updated at its meeting in December.

4.10 SaBTO endorsed the importance of carrying out these studies: their findings would inform the prioritisation of risk reduction measures, which were currently often both difficult and costly.

4.11 It was noted the findings of the recently-completed appendix study were towards one end of the scale used for estimating prevalence of vCJD in the risk assessment model. No new data were available on infectivity or virulence, which had been presented to SaBTO in March.

Item 5: Development of a transplant donor risk index

5.1 Early discussion had shown two potential approaches, which could be undertaken to different timescales:

5.1.1 To consider specific risks (such as drug-using donors who tested negative for viral infection) and quantify them according to the available evidence, as had been done for donors with brain tumours. Potential recipients were less likely to refuse an organ if they understood the real level of risk, so more organs could be utilised;

5.1.2 To consider broad risks (such as obesity), and quantify them for particular organs.

5.2 The first approach might affect smaller numbers of organs, but yield results more quickly.

5.3 The following points were raised in discussion:

5.3.1 Follow-up data in the UK was among the best in the world. However, more monitoring was needed for microbiological/virological data;

5.3.2 Patients' input could be helpful in prioritising which areas to consider;

5.3.3 There were intrinsic problems in using retrospective data which reflected historic practice;

5.3.4 Patients with undiagnosed encephalitis were unlikely to be used as donors, as it was assumed all could be herpes virus infections. If a specific diagnosis had been made a more evidence-based decision could be made to set against the risk of the recipient remaining on the waiting list for transplant.

5.4 SaBTO gave its endorsement for the work to be taken forward. The first step was to see where good quality data were available, and where the work could have greatest impact.

Item 6: Relating to microbiological risk associated with stem cell therapy

(a) Paper by Professor Marc Turner

6.1 It was noted that Professor Turner's paper summarised the areas of interest to SaBTO; noted the roles of relevant bodies (eg HTA, MHRA); and set out a categorisation, on which alternative approaches could be based. The risks/issues relating to a particular category could be considered; or alternatively, a single risk (eg transmissible spongiform encephalopathy, TSE) could be considered, and its potential impact on the different categories.

(b) Update on the request for advice from SaBTO

6.2 SaBTO received a presentation on the issues that had led to the request for advice from SaBTO from the UK National Clinical Human Embryonic Stem Cell Forum. There was a mis-perception that UK tissue products could be disproportionately affected by TSEs and should not be used; however, it was noted that human prion diseases were found worldwide. Both the donated tissue and the processing could give rise to potential risks. Contamination during IVF procedures compliant with EU tissue and cells directives (EUTCD) / the HFEA (Human Fertilisation and Embryology Authority) Code of Practice was unlikely, and the risk during freezing was very small despite open systems. In the past, a number of xeno elements had been used in processing, and though this was reducing, many lines in use were eg grown on mouse feeder cells; the UK stem cell bank did not require xeno-free conditions for submission of lines as EUTCD compliant. A basic donor viral screen (HIV, Hepatitis B and C) in accordance with Annex III of the EUTCD, was documented for IVF material, but no archived serum sample was held. The derivers of stem cells asked SaBTO to evaluate the risk of TSEs for tissues / stem cells, with particular relevance to any adverse perception of UK stem cells and tissues for clinical use. The investigation would need to look at international data and then consider whether the UK was a special case.

6.3 It was decided that this item and the next should be discussed together, as they were closely related.

(c) Draft proposal by the HTA addressing challenges for the human embryonic stem cell (hESC) sector of current donor testing requirements

6.4 The Committee received a presentation on the amendments proposed by the HTA to Annex II of the EU Tissues and Cells directive 2006/17/EC. These were designed to resolve difficulties arising from the current requirements for donor testing, when applied to hESC for advanced therapy medicinal product (ATMP) development. The HTA's remit covered donor selection for tissues and cells intended for patient treatment (including ATMPs and ATMP starting material).

6.5 SaBTO's endorsement in principle for the proposal was sought by the HTA.

6.6 It was concluded that SaBTO supported the pragmatic approach taken by the HTA, and endorsed their proposal in principle, with specific caveats.

6.7 SaBTO needed to satisfy itself whether the various risks and issues highlighted in Professor Turner's paper fell within the remit of one of the bodies involved, or whether further action was needed, either by SaBTO or another body. SaBTO would explore the assessment of microbiological risk associated with stem cell therapy, at international and UK levels. It was important not to smother innovation with regulation but the safety of a product for clinical usage was paramount.

Action 17/03: SaBTO members and secretariat to liaise with DH to establish whether the range of risks noted in Professor Turner's paper were covered by a body's remit; and

Action 17/04: SaBTO members and secretariat to explore the assessment of microbiological risk associated with stem cell therapy.

Item 7: Update on the MSM tissues & cells donor selection working group

7.1 It was reported that what had appeared straightforward initially was more challenging due to the decision to include gametes within the scope of the group's work. There were a large number of providers, and baseline information was needed. There were a number of different tissues with varying risks/benefits and parameters, so the recommendations formulated by the working group were likely to be in the form of a framework, with specific recommendations for some.

7.2 The group expected to update SaBTO in December, and hoped to report its recommendations during 2013.

Item 8: Updates on the recommendations / advice issued by SaBTO in the last year

(a) The provision of cytomegalovirus (CMV) tested blood components

8.1 NHSBT had found variation in how quickly Trusts expected to implement SaBTO's recommendations, and the anticipated reduction in their usage of CMV seronegative components. It was noted that a few Trusts did not intend to implement them, and some depended on the policy adopted by their tertiary referral centres. SaBTO had published its recommendations, but they were not mandated, and it was for the NHS to resolve any policy differences.

8.2 NHSBT would continue to provide products as requested by Trusts.

(b) Use of organs for transplantation from donors with primary brain tumours

8.3 It was too early for the impact of SaBTO's recommendations to be evident in the data, but NHSBT would continue to monitor it. Anecdotally, it was reported that note has been taken of the recommendations in the transplant field.

(c) Patient consent for a blood transfusion

8.4 It was reported that action was continuing to implement SaBTO's recommendations. The UK Better Blood Transfusion network and the National Blood Transfusion Patient Involvement Group were co-ordinating activities nationally. A national comparative audit of patient information and consent was being planned for autumn 2013. The National Blood Transfusion Committee's Patient Involvement Working Group was linking with more than 50 patient organisations to maximise the role of patients and patient groups. The UK Better Blood Transfusion Network was finalising standard text for patient information: the UK Network was producing a new leaflet on giving information retrospectively. NHSBT was leading a patient awareness programme. The eLearning module on Consent was to be launched at the British Blood Transfusion Society Annual Scientific meeting later that month. The British Committee for Standards in Haematology had been asked to endorse the recommendations, and Consent was included in the addendum to the Administration of Blood Components guideline published recently.

8.5 It was reported the recommendations had been well received. No negative feedback had been received, and requests for information continued to come in.

(d) Review of blood donor selection criteria: men who have sex with men (MSM)

8.5.1 It had been noted in the Report of the Blood Donor Selection Working Group that the safety gain from amending the blood donor selection criterion for MSM was predicated on improved compliance. This had resulted in four strands of work:

8.5.1.1 The analysis of donor demography data had not shown an increase in young urban male donors, at August 2012. It was suggested there might be a rise in older donors, who are no longer so sexually active;

8.5.1.2 The interview pro-forma used when donors have tested positive had been revised, but there was no obvious difference in the number of positive test results, risk factors, reasons for donation or donor compliance;

8.5.1.3 Preparations were in hand for an on-line survey to be conducted during 2012-13, to investigate donor understanding of the questions on the Donor Health Check, and compliance with them;

8.5.1.4 Funding was being sought for a study following that by Grenfell et al, to establish if the change in selection criteria had changed attitudes and compliance in the specific group.

8.5.2 An editorial had been published in Transfusion Medicine which gave a good summary of the review. An article on the ethics of the work had been submitted for publication, and SaBTO would be informed when it was accepted. Members of the Working Group were also to participate in a conference in Canada.

8.5.3 **Commercial sex workers:** SaBTO had not supported the change to a 12 months' deferral period for commercial sex workers because of a lack of evidence on several points. The working group had searched for further evidence, but had not been successful. SaBTO agreed that it could therefore take no further action at this time. If relevant data were provided by a study which was due to be published, or another source, then SaBTO would review it.

Item 9: Schmallenberg virus

9.1 The European Centre for Disease Prevention and Control, jointly with the Robert Koch Institute and the National Institute for Public Health and the Environment (Netherlands), had carried out a risk assessment for Schmallenberg virus in ruminants. They found that its zoonotic potential was absent or very low, and that it was therefore very unlikely that Schmallenberg virus posed a risk to humans.

9.2 SaBTO members concurred with this conclusion, and agreed that no action was currently needed.

Item 10: Recruitment to vacancies on SaBTO

10 At the closing date for applications, 29th August, thirteen applications had been received, covering all the five posts. The Chair thanked members for their help in disseminating information about the recruitment exercise among their colleagues and contacts. The Chair commented on the high quality of applications, and looked forward to being able to recruit suitable new members for all the posts.

Item 11: Members for whom this is their last meeting

11.1 The Chair expressed the thanks and appreciation of the Committee to the members who were to leave SaBTO: Professor Deirdre Kelly, Mr Elwyn Nicol, Professor Hamish Simpson and Professor Peter Braude. They had all been founding members, and the significant contribution they had made to the Committee's work was greatly valued.

Item 12: Any other business

12 There was no other business.

Dates of 2012/13 SaBTO meetings

Monday 10 December 2012
Tuesday 5 March 2013
Monday 24 June 2013
Tuesday 25 June 2013 – Open meeting
Tuesday 17 September 2013
Tuesday 3 December 2013

It was noted that the Open meeting had been postponed from December 2012 until summer 2013. It was important that Open meetings met the needs and interests of attendees, and the most suitable topic for the meeting - the work on ATMPs - would not have reached a suitable stage by December 2012.