ADVISORY COMMITTEE ON THE SAFETY OF BLOOD, TISSUES AND ORGANS

FINAL MINUTES OF THE TWENTIETH MEETING,
17TH SEPTEMBER 2013

WELLINGTON HOUSE, LONDON SE1 8UG

Present:			
Professor	John	Forsythe	Chair
Members			**Area of expertise**
Professor	John	Cairns	Health Economist
Professor	Kate	Gould	Microbiologist/Bacteriologist/Virologist
Mrs	Gill	Hollis	Patient Representative
Mrs	Catherine	Howell	Nurse
Professor	Richard	Knight	Prion Disease Specialist
Professor	Alison	Murdoch	IVF/Fertility/Stem Cells
Dr	Mallika	Sekhar	Haematologist
Professor	Richard	Tedder	Microbiologist/Bacteriologist/Virologist
Professor	Marc	Turner	Haematologist
Dr	Lorna	Williamson	Medical Director, Blood Services
Observers			
Mr	David	Carter	Medicines and Healthcare products Regulatory Agency (MHRA)
Dr	Aileen	Keel	Scotland
Dr	Sheila	MacLennan	UK Forum
Dr	Elizabeth	Reaney	Northern Ireland
Secretariat			
Mr	Andrew	Broderick	Department of Health (DH)/NHS Blood and Transplant (NHSBT)
Dr	Rowena	Jecock	DH
Mr	Mark	Noterman	DH
Mrs	Tina	Lee	DH
Others			
Mr	Ian	Beggs	Deputising for Ms Léonie Austin, NHSBT Communications
Mr	Andrew	Parker	DH Health Protection Analytical Team

Item 1:Welcome, introductions and apologies

1.1 Apologies had been received from Professor John Dark, Dr Paul De Sousa, Dr George Galea, Dr Harpreet Kohli, Dr Eithne MacMahon, Professor Joanne Martin, Professor Tom Solomon and Professor Anthony Warrens (SaBTO members); and Ms Victoria Gauden (Human Tissue Agency), Professor Adrian Newland (National Blood Transfusion Committee), Ms Triona Norman (DH, Transplantation Policy Lead) and Dr Andrew Riley (Wales) (Observers).

1.2 The Chair welcomed Mr David Carter, who had succeeded Mr Nigel Goulding as the MHRA Observer.

2 Item 2: Minutes of the meeting held on 24th June 2013

2.1 The Chair thanked members for providing amendments to the minutes via email. The discussion of donor selection criteria for men who have had sex with men as donors of tissues and cells had been the main agenda item at the June meeting. SaBTO's recommendations had been noted by Ministers in England and Scotland, and a response from Ministers in Wales and Northern Ireland was awaited. Publication of the minutes had been delayed to avoid making that process problematic; the subject occupied too great a proportion to be redacted, especially as the unpublished research findings on hepatitis E would also be redacted. Publication of the report was currently proposed to be on 17th October, and the minutes would be published shortly afterwards.

3 Item 3: Action points and matters arising from the meeting on 10th December 2012

3.1 Action point 19/01: working group to provide clarification of deferral criteria for female donors of banked tissues who are in a sexual relationship with an MSM.
This had been added to the recommendations in the report: female donors were subject to deferral for 12 months from their last sexual contact with a man who had ever had sex with another man (ie the same as for blood donation).

3.2 Action point 19/02: It was agreed that the Secretariat would liaise with the working group and the regulators with the aim of setting up a meeting of interested parties to explore the possibilities for improved bio vigilance. It was reported that early steps had been taken, but the Secretariat could not write out to invite participants until the report had been published, as the meeting followed up the observation and comments in the report.

3.3 Matters arising: there were no matters arising.

4 Item 4: Collection of 80% of platelet donations by apheresis and use of additive solution, as a variant Creutzfeldt Jakob disease (vCJD) risk reduction measure

4.1 The Chair noted this was the only substantive item on the agenda, and thanked Members for attending. It had not been possible to delay the item until the December meeting, and it was too complex to be dealt with by email correspondence.

4.2 The Chair noted that this item was the result of much work by a number of groups, and thanked in particular Mr Andrew Parker and the DH Health Analytical team, the SaBTO Prion Sub Group chaired by Professor Marc Turner, and Dr Sheila MacLennan and Mr Andrew Broderick.

4.3 SaBTO members received a presentation by Professor Marc Turner and Mr Andrew Parker. This was presented in stages, with members raising points as they arose.

4.4 The two methods of preparing platelet concentrates were:

4.4.1 From a pool of 4 whole blood donations, or
4.4.2 From a single donor, by apheresis.

4.5 In the UK, platelets were currently suspended in donor plasma, though some other countries used platelet additive solution (PAS) to replace around 65% of the plasma.

4.6 SaBTO's predecessor committee, the Advisory Committee on the Microbiological Safety of Blood, Tissues and Organs for Transplantation, set a target of 80% of platelets to be produced by apheresis, to reduce the number of donors to whom recipients were exposed, as one element of vCJD risk reduction. The underpinning assumptions were based on the understanding at the time of prevalence, infectivity and susceptibility. A review in 2009 concluded that the use of PAS would not be an effective vCJD risk reduction measure.

4.7 There had been significant changes since then, and the Advisory Committee on Dangerous Pathogens (ACDP) Transmissible Spongiform Encephalopathies (TSE) Risk Assessment Sub Group had approved revised working assumptions, consistent with the number of UK clinical cases observed to date. Infectivity per unit of whole blood was now estimated at 3 – 7 infectious doses, a one thousand fold reduction.

4.8 New modelling of the effectiveness and cost effectiveness of the use of apheresis and additive solution in the production of platelets as a vCJD risk reduction measure was presented. 30,000 scenarios had been modelled to find the number of life years that might be saved by averting potential future cases through risk reduction measures, using different assumptions about vCJD prevalence, susceptibility and incubation period. Of these, only credible scenarios had been used, ie those whose predictions for clinical cases to date were consistent with reality. The model showed the majority of potentially avoidable infections were likely over the next 20 years, with potential future cases up to 2070, peaking in the late 2040s. Not all those potentially infected would survive to develop clinical disease, as platelet recipients were often elderly and/or ill. This process was repeated for different assumptions about the level of vCJD infectivity in the plasma and the platelets, to investigate the effectiveness and cost-effectiveness of changing the proportion of platelets collected by apheresis and/or introducing the use of PAS.

4.9 The average age of apheresis donors was higher than that of whole blood donors, and research had shown higher prevalence of abnormal prion infection in older people. If the requirement for apheresis donors fell, however, it might be possible to focus on younger donors. The full age differential and no age differential had been modelled to show the upper and lower limits of the likely future impact of donor age.

4.9.1 Discussion point: It was noted that if SaBTO concluded that the apheresis requirement should be changed, this was likely to be implemented by the UK blood services gradually over time, so any change in average donor age would also be gradual. The modelling allowed for that, with decreasing numbers of potential infections for the same number of donations.

4.10 Modelling showed that the effectiveness of using PAS as a vCJD risk reduction measure varied according to assumptions about the levels of potential infectivity in plasma and platelets, and the age differential.

4.11 Points raised in discussion:

4.11.1 Platelets (devoid of plasma and leucocytes) were not known to be infective, but the possibility could not be ruled out. Previously it had been assumed they were not. There was no direct evidence of transmission in washed platelets, but some animal studies suggested platelets might potentially be infective.

4.11.2 It was noted the modelling was sensitive to the assumptions about the number of infective doses in a unit of blood. The small numbers were below Poisson levels.

4.11.3 The cost-effectiveness calculations related to vCJD only. Platelets collected by apheresis had wider benefits, and were required for specific clinical needs.

4.11.4 Reducing the availability of red cells, and therefore of donations, was not expected to be a factor, as there would still be more than enough to supply the necessary buffy coats, given the estimated minimum of 20% required to be collected by apheresis for other clinical reasons.

4.12 The cost effectiveness was modelled for different production methods, and both with and without age differential.

4.13 Overall, maintaining 80% apheresis was not cost effective in any scenario. Use of PAS was not always cost-effective, but saved life years in all scenarios. A combination of reducing the level of apheresis and using PAS was always more cost effective than the current situation, and in a number of scenarios showed life years saved and cost savings compared to current practice.

4.14 The Prion Sub Group's recommendation was that: 'SaBTO should remove the requirement to produce 80% of platelets by apheresis and platelet additive solution is used for the suspension of platelets'.

4.15 **SaBTO was asked** whether it agreed with that recommendation.

4.16 The following points were raised in discussion:

4.16.1 Using PAS would not affect the detection of bacterial contamination. However it would reduce the level of adverse reactions, which were due largely to the presence of donor plasma proteins.

4.16.2 PAS was not a necessity for pathogen inactivation, but was used in both currently available systems as the presence of plasma did reduce the effect of the light-exposure stage. SaBTO's Pathogen Inactivation of Platelets working group was considering the point.

4.16.3 The modelling was based on the best available information. It was believed the greatest future change was likely to be in the area of the prevalence of (subclinical) vCJD and, if anything, that was expected to decrease rather than increase – though this could not be known for sure. This would reduce the cost effectiveness of any vCJD risk reduction measure, as fewer life years could be saved.

4.16.4 The effect on potential infections other than vCJD was raised. Reducing donor exposure could be presumed to be beneficial in reducing opportunities for infection, but the numbers of viral infections not detected by NAT screening was believed to be extremely small. Apheresis donations were not from new donors, who presented a higher infection risk.

4.16.5 Many other countries, where vCJD was not a driver, were reducing their use of apheresis.

4.16.6 Some patients with complex conditions received extensive apheresed platelets, and the possibility of alloimmunisation was raised: one US study had found

leucodepleted apheresed platelets to be slightly better than leucodepleted pooled platelets. UK pooling methods were considered to be better than the US method, however; and leucocyte load was the greatest determinant of sensitisation.

4.16.7 Some members considered SaBTO could go further than removing the requirement for 80%, and actively encourage a reduction in apheresis. It was agreed that evidence on any wider benefits could be collected and considered separately (though SaBTO recognised that decisions on managing any reduction in apheresis would be a matter for each blood service).

4.16.8 The proposed recommendation was for the combination of reducing apheresis and using PAS, as a package, and the wording was discussed. However, as the benefit of reducing the 80% level of apheresis was not conditional on the use of PAS, no alternative wording was found to be better.

4.17 **SaBTO concluded:**

4.17.1 It agreed with the sub group's recommendation that SaBTO should remove the requirement to produce 80% of platelets by apheresis and platelet additive solution is used for the suspension of platelets.

4.17.2 It did not wish to set any other target level for apheresis: the Blood Services should set their own levels.

4.17.3 SaBTO would undertake further work to quantify any wider benefits of collecting platelets by apheresis, not related to vCJD. This would be considered by SaBTO along with the outcome of the Pathogen Inactivation of Platelets Working Group's work.

5 Item 5: Update on the Donor Organ Risk Assessment Working Group (DORA)

5.1 A written update had been circulated. SaBTO noted that the work was progressing well.

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

6.1 Professor Marc Turner, Chair of the working group, gave an update, following the group's meeting on 9th September. He reported the group had established three sub groups, to consider the infectious risks, genetic risks and issues of consent and traceability. Work was being completed and the sections of the report drafted between then and the end of December: the report would then be collated and refined, and sent out for consultation with interested bodies. The group planned to submit the report to SaBTO in April 2014.

6.2 It was noted that this work was planned as the theme of SaBTO's Open Meeting in 2014, also in April.

7 Item 7: Update on the Pathogen Inactivation of Platelets Working Group

7.1 Dr Lorna Williamson, Chair of the working group, reported that it was a short and intensive piece of work. The group planned to report to SaBTO in December 2013.

7.2 Sub groups had been set up to work on licensing and regulation, efficacy, clinical considerations, cost and benefit analysis and operational feasibility. A survey had been sent to the three manufacturers in the area, and meetings would be held with them.

8 Item 8: Any other business

8.1 Members leaving SaBTO

8.2 The Chair reported that Professor John Dark and Professor Joanne Martin were both leaving SaBTO, as their terms of appointment came to end in November. Professor Dark had kindly agreed to continue with the DORA working group, however. Unfortunately neither was able to be present, but the Chair wished to note the significant impact of their input to the Committee's work. He would write to both on behalf of the other members when their appointments ended.

Dates of future SaBTO meetings

Tuesday 3 December 2013
Monday 28 April 2014 (Open Meeting)
Tuesday 29 April 2014
Tuesday 2 September
Tuesday 9 December