

# Advisory Committee On The Safety Of Blood, Tissues And Organs

## Minutes of the Second Meeting, 29 April 2008

### Department of Health, Skipton House, London SE1

#### Present:

Mr John Forsythe **Chairman**

#### Members

#### Areas of expertise

Dr	Keshwar	Baboolal	Risk Assessment Manager/Communicator
Professor	Peter	Braude	IVF/Fertility/Stem Cell Specialist
Professor	John	Cairns	Health Economist
Professor	John	Dark	Solid Organ Transplant Surgeon
Professor	Ian	Franklin	Medical Director from Blood Services
Dr	George	Galea	Blood/Transplant Service Manager
Mrs	Catherine	Howell	Nurse
Professor	Deirdre	Kelly	Physician
Dr	Eithne	MacMahon	Microbiologist/Bacteriologist/Virologist
Mr	Elwyn	Nicol	Patient Representative
Dr	Tyrone	Pitt	Microbiologist/Bacteriologist/Virologist
Dr	Michael	Potter	Haematologist
Professor	Richard	Tedder	Microbiologist/Bacteriologist/Virologist
Professor	Marc	Turner	Haematologist
Dr	Hester	Ward	CJD Expert
Dr	Anthony	Warrens	Immunologist

#### Observers

Mr	Nigel	Goulding	The Medicines and Healthcare products Regulatory Authority
Dr	Sara	Hayes	Welsh Assembly – Department of Public Health
Dr	Aileen	Keel	Scottish Government – Chief Medical Officer Directorate
Ms	Triona	Norman	DH
Mr	Will	Scott	Scottish Government – Chief Medical Officer Directorate
Ms	Imogen	Swann	Human Tissue Authority (HTA)
Dr	Lorna	Williamson	UK Forum

#### Secretariat

Mr	Konrad	Borowski	DH
Dr	Rebecca	Cardigan	DH/NHS Blood & Transplant
Mr	Ben	Cole	DH
Mr	William	Connon	DH

#### Others

Dr	Sonya	Crowe	DH
Mr	Stephen	Dobra	DH
Mr	Peter	Grimley	SEAC secretary
Mr	John	Henderson	DH
Dr	Rowenna	Jecock	DH

**Item 1: Welcome, introductions and apologies**

- 1.1 The Chairman thanked members for attending. Apologies had been received from Dr Harpreet Kohli (member), Professor Hamish Simpson (member), Dr Elizabeth Mitchell (Northern Ireland observer), Dr Susanne Ludgate (MHRA observer).
- 1.2 The following were welcomed to their first meeting: Professor Peter Braude (member), Professor Deirdre Kelly (member); Mr Ben Cole (DH SaBTO secretariat), Mr Nigel Goulding (MHRA), Dr Sonya Crowe (DH), Mr John Henderson (DH) and Mr Will Scott (Scottish observer)

**Item 2: Minutes of the Meeting, 23 January 2008**

- 2.1 The minutes of the meeting held 23<sup>rd</sup> January 2008 were accepted as a true record of the meeting.

**Item 3: Action Points from the Meeting Held 23 January 2008**

- 3.1 A paper listing progress with action points was distributed.
- 3.2 The following were noted:
  - **Action 01/1:** Secretariat to clarify the remit of SaBTO with regard to stem cells.

The secretariat had confirmed that the remit covers the microbiological safety of gametes and all stem cells (not just haematopoietic cells).

The committee agreed that the remit should now read:

“The Committee will advise Ministers of the UK Government and the Devolved Administrations as well as UK Health Departments on the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion / transplantation. Its remit includes providing independent advice on: the microbiological safety of gametes and stem cells, in liaison with the relevant regulatory authorities; risk management options for Ministers and UK Health Departments to consider.”

- **Action 01/2:** Secretariat to update the website, notify members of key journal papers, investigate a members only area of the website

The chairman asked members to send any relevant papers to the secretariat who would disseminate to the committee where appropriate. A members' only area of the website has been investigated; the secretariat is awaiting new IT software before this can be progressed further.

- **Action 01/4:** Public summary of SaBTO meetings

The committee agreed that the Chairman would agree the content of the public summary with the secretariat to expedite it being made available on the SaBTO website. A copy of the summary will be distributed to members with the draft minutes of the meeting.

- **Action 01/5: Public access to SaBTO website**

The secretariat confirmed that a mail box has been set up on the website which can be used by the public to email queries to the secretariat. This will be checked on a regular basis and the secretariat has already received questions via this mechanism.

- **Action 01/7:** Secretariat, in cooperation with SaBTO members, to explore opportunities to raise the profile of SaBTO.

The chairman took part in an interview for an article to be published in the Sunday Herald newspaper. The secretariat and Chairman are preparing an article on the work of SaBTO for both Blood Matters and Transfusion Medicine.

- **Action 01/8:** Secretariat to organise a review of the interaction with other relevant committees.

A review has been initiated and a further update will be provided at the July meeting.

- **Action 01/9: Outstanding items from MSBTO Bone & Tissues sub group**

Dr Galea reported that a draft report had been circulated to members of the sub-group for review. Dr Galea will produce a report for the July meeting of SaBTO outlining outstanding issues from the MSBTO Bone and Tissue Sub-Group.

- **Action 01/10:** Secretariat to draw up a work plan, based on the committee's recommendations, and circulate it for comment before the next meeting in April.

The work plan was circulated with the minutes of the previous meeting and was agreed by the committee. The secretariat will now post the work plan on the SaBTO website.

- **Action 01/11: Chairman and secretariat** to identify those committee members best placed to progress the updating of the existing MSBT Guidance on the Microbiological Safety of Human Organs, Tissues and Cells used in Transplantation.

Members were asked to volunteer to serve on the sub-group to work with Triona Norman (DH) to take this forward. The following members

expressed an interest in being part of this group: Professor John Dark, Dr George Galea, Dr Eithne McMahon, Dr Tyrone Pitt and Dr Michael Potter. Triona Norman will contact members to take this work forward. The sub-group may co-opt additional experience from outside of SaBTO if necessary.

#### **Item 4: A Safety Evaluation Framework for SaBTO**

- 4.1 The Chairman thanked the members of the working group who had helped draft the paper for this item: Professor John Cairns (SaBTO lead), Mr Stephen Dobra (DH lead), Professor Ian Franklin, Mr Elwyn Nicol, Dr Kesh Baboolal, Mr John Henderson (DH economist) and Dr Janet Gibson. The chairman also thanked Dr Cees van der Poel (Sanquin, Netherlands) for his contribution to the working group.
- 4.2 Professor Cairns gave a presentation summarising the key points from the discussion paper that was circulated to the committee.
- 4.3 The purpose of the framework is to provide a transparent and consistent process to assess possible options for mitigating a given hazard. It will allow SaBTO to make recommendations on safety initiatives in the context of other decisions, and to be explicit about the assumptions that are used in reaching a conclusion. The framework will enable SaBTO to prioritise safety initiatives to make the best use of limited resources, and to take account of sufficiency and efficacy as well as safety. The framework presented was developed for The National Blood Service and adopted by the Advisory Committee on the Microbiological Safety of Blood, Tissues and Organs (MSBTO). It provides information on a range of factors, one of which is an economic or 'value for money' score. The weight attached to a given factor may vary depending upon the issue under consideration.
- 4.4 The paper highlighted four possible approaches that SaBTO could use to evaluate safety measures:
  - Cost-effectiveness analysis (as used by NICE), which quantifies the cost of an intervention and also its effectiveness in terms of Quality-Adjusted Life Years (QALYS).
  - Cost-benefit analysis (as used by Department for Transport), which quantifies, where feasible, both the benefits as well as costs in monetary value.
  - Pure "safety" (technological) criteria, where all that is technically feasible should be done to reduce risk to 'as low as reasonably practicable' or 'best available technology not entailing excessive cost'.
  - Hybrid approaches such as those adopted by Health and Safety Executive categorising risk as 'acceptable', 'unacceptable' or 'tolerable'.

4.5 Between the economic approaches the main issue is the extent to which activities should be evaluated as part of the health sector or as part of risk reduction activities within the public sector more broadly. Whatever approach is adopted, a key aspect of the decision-making framework is to ensure there is adequate scope to allow for considerations unique to blood, tissues and organs. The greater the number of special considerations the harder it becomes to ensure consistency in decision-making across the health sector or the public sector more generally. If it is decided that special considerations for either blood, tissues or organs should apply, then it is important to define when these factors are relevant and what weight they will be given.

4.6 The chairman asked the committee to consider:

- Whether the committee endorsed the use of the safety evaluation framework and whether any considerations were missing from the framework.
- What approach should be used to evaluate safety measures.
- What special considerations need to be applied to blood, tissues, organs, gametes and stem cells.

4.7 During the discussion the following points were made:

- The public perception of benefit that may be gained by the use of new drugs/treatments (e.g. by NICE), may be different to considering interventions to reduce the risk of harm to recipients (by SaBTO).
- The benefit of any safety intervention may be different for different groups of recipients and what may be regarded as an acceptable level of risk for one group may not be acceptable for another. For example, recipients of haemopoietic stem cell transplants might be willing to accept a different level of risk than those receiving a blood transfusion. Whilst it was noted that the framework would be able to accommodate such variation, brief discussion ensued on a separate issue, namely that of communication to patients of the risks associated with transfusion. Several members felt that current practices could be improved for informing recipients of such risks, and gaining their written consent.

**Action 02/01:** Secretariat to: obtain the status of work done to date on consent by NHSBT's Appropriate Use Group (via Catherine Howell) and the secretariat to bring this back to the committee at a future date for further consideration.

- It is also important to consider the number of recipients treated from an individual donor, which might be quite different for blood, tissues or organs. It was noted that this had been factored into the

framework on risk-reduction options for vCJD transmission by blood components.

- That there may be limitations in the accuracy of data in relation to estimating the level of risk.
- The framework should consider the impact on donors as well as recipients
- In addition to considering risk to recipients, the framework should consider how interventions might have a wider role in protecting public health.

4.8 In summary:

- The committee agreed in principle that the framework would be a useful tool for SaBTO to use in evaluating safety initiatives
- It was noted that the framework could be applied to tissues, organs, stem cells and gametes in addition to blood. However, some considerations used in the framework may be unique to each speciality.
- Having considered the advantages/disadvantages of the options for evaluating safety initiatives, the committee agreed in principle that a cost-effectiveness approach would be suitable, providing that they were able to take account of wider factors other than measures of 'value for money'. These may include some that are unique to blood, tissues, organs, stem cells and gametes.

4.9 The chairman asked the committee to forward any further comments on the Safety Evaluation Framework to the secretariat, and to highlight any special considerations that should apply to blood, tissues, organs, gametes and stem cells that were not listed in the paper.

**Action 02/02: Members** to forward any further comments on the Safety Evaluation Framework to the secretariat, and to highlight any special considerations that should apply to blood, tissues, organs, gametes and stem cells that were not listed in the paper

#### **Item 5i: vCJD - Possible Risk Management Strategies**

- 5.1 The Chairman thanked the members of the working group who had drafted the discussion papers for this item: Professor Marc Turner (SaBTO lead), Dr Hester Ward, Dr Lorna Williamson, Dr Rowena Jecock (DH lead), Dr Rebecca Cardigan, Dr Sonya Crowe, Mr Stephen Dobra.
- 5.2 A two-part paper was provided. The paper only considered blood components and explicitly excluded plasma products, tissues, organs

and stem cells. MSBTO had previously provided guidance on reducing the risk of vCJD transmission by tissues and organs.

- 5.3 The first paper covered an introduction to prion biology relevant to the transmissibility of vCJD via blood, current measures in place to reduce the potential risk from blood components and the assumptions that were used in developing scenarios against which potential further options to reduce risk are assessed. The second paper described the evaluation processes for prion reduction technology and vCJD screening tests. The paper then set out a series of possible options for further risk reduction, (including prion reduction filters and screening tests), together with commentary on their respective merits/drawbacks, and provided current best estimates of their cost-effectiveness.
- 5.4 Professor Turner summarised the key points covered in two discussion papers that were circulated to the committee.
- 5.5 There is now convincing evidence of human to human transmission of vCJD via blood transfusion with 3 clinical cases of the disease and one of sub-clinical infection believed to have been transmitted via this route. However, in humans little is known about the level, distribution and temporal development of infectivity in blood. Estimates of prevalence of asymptomatic infection in the UK population remain uncertain, as does the susceptibility of recipients to infection.
- 5.6 To assess the cost-effectiveness of future measures to reduce the risk of vCJD by blood components 8 scenarios relating to prevalence, susceptibility and infectivity were modelled: a prevalence of 1:20,000 (LOW) and 1:4000 (HIGH), infectivity of 0.1 ID/ml (LOW) and 30 ID/ml (HIGH), and susceptibility of recipients to development of clinical disease of 10% (LOW) and 100% (HIGH). It was noted that the high susceptibility scenario is not consistent with the observed number of clinical cases. It was noted that SEAC reviewed data available to date from The National Anonymised Tonsil Archive (NATA) Study at their meeting on 25<sup>th</sup> April 2008 and has not revised its estimate of prevalence of sub-clinical infection as a result.
- 5.7 The committee noted that a number of risk reduction measures had already been implemented on a precautionary basis. The paper presented a number of further options for consideration:
- Plasma components: extending the importation of plasma from a low risk country to all recipients (currently already in place for recipients <16 years old.); alternatives to the use of cryoprecipitate.
  - Red cell components: reducing the plasma content by choice of whole blood processing method; prion filtration; double dose red cell to the same recipient ; importation of red cells from a low risk country.

- For platelets: increasing the % of platelets collected by apheresis; use of platelet additive solutions to store platelets.
  - Options applicable to all components: screening tests; reducing inappropriate use of blood components; selection of donors that have not been exposed to BSE through diet (e.g. those resident outside the UK 1980 – 1996).
- 5.8 For some options consideration was given to implementation for recipients <16 years old as well as all recipients.
- 5.9 The chairman asked the committee to consider:
- Whether there is a need for further risk management measures to reduce the risk of secondary transmission of vCJD via blood components, taking account of current scientific knowledge and uncertainty.
  - Of the further options for risk management, which, if any, should be examined in more detail/considered for implementation, and whether any options should not be pursued further at this stage.
- 5.10 During discussion the following points were noted:
- There is discrepancy between estimates of prevalence and numbers of clinical cases. This may be because prevalence is lower than anticipated, or that due to the long incubation period of disease and genetic factors influencing host susceptibility that the clinical cases have not yet been observed.
  - It is likely that uncertainty around the level of prevalence will remain for some years.
  - vCJD is a unique disease that has thrown up unexpected challenges in the past and therefore a continuing precautionary approach to risk reduction may be prudent.
  - The estimated cost effectiveness of the risk reduction options is greatly influenced by the level of prevalence and recipient susceptibility modelled. For some options involving processing methods the assumptions about the level of infectivity also significantly affect the cost-effectiveness estimates.
  - There may be merit in considering implementing options for recipients <16 since these recipients have a long life expectancy following transfusion and some of these recipients will not have been exposed to BSE through food.
  - The committee supported the work being undertaken on appropriate use of blood components with initiatives such as Better Blood Transfusion 3. It was noted that there may be

opportunities to reduce cryoprecipitate usage as part of these initiatives. Members re-iterated their earlier view that further work was needed to ensure that blood recipients are better informed of the risks of transfusion

- There was considerable concern about the use of screening test(s) in the absence of a confirmatory test, since false positive results would have an impact on the blood supply, individual donors (potential negative impact on employment, insurance and financial factors as well as psychological) and wider public health.
- Prion filtration would not have an impact on individual donors but further data on clinical safety would be required prior to being able to make any recommendations on its use. Obtaining definitive data in humans with respect to efficacy of prion filtration is not possible, and data from animal models is therefore the best that can be achieved. It is important to understand what potential harm may be associated with any new technology and these concerns are being addressed by clinical studies underway in the UK. Further data would become available from post-marketing surveillance if Ireland implement this technology.

5.11 In summary:

- Continued effort to reduce inappropriate use of blood components is important for many reasons, including vCJD risk reduction. Future appropriate use initiatives could helpfully include alternatives to cryoprecipitate.

5.12 The option to use of platelet additive solution should not explored in any more detail because even under the most optimistic infectivity concentration assumptions it is not effective in reducing the risk of transmission because of the amount of plasma remaining in the platelet concentrate.

5.13 Further consideration of the options would be needed to enable clear recommendations to be made.

5.14 There was interest in considering the pros/cons of combinations of options in addition to individual options.

**Action 02/03: the secretariat** to work with policy colleagues to produce a revised paper for the July meeting. This will contain option appraisals, and recommendations for the committee, which reflect the discussions listed in 5.10 above.

**Item 5ii. Plans For Open Meeting On vCJD**

5.15 A short paper, reflecting the basic arrangements for the open meeting in October was tabled and noted. The content of the meeting would be developed further for the July meeting.

**Action 02/04: Members** to submit any comments on the paper to the secretariat by 16<sup>th</sup> June.

**Item 6: Any Other Business**

**Correspondence from UK Forum**

6.1 The UK Forum had raised the issue of who “owned” the policy on blood donation with respect to men having sex with men and when a review might happen? It was reported that DH, and ultimately Ministers, were the “owners” of this policy which in line with all policies is regularly reviewed. The policy would be reviewed if, for example, new data become available. There are no specific plans to review the policy at present.

6.2 The chairman asked members to raise items of any other business with the secretariat prior to committee meetings. Where possible these would be dealt with outside of the main committee meeting. All matters for the committees consideration should be submitted to the secretariat for consideration by the chairman before distribution to members.

**Item 7: Date of next meetings**

7.1 15 July & 21 October 2008, 20 January 2009