

Minutes

XXVIIIth Meeting of the Biomedical Excellence for Safer Transfusion Collaborative

Edinburgh, Scotland

July 9-10, 2004

These minutes represent presentations and discussions at the BEST meeting on July 10 as well as a synopsis of the team meetings held immediately before. They include some detail and discussions that occurred only in the team meetings in order to provide all members with as much information as possible about past and planned studies. Additional details can be obtained from the leader of each team, who prepared the summary of the team's activity given below, often with assistance from presenters.

Jim AuBuchon opened the meeting with a welcome to all attendees. First-time attendees were introduced, and a special welcome was extended to Ray Goodrich as the representative of BEST's newest manufacturer member, Navigant Biotechnologies.

Scott Murphy presented a financial report. He briefly reviewed the resources available as detailed in the BEST book and noted that BEST remained in a sound financial position.

AuBuchon reviewed the current status of the organization's structure. The BEST Collaborative has now been incorporated as a not-for-profit corporation in the State of New Hampshire. The Bylaws accepted at the Bermuda meeting (and included in the BEST book for the Edinburgh meeting) are the way in which BEST will be operated, but changes in these are, of course, possible, as needed. He noted that the Executive Committee is now defined as the team leaders of each team plus the treasurer (past chair) and the chair. He again thanked P. Rebulla, S. Slichter and C Smit Sibinga for their contributions to the leadership of BEST over their years on the Executive Committee.

AuBuchon then brought the group up to date on a meeting held the previous morning between the Executive Committee and the leadership of the ISBT to discuss the letter that had been sent to ISBT in late February. This letter (copy in the book) had offered: Continued assistance with the organization of congresses and participation as speakers; Co-location of BEST meetings with congresses whenever feasible; Dissemination of information about BEST through placement of team meeting minutes in Transfusion Today; Continued consideration of submission of manuscripts to Vox Sanguinis; Solicitation of applications for the next round of membership through Transfusion Today and the ISBT website; Provision of advice through ad hoc or scientific advisory committees as requested. The ISBT leadership stated that they would need to consider how BEST would interact with ISBT in the future and whether ISBT needed its own scientific presence and productivity. BEST members reiterated that "BEST hadn't gone anywhere" and that BEST was willing to be as involved in ISBT as ISBT wished. The "separation" had been solely for the purpose of preserving control over BEST resources and direction and not because of ideological differences. The potential for a re-affiliation with ISBT at some point in the future was also mentioned.

AuBuchon then presented several designs for a BEST logo. The group's preference was for the word "BEST" accompanied by a red blood drop showing a double helix all set over a stylized globe.

P. Rebulla rose to present several ideas. The first was to create an official means of recognizing the important assistance of colleagues and staff in the execution of BEST studies where their inclusion in manuscripts as authors was not appropriate nor feasible. He suggested, and the group wholeheartedly endorsed, that such individuals be given a certificate of participation, suitable for framing, to document their contributions. AuBuchon asked that each study leader gather the names and addresses of those who should be recognized at the completion of each study and he would see that the certificates were prepared and delivered.

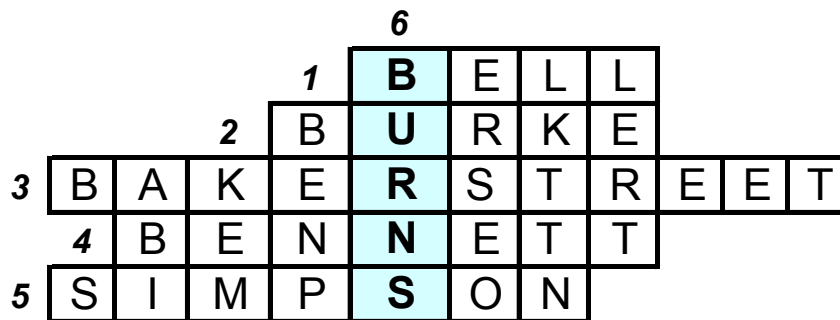
The other suggestion was that presenters be encouraged to provide their Powerpoint presentations to all members of BEST. This would allow review and capture of important data without participants having to take rapid and copious notes at the meeting. The caveat was offered that these presentations would not be used for commercial or comparative purposes. AuBuchon suggested that the presentations could be sent to him; he would convert

them to pdf files and, with appropriate attribution, distribute them to all members. This submission for distribution would, of course, be voluntary. The group supported this idea.

Future meetings were also discussed briefly. The next meeting, BEST XXIX, will be in Rome, March 11 and 12, 2005. Team meetings will commence on the afternoon of March 11 and continue the morning of March 12. The BEST meeting will be the afternoon of March 12, and the BEST dinner the evening of March 11. Details will be distributed shortly. BEST XXX will be held in conjunction with the AABB Annual Meeting in Seattle, Washington, October, 2005. BEST XXXI will be in the spring of 2006, and BEST XXXII will be held in conjunction with the next ISBT congress in Cape Town, South Africa, September, 2006.

The group appreciated the puzzler as prepared and presented by C. Prowse who was so kind as to provide bottles of single malt scotch for two winners (selected from many correct responses).

Puzzler Answer



1. Sir Joseph Bell (1837-1911) was a professor at Edinburgh University Medical School. One of his students was Arthur Conan Doyle who wrote the Sherlock Holmes stories. Sherlock Holmes is said to be modelled on Sir Joseph Bell.
2. William Burke (1792-1828), together with his partner in crime William Hare procured bodies for Professor Knox for anatomical dissection at the medical school. Rather than rob graves they found it easier to murder neighbours in the Grassmarket slums, one of whom was known as Daft Jamie (victim 14). They were discovered because they had hidden the body of their 16th and last victim under a bed, which was discovered by an Irish lodger. Hare turned King's evidence and was freed but Burke was publicly executed in 1828 and his body subjected to a public dissection by Professor Munro. His skeleton is in the museum of the College of Surgeons. Professor Robert Knox (1791-1862) was cleared of involvement, although the investigating committee said he had acted incautiously in accepting the bodies without making enquiries. A further outcome was the passing of the Anatomy Act in 1832. Those who used Google to find this answer may like to know that Jack Gillon, who wrote the article you probably came across, is a medical consultant in the Scottish Transfusion service.
3. Baker Street – superb opening saxophone riff in Gerry Rafferty's original recording. 221B was the fictional residence of Sherlock Holmes, invented by Arthur Conan Doyle.
4. John Hughes Bennett (1812-1870) is acknowledged as the first to describe leukaemia in a paper published in 1845 " (Edinburgh Medical and Surgical Journal (1845), 64, 413-423)", just beating Virchow – who acknowledged this. Bennett preferred the term leucocythemia to that of leukaemia. (Conan-Doyle published in The Lancet on leukaemia)
5. Sir James Young Simpson (1811-1870) is credited with developing chloroform as an anaesthetic, as an alternative to the rather explosive ether. This was made possible by the

availability of a method developed by a local chemist, David Waldie, that yielded a purer preparation of chloroform. Following its adoption by Queen Victoria for the birth of Prince Leopold it gained widespread use. He was President of the Royal College of Physicians of Edinburgh in 1849. The frolics refer to parties at involving inhalation of ether and similar substances – all the rage in the day.

6. The picture shows a Russian stamp from 1956 of the poet Robert Burns (1759-1796), born in Dumfriesshire, but one of the leading lights of the Scottish Enlightenment scene in Edinburgh. Worked at times for the Customs. Lot of lady friends.
7. Tie break: Simpson's father was a baker (but not from Baker Street).

Report: Transfusion Safety Team

S. Dzik, M. Murphy

The Transfusion Safety Team was well attended and went through a full agenda.

1. Membership Survey:

Sunny Dzik and Michael Murphy hosted the session. Sunny began by reviewing results of the member survey conducted in June 2004 in collaboration with the Components Team. The survey explored future topics of interest to the team. The survey identified the following topics of research interest:

- * PROBE Study
- * Use of RFID technology on blood bags
- * Descriptions of different systems of blood utilization review
- * Review of the Canadian Consensus Conference on TRALI
- * Standardized definitions of transfusion reactions
- * Number of units used in specific medical conditions
- * Effect of blood storage on RBC efficacy
- * Triggers for transfusion of routine components
- * Contraindications to the use of blood products
- * Refining data on the clinical benefit of FFP
- * Logistics of supply versus demand of blood esp in developing nations
- * Distinguishing platelet consumption from alloimmune destruction

Next Steps:

1. Initiation of the PROBE study and the bacterial detection survey.
2. Develop background for future projects taken from the members list

2. Effect of Blood Storage on Clinical Outcomes:

Paul Hebert (Associate Scientific Member, Canada) presented an invited mini-review of the clinical studies that have been done on the effect of refrigerated blood storage on clinical outcomes. Pre-clinical studies have documented that the storage lesion of RBCs results in metabolic and structural defects expected to impair oxygen delivery to critical tissues. However, clinical studies on the effect of RBC storage have been few and generally of insufficient statistical power. Heterogeneity of the study population has been a weakness of some studies. More importantly, most clinical studies have assigned patients to “overlapping” storage age groups without clear separation of short-storage versus long-storage groups. Hebert summarized the attributes of an effective clinical study on the topic of storage age. Such a clinical study should focus on a population at risk for oxygen debt (such as intensive care unit patients, coronary-care unit patients, or trauma patients). The group should receive a large volume of blood components. In addition, the population should be “at risk” for adverse events. Each of these considerations suggest that trauma patients would be an informative population. The study's intervention would be the randomization of recipients to young RBCs versus old RBCs. The clinical equipoise required for such randomization needs to be explicitly stated in order for Institutional Review Board oversight of such a

clinical trial. Most importantly, endpoints (outcomes) of the trial are among the most difficult aspects of a well-designed investigation of the storage effect on transfusion. Endpoints might include surrogate markers of ischemia-- lactate, mixed venous oxygen content, clinical evidence of ischemia (eg, angina). Other outcomes would include morbidity scores, development of multiorgan failure, and all cause 30 day mortality.

Next steps:

Dr Hebert will be developing a potential clinical trial to be conducted in Canada. He may be asked to update the BEST group on progress on this trial at a future meeting.

3. PROBE Study

M Murphy presented an update on the proposed project 'Prevention of Bedside Errors (PROBE)' study. This study aims to assess the effect of a simple intervention (a label attached to the blood bag directing the user to check the patient's wristband, and also to determine the durability of any effect. He proposed that the trial design should control for any initial effect of the observer in practice by introducing the intervention in both the clinical area randomised to receiving the intervention and the control area after a period of baseline observations in both clinical areas. The endpoint will be a composite of essential bedside checks. The aim is to detect a reduction in failure risk of bedside checking extracted from previous studies to be 25% to 50%. The variation between patients in each clinical area (cluster) in the study results in more uncertainty of results compared to a randomised controlled trial (where individual patients rather than individual clinical areas are randomised). The sample size for this 'cluster' randomised controlled trial with 10 patients/cluster is estimated to be $135/\text{arm} = 270$ patients. This means that >14 hospitals (2 clusters/hospital = 20 patients) will be needed to reach this number.

Comments included:-

- 1) avoidance of nursing staff carrying out bedside checks in both the intervention and control areas within a hospital, or more than 2/10 bedside checks in each audit section of the study. These will be included in the protocol, and will require recording the initials of the nurse carrying out each bedside check in the protocol;
- 2) record the nursing experience of each nurse carrying out bedside checking;
- 3) record the time as well as the date of each transfusion;
- 4) provide 'Instructions for Observers', and a standard information letter to inform the Head Nurse in each participating hospital about the study.

Next steps:

Murphy agreed to prepare a more detailed study protocol and circulate this to potential participants by the end of October with the intention of beginning the study early in 2005.

Potential participants include:- Murphy, England (4 sites); Dzik, Shulman, Aubuchon, Reed, Sacher, Slichter, Popovsky, Toy, USA (8 sites); Shimuzu, Japan (1 site); Olsson, Sweden (1 site); Heddle, Devine, Hebert, Canada (3 sites); Cazenave, Andreu, France (2 sites); Prowse, Scotland (1 site); Lozano, Spain (1 site); Rebullia, Italy (1 site); Wendel, Brazil (1 site).

4. Survey of Methods Used for Bacterial Testing

Chris Prowse (Scotland) presented a short survey instrument to collect information on the current approach to screening blood components for bacterial contamination. This study is being organized in collaboration with the ISBT Working Party on Transfusion-transmitted Diseases. Sunny Dzik urged members of the Safety Team to "take the survey for a test run" and send Chris Prowse comments for improvement. Chris will review team responses and expects to make final refinements prior to "locking" the version of the survey and distributing it to members in early autumn. Once the survey is distributed, all members are urged to complete the survey and report their findings to Dr Prowse.

Next steps: Chris Prowse will distribute in Sept / October a final version of the survey to all BEST members.

5. Statistical Process Control applied to patient sample collection and labeling:

Neil Beckman (UK) presented an approach his group is exploring to apply standard principles of Statistical Process Control (SPC) to the topic of patient samples and their labeling. He pointed out that the development of a practical method for monitoring the sample collection process was a natural outgrowth of the BEST Collaborative COBS Study. Working with data from two hospitals in Oxford and Birmingham, Beckman established baseline rates of mis-labeled samples and then applied standard SPC principles. On going sample tracking can then be applied to detect “in real time” the development of problems in the sample collection process. The details of how to apply SPC to sample collection are the main focus of the group and may lead to a practical recommendation for laboratories everywhere on tracking the performance of sample collection.

In the Discussion that followed, Neil Beckman was asked to consider two additional points: 1) For low-incidence events (like WBIT samples) did the standard rules of “control charts” apply for detection of process failure ? and 2) A formal analysis to select the best “set of rules” for defining process failure would be of interest.

Next steps: Neil Beckman will continue to develop the technique and report on progress at the next meeting. BEST would be well constituted for validating any technique developed.

6. Canadian Consensus Conference on TRALI

Sunny Dzik reviewed a draft version of the committee report of the Canadian Consensus Conference on TRALI—kindly provided by Steve Kleinman, chair of the Committee. The BEST Collaborative was one of the sponsors of the meeting and many BEST members attended. There was lively discussion on the Committee’s report especially focused on the definition of TRALI and “possible TRALI”. The BEST Transfusion Safety Committee members at the meeting expressed the viewpoint that the definition of “possible TRALI” was sufficiently broad that the following two comments were raised:

A) It was recommended that the document explicitly state that the definition of “Possible TRALI” should not be used for the purpose of donor deferrals. Because many donors could be implicated using the Canadian definition of “possible TRALI”, deferrals based on this definition might jeopardize the blood supply.

B) It was recommended that the document explicitly state that the definition of “Possible TRALI” should not be used in setting regulatory policy or professional Standards. As a result of the broad definition, many clinical cases could be labeled as “Possible TRALI”. If regulatory or professional standards which required specific investigation, reporting, or additional evaluation / treatment were applied to cases meeting the definition of “Possible TRALI”, then an excess of effort may be applied without productive gain and detract from focus on more serious flaws in the transfusion process.

C) “Possible TRALI” should be “optional” for use in hemovigilance programs. Hemovigilance programs may wish to use (or NOT use) the “Possible TRALI” definition. In favor of its use is the tracking of cases that might include actual TRALI. Against its use might be concern that too liberal a definition of TRALI might “swamp” the reporting and skew results in a mis-leading direction. Each hemovigilance program should be allowed to decide how to address the “Possible TRALI” category.

D) The document may wish to emphasize that the category of “Possible TRALI” should prove most valuable for epidemiologic and clinical research studies on adverse transfusion events. This goal is a valuable one but is very distinct from regulatory issues and donor deferrals.

Next steps:

Initially, it was felt that the work product of the Canadian Committee might be made available to the BEST membership for “approval and endorsement”. However, with more discussion, it became clear that the logistics of distribution, review and incorporation of BEST comments would slow the process by which the Canadian Conference results are publicly presented.

Dr Dzik would verbally report to Dr Kleinman the discussion points that emerged during the BEST meeting and suggest that Dr Kleinman is very welcome (but not required) to send a pre-publication of the Canadian Report to individual BEST members for a private reading and critique. No formal endorsement of the Canadian Report

would be done by the BEST Collaborative as this would only slow down the process for the Consensus Committee.

7. New Members for the Transfusion Safety Team:

The meeting closed with a review of possible candidates for membership on the Transfusion Safety Team. Individuals in mid-career who work in hospital transfusion medicine would be expected to be particularly suitable for the team.

Next steps: Membership is open to any individual. Interested parties should contact either Dr Murphy or Dr Dzik.

Report: Conventional Components Team

H. Gulliksson, J. Hess

Gulliksson welcomed the team and opened the meeting of the Conventional Components Team by presenting the agenda and a list of present manuscripts for publication from the Conventional Components Team.

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| BEST study #20 | <p><i>Interruption of agitation of platelet concentrates: Effects on in vitro parameters.</i></p> <p>Pieter van der Meer, Hans Gulliksson, James P AuBuchon, Chris Prowse, Ekkehard Richter, Janny de Wildt-Eggen, for the Biomedical Excellence for Safer Transfusion Collaborative.</p> <p>Status: Manuscript for publication in the Edinburgh book.</p> |
| BEST study #21 | <p>Platelet Storage Solution Effects on the Accuracy of Laboratory Tests for Platelet Function – A Multi-Laboratory Study.</p> <p>Tania VandenBroeke, Larry J Dumont, Susie Hunter, Janice Nixon, Scott Murphy, Jill Roger, Louise Herschel, James P AuBuchon, Hans Gulliksson, Thomas Dengler, Valerie Hornsey, Chris Prowse, for the Biomedical Excellence for Safer Transfusion Collaborative.</p> <p>Status: Published in Vox Sanguinis (2004) 86, 183-188.</p> |
| BEST study #26 | <p>Measuring red cell ATP, DPG, and hemolysis: The BEST #26 study.</p> <p>John R Hess and Loni R Kagen for the Biomedical Excellence for Safer Transfusion Collaborative and the U.S. Red Cell Focus Group.</p> <p>Status: Manuscript for publication in the Edinburgh book.</p> |

BEST #24 study. Interruption of agitation of platelet concentrates: Effects of shipping on platelet function and biochemical analyses. Multi-center in vitro study.

Gulliksson presented the design of the BEST #24 study and preliminary in vitro data from three different laboratories. Data from four additional laboratories will complete the study.

General background: 1) Platelet concentrates (PC) are sometimes transported in platelet storage containers for at least 24 hours, in particular in America; 2) the effects of transportation are not adequately known; 3) the principal effects are expected to be metabolic and can be monitored by conventional platelet in vitro studies.

Study design: 1) preparation either by apheresis, from PRP or from buffy coat; 2) leukocyte depletion pre storage; 3) storage in plasma; 4) primary pools for splitting in four PC (A and B: test unit containing either about 1000×10^9 platelets/l (A) or 2000×10^9 platelets/l (B); C and D: reference unit containing either about 1000×10^9 platelets/l (C) or 2000×10^9 platelets/l (D) and continuous agitation for 7 days); 5) agitation of test units (A and B) interrupted during transportation for about 24 hours but not more than 48 hours; 6) in vitro testing for biochemical and functional parameters; 7) the temperature in shipping boxes should be monitored during transportation.

Preliminary results suggest slightly but significantly higher lactate concentrations and p-selectin levels and significantly lower glucose concentrations, pH, ATP and ESC levels in transported (test) PC than in continuously agitated (reference) PC.

BEST #20 study. Interruption of agitation of platelet concentrates: Effects on in vitro parameters.

Van der Meer briefly concluded the results of the BEST #20 study. The results are summarized in a manuscript for publication in the Edinburgh book. Van der Meer showed, after analysing results from all 6 participating centres, that platelet concentrates in PASIIM, with a platelet concentration of about 1×10^9 /mL, can be kept for up to 4 days without agitation, with maintenance of acceptable pH and HSR levels. Composol, a solution lacking phosphate, gave low pH and HSR values under all conditions of interruption. However, reference units gave results similar to those of PAS-IIM. An abstract was submitted to the AABB meeting. The manuscript, after including comments from the group, will be submitted to Vox Sanguinis for publication. This is due in August.

The BEST platelet questionnaire, platelet fixation study and platelet send-around study.

At the Bermuda meeting, the Clinical Studies team showed results of a platelet counting send-around study, with different results between the 5 participating centres. It was agreed that the group should look into this matter. Van der Meer presented some of Moroff's earlier work to the group, indicating that the use of non-human fixed platelet preparations gave varying results when used in different analysers, and thus making it difficult to establish a 'true' platelet value. Human fixed platelets should be used to calibrate analysers and human platelets should be used in future send-around studies between labs as well.

Cardigan explained in more detail their experiments to find a stable human platelet fixation procedure. Paraformaldehyde (PFA) was used to fix platelets. They found that the presence of EDTA is necessary to prevent clumping. Although the fixation using 1% PFA on 5- to 6-day stored platelets seemed successful, the analyser used for platelet counting also influenced the final results. Another experiment using fresh platelets showed that unfixed platelet counts were stable for up to 3 days. Experiments using the commercially available CytoChex gave good results, but the relatively high dilution factor (1/5 to 1/10) resulted in fixed samples with reduced absolute platelet counts.

To understand in more detail the currently used procedures for platelet sampling and counting, De Wildt-Eggen and Van der Meer designed a questionnaire, which was discussed in detail. The questionnaire will be distributed amongst BEST labs in August.

For the send-around study, a proposition was presented for the types of samples (patient whole blood, platelet concentrates) and the platelet levels in the samples. Once a fixation procedure has been developed, the samples will be shipped to participating centres, hopefully no later than January 2005. The 'gold standard' for platelet counting was briefly discussed, and a flow cytometric counting method should be validated versus a manual method.

This platelet counting study is designated BEST study #35.

Glycolysis in stored platelets - donor and possible CO₂ effects.

Dumont reported on two studies conducted at Gambro, which relate to some of the platelet storage questions being explored by the group. The first study was “Donor Dependent Glycolysis Rates for Platelets Stored in Plasma” (L. Dumont, T. VandenBroeke). Study results were presented evaluating the donor repeatability of lactate production rates for apheresis platelets stored in plasma. Apheresis platelets were collected using Trima. Platelets were collected from 16 donors on two separate visits, and stored in 1L ELP bags at 22°C on a horizontal shaker up to 7 days. Glucose consumption and lactate production rates were calculated as rates normalized to platelet content ($\mu\text{mol}/10\text{E}12 \text{ plt}/\text{hour}$). There was a high correlation between repeat products from the same donor (intra-class correlation coefficient, $\rho=0.826$). Lactate generation rates from 154 unique donors were fit to a gamma distribution from which we estimate 10% of donors have a basal rate greater than $65 \mu\text{mol}/10\text{E}12\text{plt}/\text{hr}$ in the ELP storage system. The basal rates of lactic acid generation are highly correlated with donor. This may explain previous observations of some donors’ platelets not storing well.

An hypothesis was presented that CO₂ level down regulates flux through the Krebs’ cycle by non-competitive inhibition of rate limiting enzymes in the cycle. This in turn results in upregulation of glycolytic rates in stored platelets. (“Possible Role of CO₂ in Upregulation of Glycolysis During Platelet Storage” L. Dumont, A. Smart, J. Rice, T. VandenBroeke). Preliminary data was presented using apheresis platelets stored in a paired manner in standard 1L ELP storage bag (Control) and a modified bag with lower average gas permeability (Test). Glycolytic rates established over the first day of storage were consistently maintained for all products over storage. Reduction of gas exchange rate for platelet storage bags results in retention of CO₂, reduction in pH, and increased glycolytic rates in Test products. The increased utilization of glucose is not explained by O₂ starvation. CO₂ may be acting to inhibit rate limiting decarboxylating enzymes in the mitochondria, directly slowing down oxidative phosphorylation, and indirectly upregulating glycolysis. This potential effect is confounded in this study with changes in pH, although the inverse relationship between pH and glycolytic rate is inconsistent with other literature reports. This group will continue to work on this metabolic question related to platelet storage.

Documenting platelet efficacy II: Standardized radiolabeling protocol.

AuBuchon presented a brief review of the May 3 meeting convened by the FDA, Use of Radiolabeled Platelets for Assessment of in Vivo Viability of Platelet Products. All of the presenters at this meeting were BEST members, and BEST’s preliminary work had much to do with the meeting’s success. The meeting’s expert panel endorsed the application of the approach proposed by S. Murphy that the recovery and survival of stored/treated platelets be compared to fresh platelets when radiolabeled and reinfused simultaneously. The consensus had been to collect the fresh platelets via a reproducible, manual (tube) method from the subject on the day of reinfusion of the stored platelets (the last day of their defined storage period).

AuBuchon shared with the group the results of a send-around of data sets to be analyzed by each lab’s COST program. Concern had been raised that local modifications may have affected the output. However, all participating labs (American Red Cross-Norfolk, American Red Cross-Philadelphia, Dartmouth-Hitchcock Medical Center, Gambro BCT, Navigant (via COST and via SAS), Puget Sound Blood Center, and Yale) generated exactly the same results. He also shared the results of a study comparing the use of ⁵¹Cr and ¹¹¹In for radiolabeling 8d old apheresis platelets; the observed recoveries and survivals were not different; Slichter mentioned that early data in her lab using the same method as used by AuBuchon was yielding similar results.

E. Snyder then joined the group by telephone as the group reviewed a draft standard operating procedure for separation of fresh platelets from whole blood and radiolabeling of platelets. Snyder had been leading the work on this effort with assistance from AuBuchon, Dumont, Heaton, Holme, Slichter (and their lab staff) and Pam Whitley of the ARC-Norfolk lab. The discussion clarified several points, and the SOP will be taken to its next version and circulated to the BEST group for comments. It will be placed in a manuscript and submitted for publication as soon as possible to allow all labs to use the same method. The cooperation of the American Red Cross in allowing the Holme and Heaton SOP to be disseminated was acknowledged with appreciation.

Many technical details were not considered in detail at the FDA meeting but were understood as important. The current consensus on these points is as shown below:

Radioactivity dosage: As low as consistent with counting capabilities, usually 10-15 μ Ci/label
Platelet content: Not defined
Labeling environment: ACD-A/saline
Labeling vessel: Tubes, using the method of Holme and Heaton
Blood volume estimation: Mathematical (Nadler)
Sampling times: 2 hr, then daily out to 1 week, omitting weekends, and Day 10
Recovery calculations: Extrapolated, via COST
Recovery curve modeling: Multiple hit
Corrections: Elution before injection, plasma radioactivity and labeling of other elements
Comparison method: Non-inferiority to standard as defined by Murphy's Law
Standard: Test platelets to have \geq 67% of the recovery and 50% the survival of fresh platelets

Measuring red cell ATP, DPG, and hemolysis (BEST #26 study) and follow-up on other RBC activities.

Hess presented the results of the BEST #26 study. This study was a split sample send-around study comparing measurements of RBC ATP, 2,3-DPG, and hemolysis in 14 laboratories representing BEST and the U.S. Red Cell Focus Group. The study was approved at the October 2003 meeting in San Diego, finalized at the Feb 2004 meeting in Bermuda, specimens were mailed from the Blood Center of Southeastern Wisconsin on 15 March 2004, and primary sample processing was accomplished at all centers on 18 March 2004. Sites reported data between early April and late May. Questions raised by the varying modes of data reporting were resolved in late May, and distribution of initial data results and a draft version of the manuscript, version 1a, was sent to all groups in the first week of June. This is the version that appears in the BEST XXVIII book.

With the review of the original data, several groups recalculated their results and reported corrected results along with appropriate explanations of the mathematical errors that led to erroneous results. Also, excellent suggestions for the manuscript were received from Pieter van der Meer, Jim AuBuchon, Tibor Greenwalt, William Lockwood, Pam Whitley & Harry Taylor, Loni Kagen & John Adamson, Rebecca Cardigan, and Claes Hogman.

At the meeting, discussion focused on the size of the differences observed between participating laboratories. The study identified a hierarchy of sources of error: 1) mathematical errors, 2) novel methods, 3) differences between sites representing a lack of shared standards, and 4) fluid handling errors. Discussion centered on the appropriateness of acknowledging mathematical errors, why some methods did not give good results, appropriate standards for calibration of testing systems, and methods to reduce fluid handling in assays.

After the meeting, John Hess collated the comments, rewrote the manuscript, and sent version 3 to all participating investigators on 1 August 2004.

Follow-up on other RBC activities.

The use of tandem mass spectrography was on the agenda, but was not discussed due to lack of time. John Hess has shared his methods with six other members of the BEST at this time and continues to attempt to refine the methods.

Extended or improved RBC storage was not on the agenda for this meeting, but talks are underway with manufactures about commercialization of the EAS-81 8-week normal volume RBC additive solution, which has demonstrated improved recovery and reduced microvesiculation in initial testing as discussed in Oct 2003 in San Diego.

Gulliksson then adjourned the meeting after thanking the members for excellent contributions.

Report: Cellular Therapy Team

G. Moroff, H. Eichler

Participants: BEST Members: A. Brand, S. Coker, H. Eichler, D. Elfath, O. Engelking, J. Hess, R. Kekomaki, N. Kitaguchi, H. Klein, H. Meryman, G. Moroff, D. Pamphilon, D. Paunovic, M. Ras, P. Rebull, W. Reed, J. Reems, R. Sacher, Z. Szczepiorkowski, T. Takahashi, S. Wortham.
Guest: X.D. Nguyen

1. Administrative Issues and Update on Cellular Therapy Team Projects and Manuscripts (Gary Moroff)

Gary Moroff welcomed all participants of the Team Meeting. The summary of the meeting, including plans for study activities to be conducted, will be published in the September issue of *Transfusion Today*. Gary gave an overview of the agenda and current cellular team projects. The study on the preparation of cord blood cells using standard and filter methods, that involved comparative assay studies, has been completed. The manuscript of this BEST Study #15 entitled "Multi-Laboratory Evaluation Of Procedures For Reducing The Volume Of Cord Blood: Influence On Cell Recoveries" has been reviewed by *Vox Sanguinis*, but the revised manuscript will be submitted to *Cytotherapy*. The results of BEST #19 (Study parts A,B,E,F) will be summarized in the manuscript "Multiple Laboratory Comparison Of In Vitro Assays Utilized To Characterize Hematopoietic Cells In Cord Blood". The manuscript is being drafted and will be submitted to *Transfusion*. Gary Moroff suggested to compose a list of authors in alphabetical order naming one principal investigator for each site that participated in at least one exercise. In addition, all technical staff that participated in the BEST #19 exercises will be acknowledged. The two technical staff from the Rockville site will be co-authors because of their major contribution in planning and executing the exercises. The second manuscript from BEST #19 (study part D) entitled "Comparison Of Total Nucleated Cell Measurements Of Umbilical Cord Blood Samples Using Two Hematology Analyzers" has been accepted by *Cytotherapy* in June 2004.

2. Collaboration with International Society of Cellular Therapy (ISCT) (Hermann Eichler)

The results of the discussion during the Dublin meeting on May 8th, 2004 about a possible collaboration between the BEST Cellular Therapy Team and the ISCT were presented. The first suggestion from Lee Buckler, ISCT Executive Director, to share a liaison group for the discussion of regulatory issues with the FDA does not seem to be appropriate. As a first step to provide information about the BEST Collaborative organization to the ISCT membership, it was agreed that an article should be submitted to the *ISCT Newsletter* reviewing the structure of BEST including the activities of the Cellular Therapy Team. For future collaboration, the overall concept is to identify laboratory-based projects that are suitable for a BEST Cellular Therapy Team /ISCT collaboration involving multiple center studies. The discussions indicated that direct contact with leaders of ISCT Committees such as 'Immunotherapy and Dendritic Cells' should be encouraged. Lee Buckler invited BEST to consider the ISCT journal *Cytotherapy* as a medium for publishing BEST study results. It was further considered that the leader of the ISCT subgroup dealing with dendritic cells (Jeff Mollndrem, MD) should be contacted first to discuss a possible collaboration in this field.

3. Quality Control Data for Thawed Cord Blood Samples (Anneke Brand)

Anneke Brand gave an overview on the results of the questionnaire sent out to twenty different cord blood banks asking for recent quality control data on thawed cord blood cells. Six cord blood banks responded and five submitted results that could be used for further evaluation. The cord blood banks performed volume reduction methods by HES or a buffy coat technique prior to freezing. The data collected included cell recovery and viability levels after freezing/thawing. The levels of TNC, CD34+ cells as well as cell viability differed between the centers. The analysis of QC results showed a high level of intra-laboratory variation and a large variation between laboratories. In the following discussion, participants agreed that a cord blood send-around study with identical frozen samples may help to generate more reliable information about the nature of the large variations in QC data of frozen/thawed cord blood samples. It was suggested that NETCORD banks could also be asked to participate in such a study. Anneke Brand mentioned that currently available data from BEST members are not sufficient to draft a full manuscript on this issue, but it was agreed that she should draft a letter to an appropriate journal to convey the overall message. Anneke will also draft a protocol for a send-around study with frozen cord

blood samples. These frozen CB samples could be delivered together with the frozen dendritic cell samples for the planned BEST #28 study.

4. Discussion on the Responses to the Questionnaire on Release Criteria used with Cellular Therapy Products (Ron Sacher)

Ron Sacher presented the results of a questionnaire on release criteria for cellular products including information on more than minimally manipulated cellular products. The questionnaire that was sent out to BEST and FACT laboratories contained 11 narrative questions. 24 of the returned questionnaires could be analyzed (8 by BEST and 17 by FACT). A summary of the results showed a wide variation of the release criteria with very little consistency. It was pointed that the questions themselves might have caused some of the variability since they were only partially specific. More product-specific questions might have helped to get a deeper insight into the current practice at US and European laboratories. For this reason, Ron Sacher will lead a working group consisting of William Reed, Zbigniew Szczepiorkowski and Hermann Eichler to draft a more specific questionnaire. The decision was made that the current results – from responses to the first questionnaire – should be summarized and published in a letter to the editor or a short communication in a recognized scientific journal.

5. Multi Center Study on the Characterization of Dendritic Cell Quality Parameters, BEST #28 (Hermann Eichler)

Dendritic cells (DC) are the most potent antigen-presenting cells, and human clinical trials are ongoing to use these cells for the induction of immunity against different types of cancer. Transfusion centers worldwide are increasingly involved in clinical trials by providing apheresis products and/or GMP conform processed DC products. BEST Cellular Therapy Team therefore started activities to further investigate this kind of in vitro generated cellular products that are increasingly considered for immuno therapeutic treatment. The decision was made to perform – as a first step – a prospective multi-center study on various DC quality parameters. Assay results between participating labs will be compared by sending around identical pre-cultivated and frozen DC samples. The objective is to compare the results of quality assays (non-functional) performed by different laboratories on identical frozen/thawed DC samples. In addition, re-cultured DC will be analyzed for storage stability at different post-thaw time points. Details of the DC study protocol were discussed, and a revised protocol will be finalized in August 2004 by the study planning group. The frozen samples will be shipped to ten participating labs in Europe, Japan and the US [European centers: NBS, Bristol (Derwood Pamphilon), London (Marcella Contreras); Sanquin Bloodbank, Leiden/Groningen (Anneke Brand, Janny de Wildt); Finland Red Cross, Helsinki (Riitta Kekomaki); German Red Cross, Mannheim (Hermann Eichler, Duc Nguyen); Japan: Institute of Medical Science, Tokyo (Tsuneo Takahashi); US centers: Hoxworth Blood Center, Cincinnati (Ron Sacher); Dartmouth Hitchcock, Lebanon (Ziggy Szczepiorkowski); NIH, Bethesda (Harvey Klein); University of Maryland, Baltimore (John Hess); Blood Systems Research Institute, San Francisco (William Reed)]. It is planned to perform MNC apheresis procedures from three volunteer donors in August 2004 at the coordinating site in Mannheim. CD14+ cells will be selected by immuno magnetic cell selection (CliniMACS), and purified monocytes will then be cultivated with IL-4/GM-CSF + TNF alpha to generate peptide-loaded and unloaded mature DC. In fall 2004, frozen DC samples will be shipped on dry ice together with donors' sera, donors' lymphocytes, cell culture medium and monoclonal FACS antibodies to the participating laboratories. Each site will evaluate defined quality parameters, e.g. DC antigen expression of CD1a, CD14, CD16, CD83, CD86, and HLA-DR. The goal is to present preliminary results at the next BEST meeting in Rome (March 2005).

6. Guest Presentation: Functional in vitro Testing of Dendritic Cell (DC) Products (Duc Nguyen)

As part two of the DC study, it is planned to integrate functional DC testing into the study protocol. However, it is not clear which kind of assay should be performed. Although T cell proliferation using [3H] thymidine incorporation assay is currently widely used to test DC function, this technique is difficult to handle and provides only limited information about T cell proliferation. Duc Nguyen presented his results on using a new flow cytometric assay for testing functional properties of in vitro generated and peptide-loaded mature DCs (Nguyen XD, et al. J Immunol Methods 2003;275:57-68). This method was developed to quantify DC-mediated T cell activation as well as proliferation simultaneously. CD14+ peripheral mononuclear cells were cultured to generate fully mature DC. These cells were co-cultured with allogeneic naive T lymphocytes with known HLA class I and II antigen mismatches, and T cells were harvested on days 0, 3, 5, 7, 9, and 11 for flow cytometric analysis. T

cell activation was quantified by staining for CD71 expression on CD3+, CD4+, and CD8+ cells. Fluorescent beads were used for cell counting. In summary, this FACS based assay delivers precise and quick quantification of T cell activation and proliferation triggered by incubation with peptide-loaded mature DCs, yielding information on in vitro function of DCs. Compared to the BrdU-incorporation assay, quantification of CD71 expression on T cells can be used as activation marker. In addition, specific T cell subsets involved in antigen-specific proliferation can be evaluated in detail.

7. Cell Processing in the United Kingdom (Derwood Pamphilon)

Derwood Pamphilon presented current activities and regulatory challenges in the field of cell processing in the UK. Methods currently used in the Bristol stem cell facility such as red blood cell depletion, monoclonal antibody purging and CD34+ cell selection were presented. He mentioned developmental work on immuno therapeutic approaches such as generation of virus specific T cells for the treatment of CMV+ patients. Another field of action is the research on immunotherapy of leukemic patients, for example by the use of pulsed dendritic cells. These DCs might be generated from immuno magnetically selected CD34+ cells. In summary, the immuno therapeutic activities are still increasing in number and complexity. Due to the European regulations it is necessary to build up fully accredited GMP facilities for the clinical use of such procedures.

8. Revised Version of Asahi Medical Filter System for Volume Reduction of Cord Blood (StemQuick™-R) (N. Kitaguchi)

Dr. Kitaguchi presented initial results of preparing cord blood products using the revised StemQuick filter device developed by the Asahi Company. This system is a modification of their previous system for the processing of cord blood samples. A larger filter area, the implementation of a pre-filter to remove cell aggregates as well as a new syringe-pressing device, characterizes the new system. The recovery of CD34+ cells showed a value of around 90%. It also seems to be possible to recover non-hematopoietic cells such as vascular progenitor cells from bone marrow. The filter device is not available on the market at the moment.

9. Concept for a Multi Center Study on Mesenchymal Stem Cells (JoAnna Reems)

JoAnna Reems gave an overview on the current state of the definition and possible clinical use of mesenchymal stem cells. These cells can be expanded exponentially under favorable conditions and can subsequently be differentiated into a number of various non-hematopoietic cell types such as adipocytes, chondrocytes and others. Currently there are various ongoing activities in several laboratories of Cellular Therapy Team members. It was therefore decided to carry out a laboratory pilot study to evaluate different culture conditions to expand mesenchymal stem cells. JoAnna Reems will lead a group to draft a protocol and to perform this pilot study before the meeting in Rome in March 2005.

10. Information on Guava Flow Cytometry Technology for Cell Counting and Phenotyping (William Reed)

William Reed reported on a newly developed system for cell analysis based on principles referred to as micro-capillary cytometry. This "Personal Cell Analysis" device (developed by the GUAVA Company) is able to analyze different cellular parameters in multi-parameter assays (for example cell count and viability). Other applications are analyses of antigen expression of cells, cell cycle markers, ABO/Rh grouping or the detection of bacteria. In the field of cell therapy this device could be used for QC product characterization (immuno phenotype, viability, sterility). Advantages are the very small volume requirement, high reproducibility and walk-away simplicity. A disadvantage may be the limitation to simultaneous parameter measurements and cost.

11. Cell therapy for cardiac repair treatment (Paolo Rebulli)

Paolo Rebulli gave a short state-of-the-art presentation on cell therapy for myocardial repair. The rationale of cell therapy after acute myocardial infarction is to enhance the number of progenitor cells that could physiologically migrate to the damaged reperfused myocardium and positively affect/influence myocardial repair, and to reduce the migration of inflammatory cells negatively affecting myocardial repair. He discussed the current knowledge of different cell types to induce cardiac repair such as skeletal myoblasts or bone marrow

cells. Dr. Rebullia also presented an overview on published as well as on ongoing clinical trials. He stressed the need for a controlled randomized trial and standardized functional techniques for the evaluation of differences in metabolism and perfusion. A clinical trial with the application of CD133+ cells on this issue will be performed in Milan.

Report: Clinical Studies Team

L. Williamson, N Heddle

1. RESULTS OF 'GETTING TO KNOW YOU' QUESTIONNAIRE – CLINICAL STUDIES RESPONSES.

N. Heddle summarized the results of the questionnaire which was circulated to BEST members to get an understanding of the areas of interest for clinical research projects. A series of questions related to blood components were asked including: whether the focus should be on platelets for the next few years; whether the team should perform studies on red cells; and to determine if there was an interest in standardizing methodology to be used for clinical studies i.e. assessment of bleeding. The responses indicated a diverse interest with some responders showing a moderate to high degree of interest in all of these areas. Section B of the questionnaire asked individuals to specifically rate their level of interest for studies related to: neonates; surgical patients; development of a bleeding tool for patients receiving FFP; or projects related to utilization. The summary of responses were included in the book prepared for the Edinburgh meeting; however, once again there was a wide range of interest varying from a score of 2 to 10 with 10 indicating a high level of interest. The third section asked the responders whether they would be interested in taking part in studies including: assessment of a bleeding tool; data on FFP use; an N of 1 study for febrile transfusion reactions; quality of life studies; and post transfusion tracking of platelets using flow cytometry. Based on the responses, there appeared to be moderate to high interest for each of these areas. The individuals who responded to the questionnaire also provided some suggestions for studies related to fresh frozen plasma and studies on neonates (see Edinburgh book for details). It was decided that the group should continue to focus on platelet studies as there appeared to be interest and leadership in this area; however, the individuals who are interested in some of the other areas (i.e. neonates, measurement tools, etc.) should come forward with suggestions for various studies and protocols at future meetings.

2. SToP STUDY

N. Heddle gave an update on the current status of the SToP study. There have been a number of issues which has slowed or stopped recruitment at two of the sites (Aubuchon and Herzig). Two of the Canadian sites are awaiting final ethics approval and the third Canadian site is actively enrolling patients. There is also a possibility of getting another US site in California who may be interested in participating in the study and N. Heddle will follow up on this. The logistics of the study seem to be moving along well. If there are any other BEST participants who are interested in joining these studies it is not too late for them to do so.

3. UPDATE FROM RADIOLABELLING MEETING AND FDA WORKSHOP: DEFINITION OF THE ISSUES (see inclusions in Edinburgh book).

AuBuchon summarised the FDA workshop on radiolabelling. It seems that the FDA is willing to accept most of the BEST proposals for a standard method for radiolabelling and analysis of the results. This will be discussed in detail in the Conventional Components Group (see their minutes for this discussion and more detailed information on the workshop outcome).

4. PREPARING PLATELETS FROM A SINGLE BUFFY COAT SUITABLE FOR AUTOLOGOUS RADIOLABELLING STUDIES.

Dr Lisa Cooke (Williamson's research fellow) outlined preparatory work she was undertaking to validate preparation of platelets from a single buffy coat suitable for autologous radiolabelling studies. Buffy coat platelets are normally prepared from pools of 4-6 BC and stored in a 500-1000 ml bag. To prepare a product of

similar platelet concentration and SA/volume ratio in the bag, Dr Cooke had investigated several published protocols for preparation of platelets from 1 BC, and several storage bags. A method had been developed to achieve optimal results, and the single BC product was now being compared to standard pooled BC platelets in various platelet function assays. Radiolabelling studies using plasma and a platelet additive solution would then begin.

5. NON-RADIOACTIVE TRACKING OF TRANSFUSED PLATELETS IN PATIENTS.

Williamson and Brand presented similar methods for identifying the transfused platelet population in patients based on using specific monoclonal HLA antibodies to differentiate between patient and transfused platelets. Williamson had used anti-HLA-A2 to study both combinations of an HLA-A2 pos donor/neg patient and HLA-A2 neg donor/pos patient. Both combinations showed *in vitro* sensitivity of 2%, although there was a tendency to overestimate the transfused population in the neg donor/pos patient scenario, perhaps due to adsorption of soluble HLA on to the platelet surface. Williamson's study had also various second monoclonals in dual label studies to examine surface markers post-transfusion. It was agreed that it was probably better to focus on the method as a possible means to study platelet recovery and survival in patients. Williamson proposed a study to validate this method against radiolabelling in patients and several people expressed interest in this (subsequently designated BEST #33).

Brand's studies were aimed at using the method to investigate refractory patients, so she had examined several different HLA monoclonal antibodies for sensitivity and specificity.

It was agreed that Brand and Williamson would take these respective objectives forward.

6. UPDATE ON STUDY IN REFRACTORY PATIENTS

Brand updated the team on the studies on refractory patients. The retrospective study is now closed, but there were not many submissions. The possibilities of a prospective study were discussed.

7. FRESH FROZEN PLASMA

A. AUDIT FROM CANADA.

N. Heddle presented a summary of fresh frozen plasma use in Hamilton, ON as a way of illustrating some of the tools that are available to gather information, and to determine if there is any interest in looking at epidemiological patterns of fresh frozen plasma use across the country. The system in Hamilton pulls the information electronically from the laboratory information system as well as demographic and clinical information from the medical records database. In total over 75 data elements related to plasma use have been pulled for each patient and/or transfusion of plasma that occurs. This project has also been extended to one other hospital (London Health Sciences Centre) in Ontario which illustrates the feasibility of using this approach at multiple hospitals. Examples of the types of information that could be obtained from this database were also presented such as the percentage of procedures by case mix grouping (CMG) category that use plasma, and the volumes of plasma that are used for these procedures. The data allows one to start at a high level and drill down to a more basic level looking at individual patient use. Specific examples using cardiovascular procedures were used to illustrate the potential of this approach.

B EPIDEMIOLOGY AND SURVIVAL OF TRANSFUSED RECIPIENTS (EASTR).

Williamson summarised a study which she and M Murphy are running which aims to capture transfusion data on 12,000 patients in 29 hospitals, focussing on the uses of each blood component, including FFP and long term survival of recipients. This study uses ICD10 and OPCS information but as it does not link into the laboratory system, data on coagulation results are not included. Preliminary data from 5 hospitals were used to establish the methodology, which includes a novel algorithm to ascertain the 'reason for transfusion'. The main study will report in 2005.

Conclusion

At the conclusion of the meeting, AuBuchon reviewed the status of several other projects and assigned study numbers to the new projects that had been discussed at this meeting. Study 23 is continuing under development, but Study 32 will not be pursued as considered in Bermuda. Therefore, the new studies launched at this meeting include:

31: Randomized controlled trial of a simple intervention to improve performance of the pretransfusion bedside identity check (PROBE Study) (M Murphy)

32: Mesenchymal stem cells send-around (Reems)

33: Platelet tracking (Williamson/Brand)

34: Bacterial contamination detection questionnaire (Prowse)

35 : Platelet quality control questionnaire/standardization (van der Meer/Cardigan)

AuBuchon closed the meeting by thanking all for their participation in a productive meeting.

Notes from Executive Committee Meeting

July 10, 2004
Edinburgh, Scotland

Members present: AuBuchon, Dzik, Eichler, Gulliksson, Heddle, Hess, Moroff, M. Murphy, S. Murphy, Williamson

Staff present: Susan AuBuchon

The Executive Committee (EC) met immediately following the conclusion of the BEST meeting.

Administrative Issues

AuBuchon first led a review and discussion of the current legal status of BEST.

BEST has been incorporated and recognized by the State of New Hampshire as a not-for-profit (i.e., charitable) corporation. It has a federal Employer Identification Number (EIN) and will soon apply to the US Internal Revenue Service for validation of its not-for-profit status from a national perspective. No difficulties are expected.

The existing conflict of interest and operational policies were agreed upon without dissension. AuBuchon noted that New Hampshire law requires disclosure of financial interests by boards of directors of nonprofits (i.e., the Executive Committee of BEST) whenever the corporation does business with an entity in which a director holds more than \$500 of equity or receives this in annual compensation. This disclosure requirement would pertain to the companies through which our books are produced (Staples) and to hotels or caterers with which we contract to hold meetings but would not apply to entities that are manufacturer members, as BEST does not “do business” with them. No conflicts were apparent.

The Executive Committee re-endorsed placing BEST’s funds with the Hitchcock Foundation and was pleased that interest is now being received.

The financial status of BEST was reviewed briefly. Ample funds are available for projects of greater scope and complexity than might be accomplished with the annual \$25,000 team allocation. Several approaches to directing assets to these projects were discussed. It was concluded that the approach currently being used (requesting the support of the Executive Committee for additional funds, when and if needed) would be continued, but it was clear that there was support for not limiting worthwhile projects unnecessarily.

The concept of establishing a BEST website was also considered. This would allow postings and communications among teams or the posting of presentations, for example, if a secure website were established. Even if just a public site (without secure areas) were created, the site would allow demonstration to all our activities and accomplishments. AuBuchon will begin investigation of the cost of setting up such a website.

Membership

The manufacturer membership base was reviewed. PDS has left BEST as it appeared to have gained what it was looking for and was pleased to have been able to be part of BEST. ZymeQuest and now Navigant have joined BEST in the last year, and several other companies with interests in the cellular therapy area are considering BEST membership. (H. Eichler will follow up with these.) Contact will be made with Ortho Clinical Diagnostics in an attempt to keep their involvement following D. Ciavarella’s leaving OCD. The possibility of having a prospective manufacturer member visit a BEST meeting was discussed, and this will be handled on a case-by-case basis.

The Scientific Membership of BEST was also discussed briefly. The desire expressed by G. Andreu to move to “honorary” membership status was accepted with thanks and regret, acknowledging the requirements of his new position. Several Associate Scientific members were considered for transition to Scientific Member status, but none of these would provide the Transfusion Safety Team with the same focus that had been supplied by G.

Andreu. After discussion, it was decided that the Transfusion Safety Team would have the opportunity to identify a new Scientific Member to take the slot vacated by G. Andreu.

AuBuchon expressed concern that some Scientific Members were apparently attending only the team meeting with which they were most closely associated. He will reiterate to them the expectation that they participate fully so that BEST may take advantage of this skills to the greatest degree possible.

Team Leadership

The leadership of the Cellular Therapy Team was then discussed. H. Eichler and G. Moroff have discussed at some length who would best be suited to follow G. Moroff, and they are in agreement that this would be Z. Szczepiorkowski (who is willing). This change will take place after the Rome meeting. At that time, G. Moroff expressed his desire to transition to "honorary" membership status, with the new team co-leader becoming a scientific member. All were in agreement.

ISBT Relationships

A brief further discussion of the meeting with ISBT leadership was held. As BEST had offered all the support of ISBT that it had provided in the past, what more could be done to support ISBT was not clear, but the Executive Committee will await suggestions from ISBT about how it may be able to assist ISBT in meeting its goals.

The Cellular Therapy Team (H. Eichler) will adapt their minutes for submission to Transfusion Today. After the Rome meeting, this will be Transfusion Safety's responsibility, and, after the Seattle meeting, Conventional Component's. The deadline for submission of minutes from BEST XXVIII was set as September 1.

Meeting Improvement

The Executive Committee then discussed a variety of issues intended to improve the meeting and our communications. To reduce redundancy and to use our time together most effectively, it was agreed that, beginning at the next meeting, each team's report at the BEST meeting would be reduced to approximately 20 minutes and would be presented in its entirety by one of the team's leaders. The intention would be to provide an overview of the highlights rather than extensive detail. (Those who had a strong interest in a particular project would already have had the opportunity to participate in the team's discussion.) This approach would be facilitated if leaders asked for preliminary slide sets to be submitted to them ahead of the meeting so that they could begin preparation of their summary ahead of the meeting. This concept would also free up some time surrounding the meeting for the small group conversations that are necessary to work our details of studies after team meetings. (The Executive Committee would not convene, for example, until an hour or so after the BEST meeting.)

Future Meetings

XXIX will occur in March, 2005 in Rome. The suggestion that the meeting be held in the national health institute (P. Rebulla) was discussed, and, if this is convenient and can be set up expediently, will be taken up providing there is sufficient rationale for doing so.

The date of XXX may have to be altered to avoid Yom Kippur. This will be discussed further by the Executive Committee.

(Following this meeting, the executive Committee discussed the dates of BEST XXX via e-mail and agreed to hold this meeting immediately after the AABB Annual Meeting in Seattle. Team meetings will occur on Wednesday, October XX, 2005, and the BEST meeting will be in the morning of Thursday, October XX.)

The process for selecting the next round of BEST leadership will begin at BEST XXX. At this meeting, a Nominating Committee will be selected. The election of the next chair and Executive Committee members (team leadership) will

occur at BEST XXXI (Spring, 2006) with the new chair taking over after BEST XXXII. (This will allow the new team a full year to effect the transition before having to stage their first meeting.)

Several sites were mentioned for consideration for the location of BEST XXXI. Among these were sites in Spain and Greece, and preliminary investigations will be begun.

Other Collaborations

J. Hess brought up the possibility of collaboration with WHO's Global Blood Safety Initiative and indicated that he had invited N. Dingras to speak to the Executive Committee at dinner about this. Support was expressed for the efforts of this initiative, and BEST would be happy to explore how it might be of assistance.

The meeting adjourned at 6:00 pm.