

Minutes

XXXIIIrd Meeting of the Biomedical Excellence for Safer Transfusion Collaborative
Amsterdam, The Netherlands
April 27-28, 2007

These minutes summarise presentations and discussions at the full BEST meeting on April 28 as well as a synopsis of team meetings held immediately beforehand. Additional details of studies can be obtained from team leaders. All slide presentations can be found on the website.

Lorna Williamson opened the meeting with a welcome to new members and guests and outlined the membership list as it currently stood. There are still some open slots for Associate Scientific Members associated with Cellular Therapies and Transfusion Safety. It was hoped to fill these soon. She gave thanks to all those involved in organising the meeting and making it such a success, in particular the help from Martin Ras and Fresenius was gratefully acknowledged – not to mention the BEST Band.

Peter van der Meer presented the BEST Puzzler (see website for solution) and the prizes were presented. He was thanked for providing such an interesting and challenging Puzzler.

Members were reminded to return Conflict of Interest forms to Gill Cook and to notify her of any changes to contact details. Members were reminded of the reimbursement arrangements being \$1500 for a meeting on one's own continent and \$3000 for a meeting on another continent irrespective of whether the membership was Full or Associate.

Jim Aubuchon presented the Treasurer's Report demonstrating an end of year balance for 2006 of \$205,602.48. He presented a useful breakdown of expenses showing that 66% were for travel and 14% for cost of meetings. It was noted that the BEST dues had increased to \$20,000 in 2007, the first increase in the history of BEST. Manufacturers who had already paid were thanked.

Lorna Williamson noted the successful Canadian Consensus Conference on Pathogen Inactivation and informed members that a preliminary report from the Consensus Panel had been accepted as a rapid communication in *Vox Sanguinis*.

Lorna Williamson invited members to stand in silence for a few minutes in memory of Claes Hogman who had passed away in late 2006. Many BEST members had been present at his wonderful lecture at ISBT Cape Town and we were proud to notice that he was wearing his BEST badge when he delivered this lecture.

On a happier note members congratulated Ruby Pietersz on receiving the Order of Orange from The Netherlands Government. A symposium to mark Ruby's retirement had been held the previous day and she had received a special musical send-off from the BEST Band.

This was followed by the Scott Murphy Guest Lecture given by Sandra Cauwenberghs from Sanquin in Maastricht, Netherlands. The title of her lecture was "Platelet responsiveness and function during storage: implications for platelet transfusion therapy". Sandra's lecture stimulated much discussion and questions and she was thanked for a marvellous introduction to the Scott Murphy Lecture Series.

Team leaders then presented proposals for future studies. Subject to ratification at the Executive Committee meeting immediately afterwards, the following were proposed:

Haemoglobin measurement of blood units to matched patients (Tor Hervig #43)
Questionnaire on ABO incompatible platelets (Lozano #44)
Guidelines for reporting trials in transfusion medicine (Heddle #45)
Transfusion reaction survey (Dzik, Heddle #46)

There was then discussion of future meetings. BEST XXXIV has been scheduled for Thursday, 18th and Friday, 19th October 2007 prior to AABB and will take place at the Laguna Cliffs Marriott Resort and Spa, Dana Point, California. In view of other commitments of BEST members prior to the main AABB meeting, it was agreed to hold the team meetings on Thursday morning and Thursday afternoon with the main BEST meeting on Friday morning. BEST would arrange transport to AABB on Friday afternoon. There was discussion around possible venues for BEST XXXV in the Spring of 2008 and it was eventually agreed to hold this in Cambridge, UK. BEST XXXVI in Autumn 2008 will be held in Montreal, Canada prior to AABB.

Lorna Williamson closed the meeting by thanking everyone for their support particularly the active contributions from the guest lecturer and new members.

Minutes of the Transfusion Safety Team at BEST (Amsterdam)

Sunny Dzik, MD
Michael Murphy, MD

Sunny Dzik opened the session by welcoming back Dr Georges Andreu (France) to BEST. The group is delighted that Dr Andreu has been able to return to BEST and looks forward to collaborations with him on BEST studies. Drs Murphy and Dzik will be making recommendations to the Executive Committee for individuals to serve as Associate Members on BEST. Dr Dzik welcomed any suggestions from the group and several were provided. Invitations to new Associate Members will be made in time for their attendance at the autumn meeting in California.

Old Business:

1. Bacterial Detection Survey

Dr Silvano Wendel gave an update on the survey (previously done) regarding current practices in use for bacterial screening of platelet products. This project is being done in collaboration with the Transfusion Transmitted Infectious Disease working party of the ISBT. Silvano noted that the content of the survey was reported publicly at ISBT (Capetown) and at AABB (Miami) and that these presentations provided feedback useful to manuscript preparation.

Next Steps:

A manuscript is in progress and is expected to be available for review by the primary authors in June. The group meeting in Amsterdam discussed the fact that the survey data was now a bit old, but noted that it included unpublished information especially from European centers. The group agreed that publication of this survey should go forward and suggested that Vox Sanguinis might be a suitable journal given the available European data. The manuscript may serve as a “baseline” for future bacterial detection surveys to be conducted by ISBT.

2. Statistical Process Control for Sample Labeling Errors

Sunny Dzik summarized the current status of the project. The goals of this project are:

- a. to demonstrate the practical use of statistical process control (SPC) for monitoring the rate of sample errors in the form of “control charts” (errors over time).
- b. to offer a free software tool for hospitals who wish to use SPC for preparation of control charts.
- c. to make recommendations regarding use of SPC technology among multiple hospitals in a region for the eventual development of national or regional performance standards.

10 hospitals from 5 nations have contributed data on sample errors which have been presented in the form of control charts and runs charts.

A DRAFT manuscript has been prepared.

Neil Beckman is identifying a suitable free software to make available on the public area of our website.

A discussion ensued on the messages of the manuscript and the target journal to which the manuscript would be submitted.

Next steps:

1. Joseph Sweeney, Zbigniew Szczepiorkowski, and Ronald Sacher agreed to critically review the current draft manuscript.
2. Neil Beckman will identify a suitable free software to make available on the public site.
3. Sunny Dzik, Mike Murphy, Neil Beckman, and Nancy Heddle will review the changes suggested by the critical review.

3. Transfusion Medicine: Prevention of Bedside Errors (PROBE-TM) Study

Mike Murphy gave an update on the PROBE-TM study which was published in the May 2007 edition of Transfusion.

A discussion followed on the potential to have a series of “focus group” meetings with nurses involved in the study. A facilitator would run the focus group to conduct a semi-structured interview with nurses to understand the strengths and weaknesses of the process of the bedside check. The group pointed out that other disciplines have taken advantage of existing methodology for the conduct of qualitative research. These methods may be of value to explore for the focus group project.

Next steps:

Drs Murphy, Heddle, and Tinmouth agreed to discuss this approach in greater detail and report back to the group.

4. The Decision to Transfuse: Survey of Practices in Blood Utilization Review

Alan Tinmouth (Canada) and Simon Stanworth (UK) provided an update on the web-based survey on current practices used for blood utilization review. The survey has undergone several pilot trials and refinements and is nearly ready for distribution.

Discussion centered on the proper balance of sites in relation to achieving a balance in relation to the –geographical spread of participating centers and their representation proportional to the population base of a nation, and also in relation to hospital size and complexity. The group agreed that the study should remain within BEST. It was recommended that Drs Tinmouth and Stanworth develop a sampling plan and indicate to BEST member participants how many sites they should enroll for the survey.

Next steps:

- a. Drs Tinmouth and Stanworth will make final revisions to the survey based on feedback from selected participants.
- b. A sampling strategy will be developed so that survey participation will be balanced.

New Business:

The second-portion of the meeting was devoted to an open and interactive discussion of possible new projects for the Transfusion Safety Team. Members “scored” the suggested projects for feasibility, scientific merit, and likelihood of participation. The following topics were discussed.

1. BEST practice for evaluation of transfusion reactions

The goal of this project would be to build a consensus opinion for the best way to evaluate a suspected transfusion reaction based on the cardinal symptoms of the patient. The project could be done in conjunction with the Clinical Studies Team who share interest in this topic.

There was broad agreement in the value of this approach and it received an enthusiastic score by the members in the room.

2. TRALI

The opportunities to study TRALI were discussed. These included surveys of current practices to reduce the risk of TRALI, creation of a sample repository, send-around testing studies, and clinical case-review studies. Written feedback from the group suggested that this topic, while an important transfusion hazard, may be difficult to study in the context of BEST.

3. Performance measures for key aspects of transfusion

Dr Szczepiorkowski presented a quick survey of the American Society of Hematology’s effort to develop performance measures for key aspects of the management of ITP. He noted that much of the motivation for ASH came from the need to create a basis for financial reimbursement. He described the potential for apheresis services and transfusion services to establish similar measures that would be common to all facilities that perform basic transfusion practices. This project received a medium enthusiasm written critique and may be reconsidered at the next meeting.

4. Consultants to developing nations

Sunny Dzik suggested a program of “adopt a hospital” in which BEST members with current relationships to specific hospitals in developing nations could apply to BEST for support and resources to further develop the transfusion service of that specific hospital. This approach (bottom up) would not be programmatic at the national level but would be more in the form of direct assistance and teaching to a specific hospital.

Verbal discussion on this topic suggested other avenues for participation that would engage BEST at a higher level such as the WHO Global Blood Safety program which has BEST members at the table.

The written feedback on the proposal to “adopt a hospital” was mid-range enthusiasm. Several respondents felt the idea was not sufficiently developed for them to form a good opinion. The possibility of a presentation at the next meeting by Tor Hervig who is working in Tanzania was suggested.

5. “Decision to transfuse”

Further studies on the “decision to transfuse” are expected to occur through the Transfusion Safety Group. It is expected that the results of the survey will be used as a the basis for follow up studies. The cluster randomization design used in the PROBE-TM study may serve as a good template for the conduct of those studies. Data driven evaluations of different methods to affect the “decision to transfuse” are likely to be a major focus of follow up studies.

- Sunny Dzik and Mike Murphy

MINUTES
CLINICAL STUDIES
FRIDAY APRIL 28, 2007

The Clinical Studies team met on the afternoon of Friday April 28, 2007. The following presentations and topics were discussed.

a) SToP Update: N. Heddle presented an update on the SToP Study. At the present time there are 126 patients who have been randomized to the study. The recruitment is proceeding slowly and various options for dealing with the low level of recruitment were discussed. One of the options that will be considered is a recalculation of the sample size for the SToP study using the recurrent event analysis as the primary outcome rather than a comparison of the proportion of patients transfused. If this decreases the sample size considerably, then this may be an option for achieving a reasonable level of recruitment and completing the study within a reasonable period of time. N. Heddle also presented the idea that a manuscript should be written describing the design of the SToP study similar to what Dr. Slichter had done in the Journal of Apheresis for the Transfusion Medicine Hemostasis NHLBI Platelet Dose Study. A final decision on writing such a manuscript will be left until the recalculation of sample size and a decision is made on how the SToP study will proceed.

N. Heddle also described the bleeding adjudication system that has been set up. This is a system where each of the adjudicators within BEST will receive a file which includes a database and a series of forms that provide the information on daily bleeding assessment, platelet count, etc. The data safety monitoring board has requested that the bleed be adjudicated as soon as possible so that they have accurate information on which to base any decisions that they may make related to safety. Rebecca Barty, the Coordinator for the study, will be sending out batches of files to be adjudicated and BEST members who are participating are requested to return these files as soon as possible.

ACTIONS:

1. Sample size recalculation based on recurrent event analysis model – N Heddle
2. Decision on study design manuscript following #1 – N Heddle
3. Bleeding adjudication ASAP – BEST Scientific Members

b) Buffy Coat / HLA Projects: L. Williamson gave an update on the preparation of single buffy coats and the protocol for HLA tracking. Buffy Coat Project: Additional work has been done on the validation of single buffy coats stored for 7 days in plasma. For each of the markers tested the single buffy coat platelet product always had higher levels than the corresponding platelet pool (See slide presentation posted on website). Lorna requested volunteers from members of BEST who would be interested in doing radiolabeling studies.

ACTIONS:

1. Volunteers for this study should contact Lorna by email prior to June 15, 2007

c) Hemoglobin Dosing (BEST #43): Tor presented the protocol for a pilot study on hemoglobin dosing and patient matching as printed in the BEST book. Comments on the protocol must be sent to Tor before May 10th. Immediately after the final revision, the

pilot study will begin - in order to present data for the Anaheim meeting. BEST members who can provide data on hemoglobin content in the red cell concentrates, pre- and post-transfusion hemoglobin data and height and weight of the patients are invited to participate. It was recommended that the weight of the unit also be captured; bedside leukoreduction and transfusions involving microaggregate filters should be exclusion criteria. Additional thought also needs to be given to how to ensure that the patient is not bleeding. The sample size in each centre will be 10-20." Ziggy and Joe Sweeny have already agreed to participate at the time that the minutes were prepared.

ACTIONS:

1. Comments to Tor on Protocol prior to May 10 – BEST members
2. Initiation of pilot study – Tor
3. ?Additional volunteers?

d) ABO Compatibility of Platelet Transfusions (BEST #44): There is no unanimous practice regarding ABO compatibility and platelet transfusion. In many centres ABO identical platelet products are not always available; hence, ABO mismatched transfusions are administered. ABO mismatched platelet transfusion are associated with several drawbacks: in the case of a major ABO incompatibility, the transfusion response may be compromised and in contrast with a minor ABO incompatibility a severe hemolytic reaction might be elicited.

A survey is being prepared intended to capture current practice with respect to prescribing of platelets from a different ABO group from that of the patient. The survey is divided into three parts: first - description of your institution and your transfusion service; second - details to define the type of product used; and finally - to define the practices around platelet transfusions and ABO incompatibility. BEST members are requested to provide feedback related to the questionnaire including the format of part 3.

ACTIONS:

1. Feedback on questionnaire to Miguel by June 15 – BEST members
2. Pilot run of questionnaire - Miguel

e) Antibody Titration Study: AuBuchon reviewed the plans for BEST40 as included in the book. There has been an excellent response, and almost 40 labs are expected to participate in the study the first week of June. Results will be reviewed with CAP and BEST at early fall meetings before being submitted for publication. The group reviewed the uniform procedure and made a few suggestions.

ACTIONS:

1. Initiate study - AuBuchon

f) Systematic Review Apheresis and Whole Blood Derived Platelets: L. Dumont gave a presentation on a recent systematic review and meta-analysis that was performed by McMaster University in collaboration with Gambro BCT. The review was designed to look at randomized control trials that compared apheresis platelets to whole blood derived platelets (Buffy Coat or PRP methods). The review looked at clinical outcomes including acute reactions, time to next transfusion, alloimmunization and refractoriness, bleeding, corrected count increments at one hour and 24 hours post-transfusion, and radiolabeled survival and recovery studies. The results of this systematic review are

being compiled into a report which will be sent to the sponsor and a manuscript will be drafted to present the results. The results of the review identified a lack of comparison data between buffy coat platelets and platelets prepared from PRP and apheresis platelets.

ACTIONS:

none

g) System for Classifying Acute Transfusion Reactions: N. Heddle gave a presentation related to a system for classifying acute transfusion reactions that has been developed by the ISBT. The ISBT working group has put together standardized definitions for non-infectious acute transfusion reactions. The definitions have recently been approved by all members of the ISBT working group and the next phase will involve a validation phase where a number of ISBT members and experts in the field will receive various cases to determine if the classification system is workable and valid and reproducible. N. Heddle raised the issue as to whether this classification was suitable for clinical research studies and whether there is any additional role for the BEST Collaborative in validating this classification. The members of the BEST Collaborative felt strongly that there should be one single classification and if ISBT has developed this that there should not be another classification that is also developed; however, the potential to do some validation studies was of interest to some members of BEST.

ACTIONS:

none

h) Discussion of Other Proposals/Ideas: The group requested input from members of BEST as to other proposals or ideas that could be undertaken by the clinical studies team. If any such ideas arise, please contact N. Heddle or L. Dumont.

ACTIONS:

1. Forward ideas and proposals to Nancy or Larry – BEST members