Community Blood Center of the Ozarks
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January 16, 2006

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket NO. 2005D-0330

Dear Dr. Orton & Dr. Vostal,

The Community Blood Center of the Ozarks (CBCO) is a non-profit community blood center providing blood products to thirty-six hospitals in thirty-eight counties in southwest Missouri, northwest Arkansas and southeast Kansas.

We appreciate the opportunity to submit comments and data on the Draft Guidance for Industry and FDA Review Staff; Collection of Platelets by Automated Methods.

Like you, our priorities are the safety of our donors and the quality of the products we release for transfusion. If the referenced guidance is implemented in its' current form, we are concerned that it will have unnecessary affects on the availability of platelets for transfusion and will not enhance donor safety.

CBCO has been collecting Platelets Pheresis since 1995. We have been using one Apheresis collection technology (Gambro Trima Accel) since 3-12-2004. Our 10 years of data also includes collections using Baxter CS 3000, Baxter Amicus and Cobe (Gambro) Spectra instruments. CBCO has collected 37,832 Platelets Pheresis in the past 10 years.

Our comments to the draft guidance are divided into two sections; the first section addresses the draft guidance (pages 2-7) and the second section is our Apheresis Donor Study (pages 8-21) for your review and consideration. Thank you for the opportunity to comments on this guidance and also for allowing the delay in our submission.

Sincerely,

Don Thomson

Don Thomson
Executive Director

DT/bf

2005D-0330

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Page and Section	Draft Statement	Comment	Recommendation
Page 2 Section II.A	"This guidance applies to collection by automated methods of the following components:	Does this Guidance apply to collection of Platelets, Pheresis with concurrent collection of red blood cells?	No recommendation
Page 2 Section II.A	"you should include additional criteria at the time of process validation and QC testing . . . .to include evaluation of pH at 6.2"	This statement is unclear. Blood centers perform validations to prove that the process obtains the expected results.	We recommend changing the CFR requirements to ≥ 6.2 and remove the requirement to evaluate at 6.2 pH
Page 2 Section II.A Page 3 Section II.A	"evaluation of pH at 6.2" **vs.** "pH of not less than 6.0"	Consistency is needed	Standardize the requirements. Revise CFR requirement to ≥ 6.2
Page 3 Section II A Page 5 Section III. A	". . . .donors for medication use (Ref.9)" NSAIDS, Plavix and Ticlid (Ref 9)	We do not think it is appropriate to mandate use of ASBPO drug lists unless it is scrutinized by experts and discussed in public.	Provide an FDA approved list of unacceptable medications
Page 5 Section III.A	5-day deferral for ingestion of Aspirin containing drugs	This is inconsistent with requirements for whole blood platelet collections	Standardize the requirements for whole blood and Apheresis collections
Page 5 Section III.B.1	Platelet Count: "collect only single Platelets, Pheresis . . . from first-time donors with no pre-donation platelet count	Does not address concurrent RBC and/or plasma collections	Scientific data should support this limitation. Clarify if concurrent collection of other products is acceptable.

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Page 5 Section III.B.1	Platelet Count: "a post-donation count from a previous collection should be used to set the target platelet yield if a pre-donation platelet count can not be done".	Use of post collection counts can result in inaccurate instrument programming and possible loss of product due to over or under collecting.	Do not allow use of post donation platelet counts for instrument programming.
Page 5 Section III A, Page 6 Section III B 2 Page 17 Section VII B.1	Post-donation platelet and white blood cell counts	What is the significance of post counts? Are there acceptable post donation WBC counts?	Examine data and publish acceptable post-donation platelet and WBC counts before requiring testing. Monitor donor with pre-counts and Medical reviews.
Page 6 Section III.B.2	Donation Frequency: "To protect the safety of the donor:"	Our data from 50 donors who have each donated more than 100 products during the last 10 years does not indicate a donor safety issue. See attached data	A public session for comment and discussion is needed. Development of criteria for data collection from blood centers would be beneficial in determining if there is a need to reduce the number of products that can be safely collected per year.
Page 6 Section III B 2	Interval between donations	Safety of donors can be controlled by pre-donation platelet counts and medical record review	Limit interval between donations to 3 days and 150,000 platelet count
Page 6 Section III. B.3	A unit of whole blood (450mL)	More blood centers are using 500 mL collection bags	We recommend using 500 mL as the unit of red blood cells

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Page 7 Section III.B.3	Total volume of blood components retained per collection should not exceed . . .	This is contrary to some manufacturer approvals. Gambro Trima was approved by FDA for 15% TBV.	Allow use of manufacturer's recommendations if available.
Page 7 Section III D	Medical Coverage: "presence on the premises" to include a qualified physician able to arrive at the premises within 15 minutes"	Donor treatment can be served better by trained and equipped emergency teams who attend patients on a regular basis as opposed to blood center physicians who have little or no training in responding to emergencies.	Require collection facilities to develop a written plan for emergency treatment.
Page 8 Section IV	Donor Information: "A statement that the long-term effects of repeated platelet pheresis on the donor's platelet and leukocyte count is not understood."	See attached data	See attached data
Page 8 Section IV	Donor Information: "A description of the number of Whole Blood, Apheresis Red Blood Cells. . . .components that may be collected per year . . ."	Providing the multiple donation scenarios to donors provides no benefit to the donor	Collection facilities should be responsible for controlling donation intervals per published guidelines.
Page 8 Section VB	Target Platelet Yields: "should use the following targets when collecting: doubles set at 6.5 x 10^{11} and triples set at 10.0 x 10^{11}.	Different technology requires different targets in order to obtain acceptable values. Donation history of individual donors may dictate different target values.	Manufacturer and donor collection history should dictate target settings

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Page 10 Section VI.C	Process Performance Qualification (Operator): "Personnel training should include the successful, consecutive performance, under supervision of an appropriate number of procedures. . ."	Initial personnel training should include performance but software upgrades may not be significant enough to require performance	Differentiate between initial training and training needed for software upgrades
Page 10 Section VI.D	Product Performance Qualification (Component Collection): Required testing of products during validation at 1-2, 3-4 and on 5th day".	This would require detailed tracking systems. If products meet the requirement at 5 days, they would meet it at days 1-4.	No recommendations
Page 11 Section VI.D	Product Performance Qualification:	Statement is unclear. If collecting singles, doubles and triples how many products should be tested? Is this for initial validation and/or software upgrades?	Clarify the number of products to test. Reduce required number to 20 products. Require fewer products for software upgrades.
Page 12 Table 1	Collection Performance Qualification Criteria: Doubles volume ± 5% and Triples volume ± 3%	21 CFR 606.121 (c) (6) says volume should be accurate to 10%	Make guidance compatible with CFR requirements or revise CFR
Page 15 Section VII A.2 Page 22 Section IX	Actual Platelet Yield: "should be provided to transfusion facility" Labeling: "should be available to transfusion service"	Products must have a platelet count of at least 3.0×10^{11} to meet Circulator of Information requirements.	Statement should say yields "should be available" to transfusion facilities. Maintain consistency though out document.

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Page 17 Section VII.B.1	Platelet Counts: "notify Medical Director when a donor has a post collection platelet count.....	Intravascular fluid changes during pheresis combined with individual donor hemodynamics renders immediate post donation platelet counts inaccurate.	We recommend no post-procedure counts be required.
Page 17 Section VII.B.2	Adverse Donor Reactions: Requirement is not clear	Not all reactions require reports and subsequent investigation. Blood centers often classify reactions as mild, moderate, etc	Clarify statement.
Page 19 and Page 30	QC Monitoring: Minimum of four. vs. 10% of annual collections.	QC is performed monthly, annual requirement will unknown until the end of the year. Does not require testing of all instrumentation.	10% of average monthly collections. Remove requirement to test different donors
Page 20 Section VII.C.2	Test for residual WBC within 24 hours.	Gambro's sampling protocol states samples for WBC count can be done within 48 hours of collection	Remove the time frame for sampling and allow blood centers to follow manufacturer's approved protocols
Page 20 Section VII.C.2	Acceptance Criteria: "The volume in each container for double collections should be 50% ± 5% and triple collections should be 33 % ± 3%".	Statement is unclear.	Please explain 50% and 33 % of what.
Page 21 Section VII.F	Quality System Audits: Check performance of the scale, tare weight of empty container	It is not normal practice for Guidances to specify that audits include checking performance of instruments. GMP requires regular equipment QC and maintenance	Delete statements on how to perform audits.

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Page and Section	Draft Statement	Comments	Recommendation
Page 21 Section VII.E	Operator QA: Performance . . . . . should include proficiency testing		Delete proficiency testing
Page 23 Section X.A	Reporting Changes….: Increasing Platelet yield requires prior approval.	Manufactures have suggestions for increasing platelet yields	Allow blood centers to use manufacturers' recommendations for increasing yields without notifying FDA.
Page 24 Section X.B.	Reporting Changes…: Instrument upgrades requires CBE-30	Manufacturer's upgrades are approved by FDA	Allow reporting of upgrades in annual report.

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Apheresis Donor Study

I. Reason for study:

- The changes to criteria for collection of plateletpheresis in the FDA Draft Guidance limiting the number of products that can be donated per year indicate a concern for the safety of donors with high frequency and multiple product donations.
  - The draft guideline referenced a study published in Transfusion (Guidance Reference 21) that found a decrease in platelet counts of individuals undergoing serial plateletpheresis donations.
- Discussions with individuals involved in evaluation of the draft guidance also indicated that FDA would like to receive data of donor counts from blood centers.
- We evaluated changes to platelet counts of our high frequency plateletpheresis donors as a comparison to the Transfusion study.
- We wanted to provide FDA with data to support our comments regarding the criteria changes in the draft guidance.

II. Donors studied:

A. High frequency database:

- All active donors with 100 or more product donations in our donor recognition database.

  Note: The actual number of products donated by these donors ranged from 96 to 397. Donation dates ranged from September 1995 to December 2005.

- All donors that donated triple plateletpheresis products during 2005 (a total of 13 donors).

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B. Low platelet count and white blood cell count database:

- All donors in the current computer system with donation records indicating platelet and white blood cell counts outside our acceptable ranges. This included all donations from June 2002 to December 2005.

- A total of 385 donors were identified. These included white blood cell and platelet counts of pre and post-donation donor blood samples.

- Collection of post donation blood samples was discontinued in December 2003. In 2004 & 2005 all counts performed were from pre-donation samples.

III. Method of study:

A. Computer and paper records were retrieved of donors in the study groups.

B. For each donation, of each donor, the donation date, platelet and white blood cell counts were entered into a Microsoft Access database.

C. The difference in the donor's first platelet count and last platelet count in the database was calculated to determine change in platelet count.

D. Donors were grouped into various categories (see charts of individual studies for categories) and a mean change in platelet count was calculated for the donor groups.

- The Transfusion report included mean changes to donor's platelet counts based on the number of procedures performed. We also determined changes based on the total number of platelet products donated.

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IV: Study results, high frequency donors:

Donor Database:

- All active donors with 100 or more product donations in our donor recognition database. The actual number of products donated by these donors ranged from 96 to 397. Donation dates ranged from 09/1995 to 12/2005.
- All donors that donated triple plateletpheresis products during 2005 (a total of 13 donors).

A. Mean Change in Platelet Count per Number of Products Donated

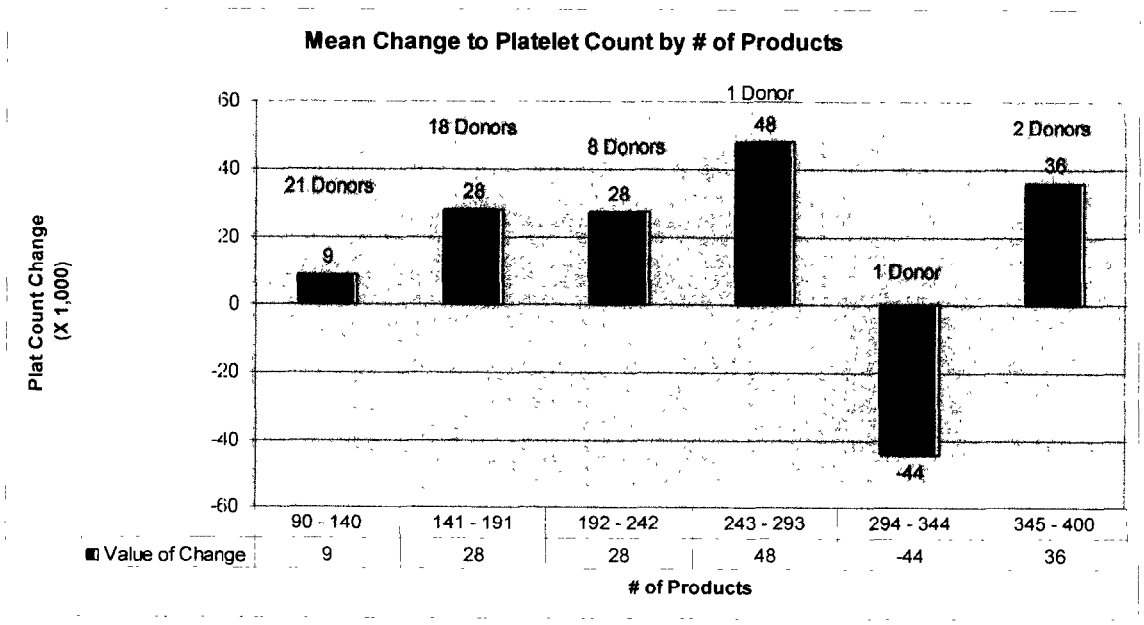
We studied the mean change to donor's platelet counts as a function of the total number of products donated over the 10-year time period.

The range of products donated per donor in this group was 96 to 397.

Donors were grouped based on the total number of platelet products donated by the following categories:

90 – 140, 141 – 191, 192 – 242, 243 – 293, 294 – 344 & 344 – 400.

Only one category (consisting of one donor) showed a decrease in count.



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B. Mean Change to Platelet Count per number of procedures

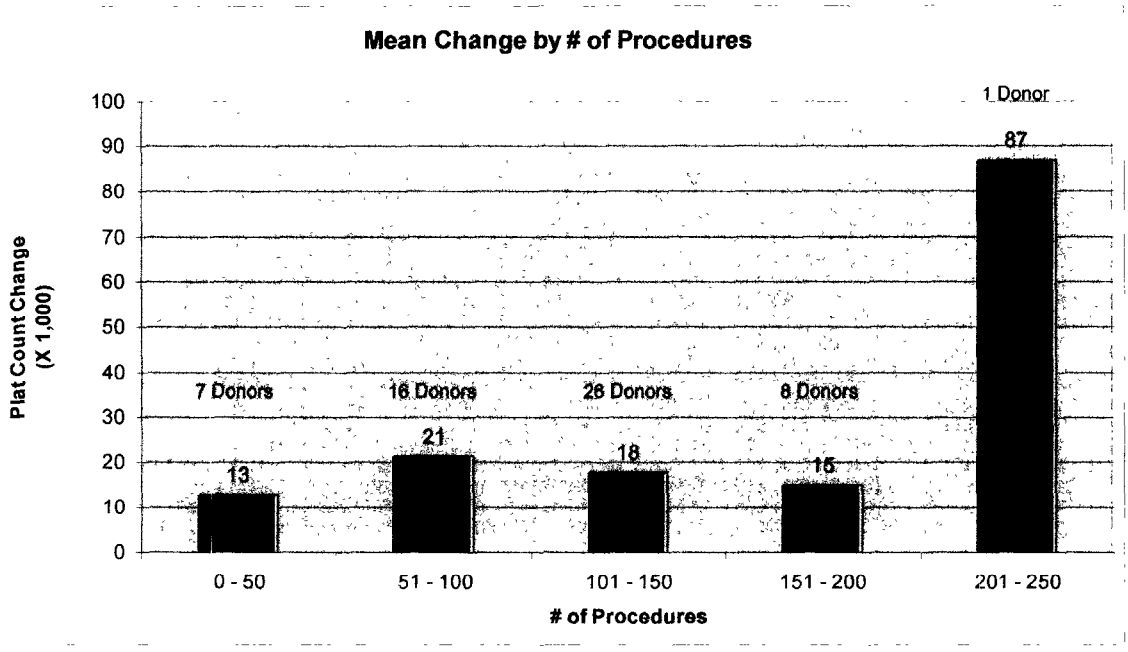
We studied the mean change to platelet counts as a function of the total number of procedures performed.

The range of procedures was 2 to 215. Donors with a low number of procedures were triple plateletpheresis donors.

Donors were grouped based on the total number of procedures performed and included all donors in the high frequency database as well as all donors that have donated triple plateletpheresis products. Total procedures were grouped in the following categories:

0 – 50, 51 – 100, 101 – 150, 151 – 200, 201 – 250.

In all categories the mean change to platelet count was an increase. This is in comparison to the Transfusion study result of a decrease in all categories of donation frequency.



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C. Mean Change to Platelet Count per Type of Procedure

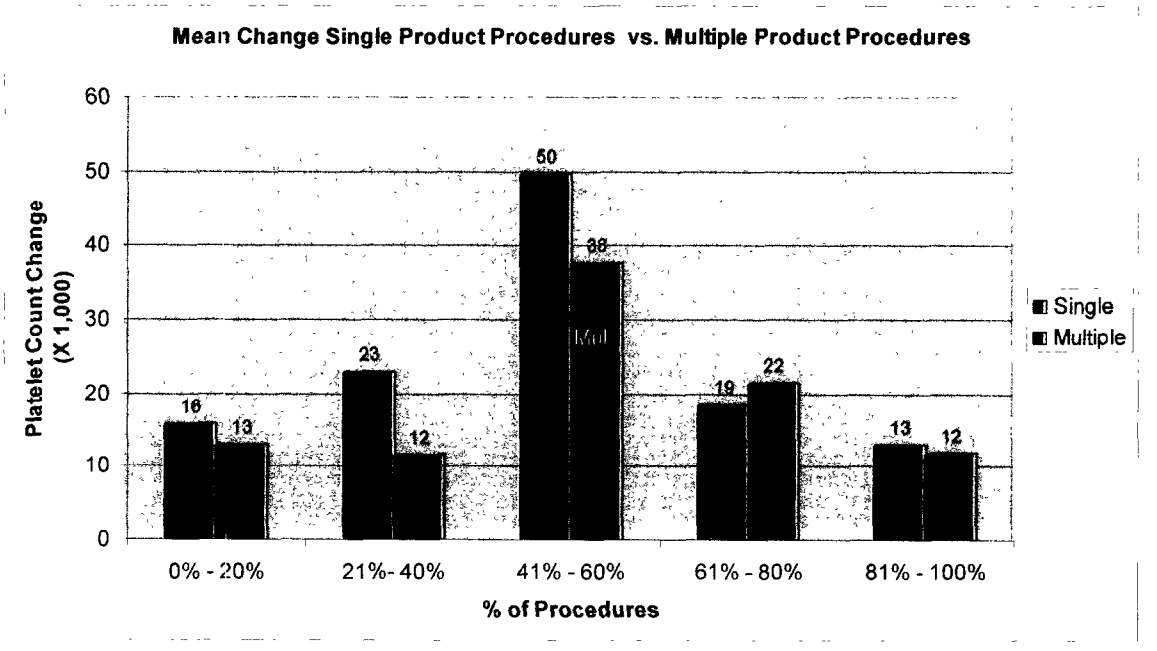
We studied the mean change in platelet counts as a function of procedures by the percentage of single product procedures compared to the percentage of multiple product procedures.

The total number of procedures ranged from 2 to 215.

- The range of %, per donor, of procedures with single platelet product procedures was from 0 to 99%.
- The range of %, per donor, of procedures with double or triple product procedures was from 0 to 99%

In all categories there was a mean increase in platelet counts.

- The category with the greatest change in donor's counts was the group with approximately half of the total procedures single product donations and half of their procedures multiple product donations.
- The mean change is similar when comparing the change to platelet counts of donors donating primarily single products vs. the mean change of donors donating primarily multiple products.



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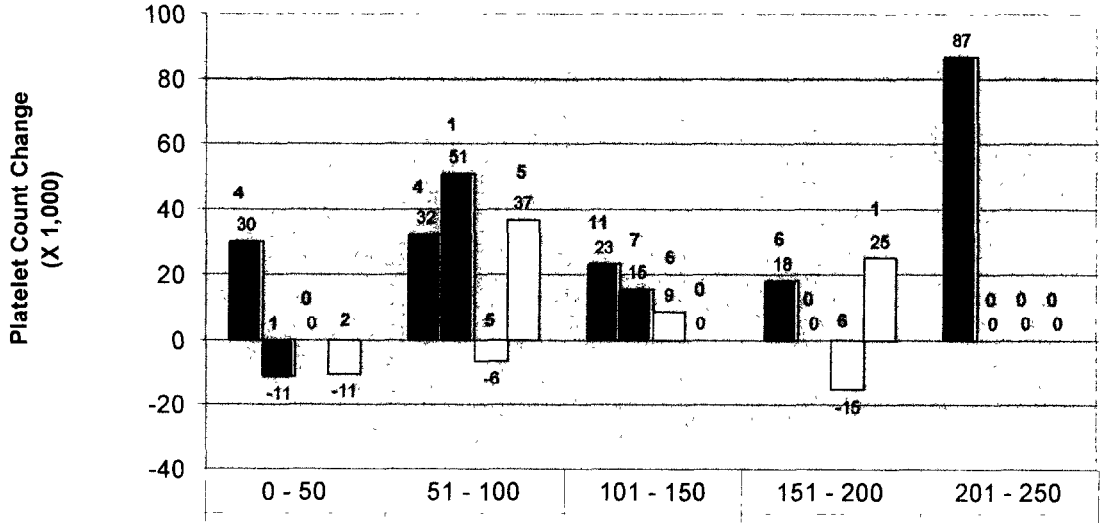
D. Mean Change to Platelet Count by Age and Gender

We studied the mean change to platelet counts as a function of donor gender and age.

In all but four categories there was a mean increase in platelet count. There does not appear to be any particular correlation to mean change based on gender or age.

Note: Numbers on the graph in orange are the number of donors in the group.



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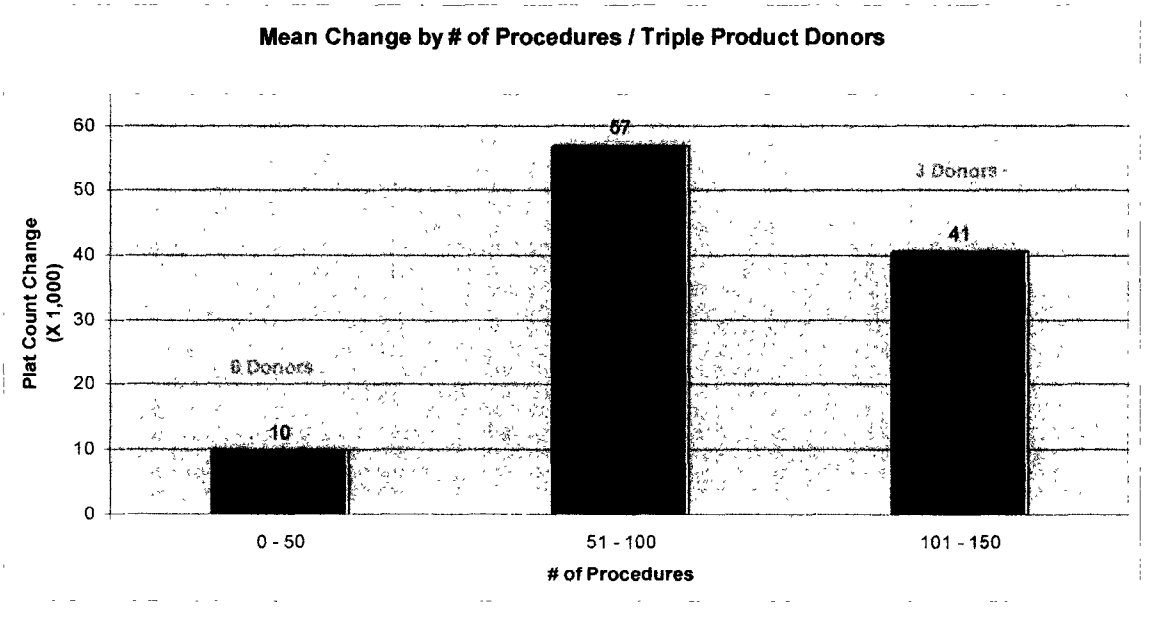
E. Change in counts of donors donating triple plateletpheresis products

1. We studied the mean change of donors that have donated triple plateletpheresis.

   This group included a total of 13 donors; all triple procedures occurred in 2005.

   - The total # of procedures in the group, per donor, ranged from 2 to 130.
   - The data included all the donor's procedures in 10 years.

   In all groups the mean change was an increase in platelet count.



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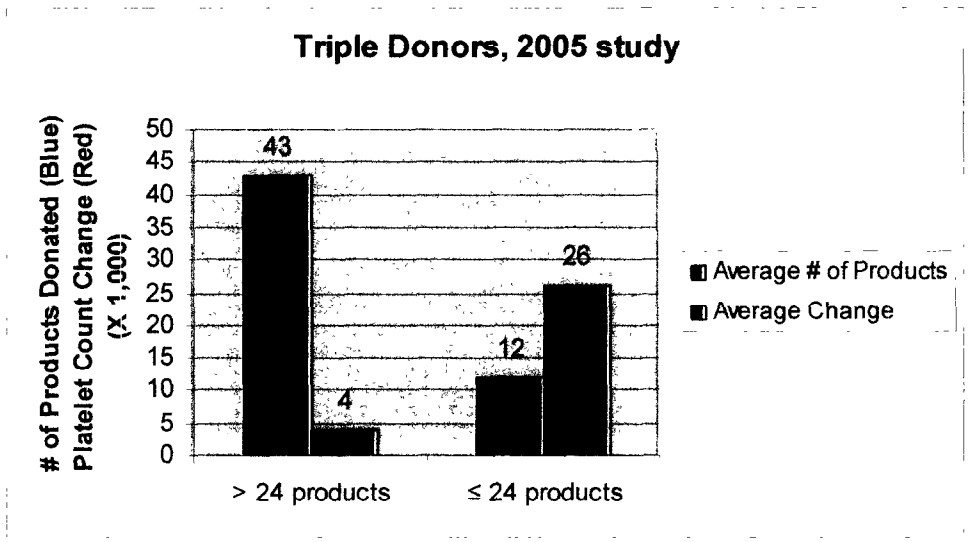
2. We studied the mean platelet count change of donors, with more than one triple donation, during 2005.

   We studied two groups; donors with more than 24 products donated during the year and donors with 24 or fewer products donated during the year.

   The mean change to platelet counts of both groups was an increase.



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V. Study Results of Donors with Platelet and White Blood Cell Counts Outside Defined Criteria

Donor Database

- All donors in the current computer system from June 2002 to December 2005 with donation records flagged for platelet and white blood cell counts outside our acceptable ranges.
    - Acceptable range for platelet counts is 151,000 – *600,000.
    - Acceptable range for white blood cell counts is *3.5 X 10^3 – *12 X 10^3.

      * Criteria determined by Medical Director.

- A total of 385 donors were identified with white blood cell and/or platelet counts outside acceptable range.

- Collection of post procedure blood samples was discontinued in December 2003. During 2004 & 2005 all blood samples were pre-procedure.

  Note: SOP requires discontinuation of the procedure and/or contact with the Medical Director when donor counts are outside defined criteria.

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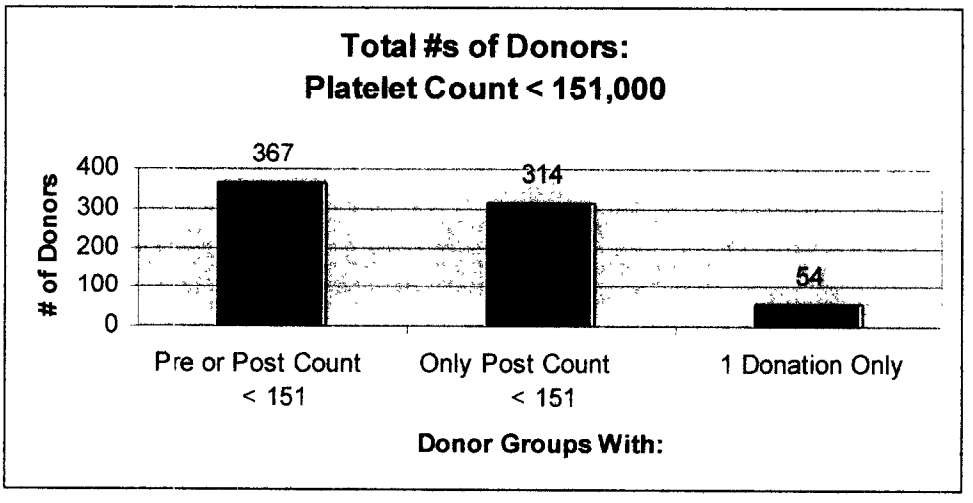
A. Number of donors with pre or post-procedure platelet counts < 151,000

We studied the total number of donors with pre and post procedure platelet counts < 151,000 and the number of these donors that presented for only one plateletpheresis procedure.

- 367 donors had either a pre or post-procedure platelet count less than 151,000.
- Of those, 314 donors (86%) had only post-procedure counts < 151,000. In this group all pre-counts were greater than 151,000 at all procedures.
- 54 of the 367 donors had only one plateletpheresis procedure.



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B. Occurrences of pre-procedure platelet count < 151,000

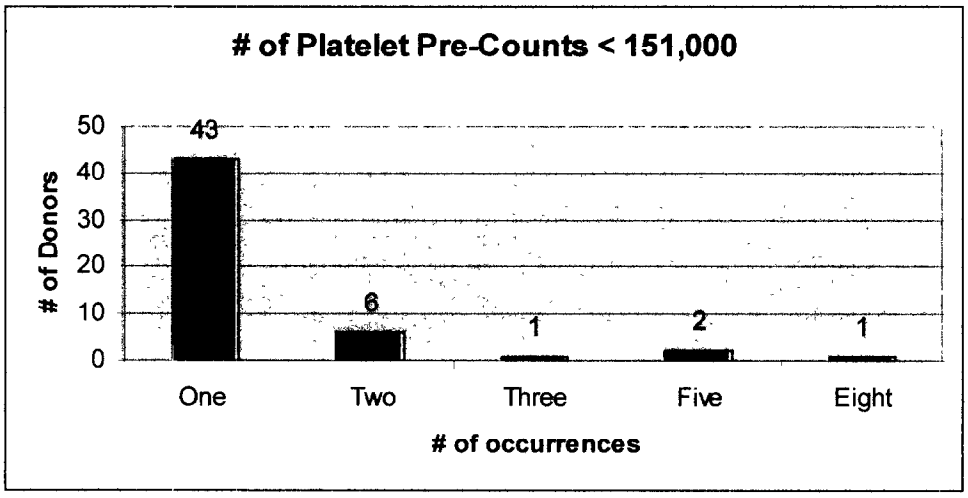
We studied donors with pre-procedure platelet counts of < 151,000. We counted the frequency of occurrence and the average number of total plateletpheresis procedures.

We studied the number of times donors had multiple pre-counts less than 151,000.

53 donors had pre-procedure platelet counts less than 151,000.

- 43 donors had one occurrence of a pre-procedure platelet count less than 151,000.
  - Of these 43 donors, 12 did not return.

- 10 donors had 2 to 8 occurrences of pre-procedure platelet counts less than 151,000. The average # of plateletpheresis procedures of these 10 donors is 51.



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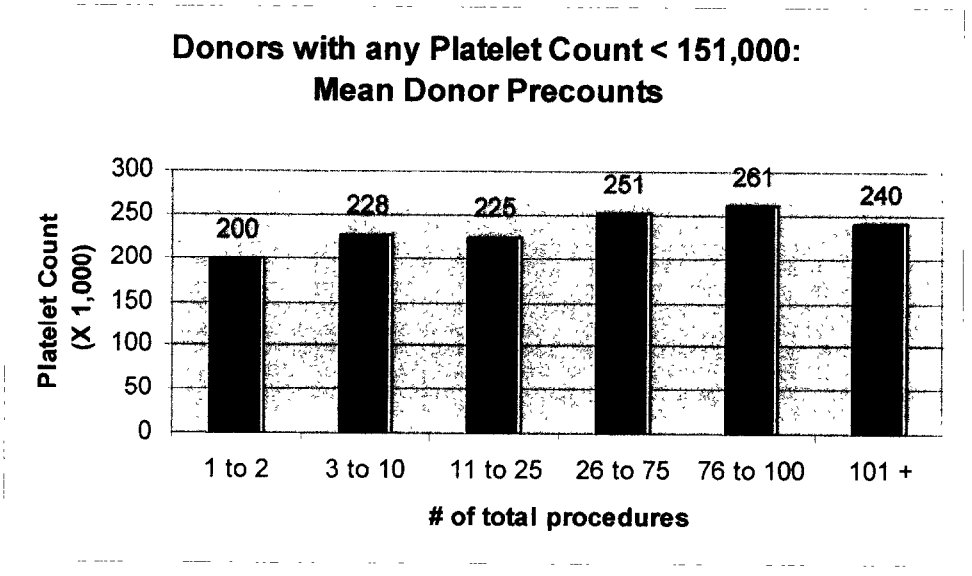
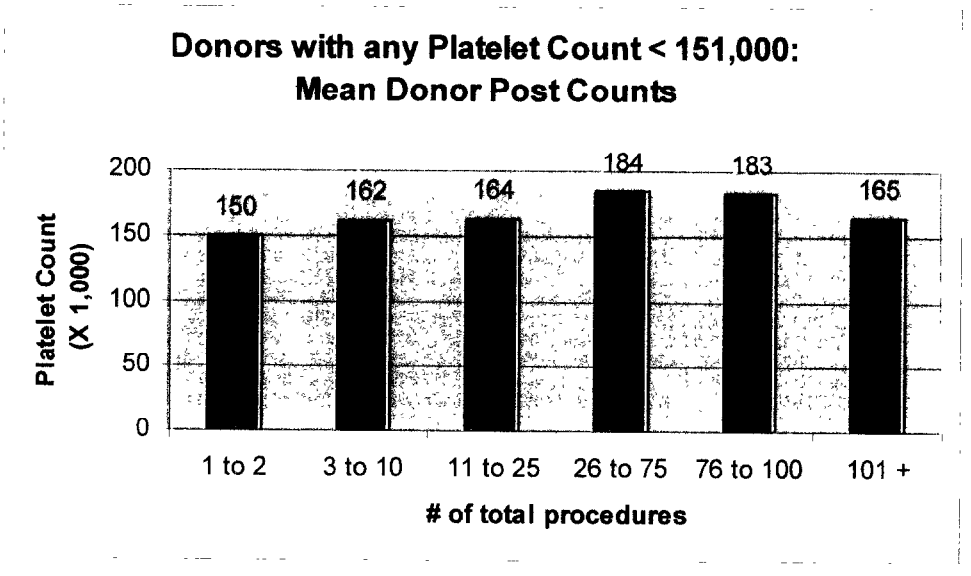
C. Average platelet count of low platelet count donors

We studied the mean pre-procedure and post-procedure platelet counts of donors with any platelet count less than 151,000.

The range of mean pre-count for this group was 200,000 – 261,000 and the mean post-count for this group ranged from 150,000 – 184,000.





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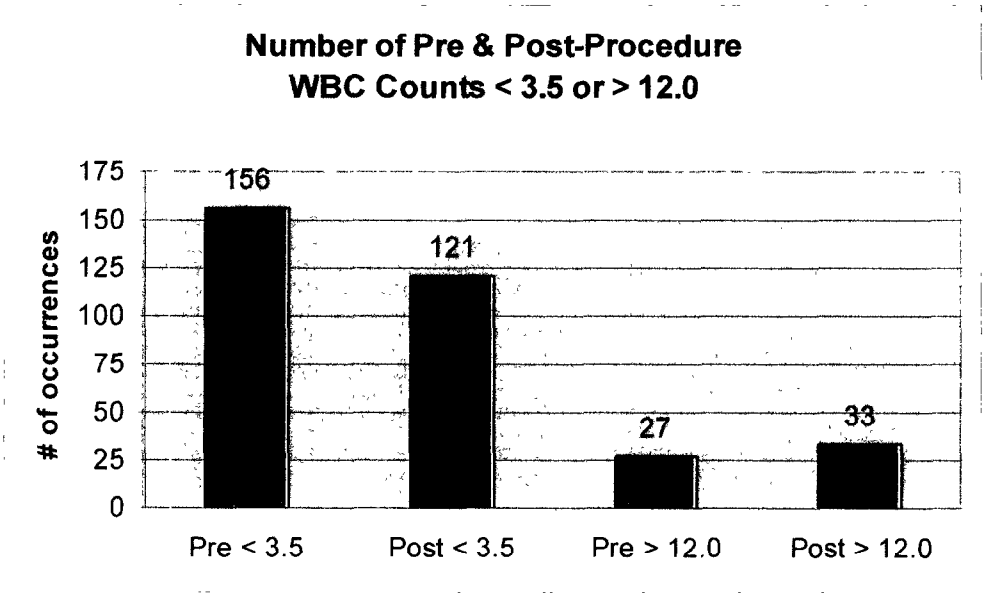
D. Occurrences of WBC counts outside defined criteria

We studied over 11,000 procedures to identify how often donor pre or post-procedure WBC counts were outside our defined criteria ($3.5 \times 10^3 - 12.0 \times 10^3$).

- There were a total of 156 occurrences of pre-procedure WBC counts < 3.5. The total number of donors represented in this group was 47.
    - Of the 47 donors 26 presented for apheresis donation only one time.



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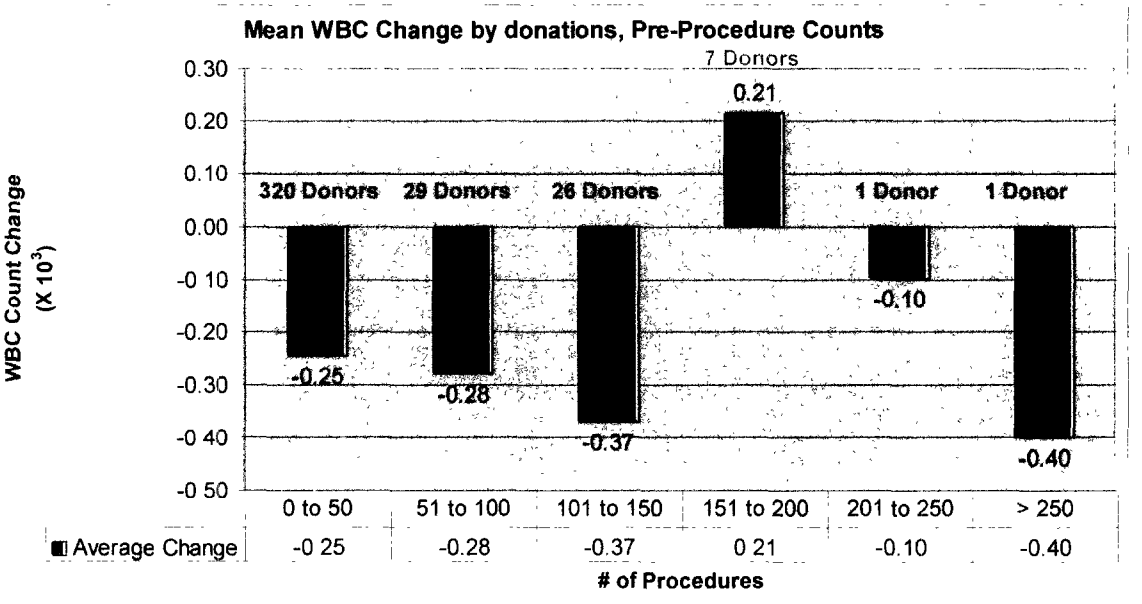
E. Mean Change to donor WBC counts

We studied all donors in the database to determine a mean change in WBC count as a function of the number of procedures.

A small decrease in count was noted in all groups but one. The majority of donors had a mean decrease of 0.25×10^3.

The range of decrease was $0.25 \times 10^3 - 0.4 \times 10^3$.