

# Product Collected, Data Forms Completed, What Happens Next?

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# Disclosures

The following faculty and planning committee staff have no financial disclosures:

Name	Institution
Roberta King, MPH	CIBMTR/NMDP
Marie Matlack, BS	CIBMTR/NMDP
Rachel Schuler, M.S.	NMDP/Be The Match
Kuchen Hale	NMDP/Be The Match

# Learning objectives

At the conclusion of this session, attendees will be able to:

- Describe types of donor data collected
- Describe how donor data are used
- Network with representatives from CIBMTR to gain further insight

# Types of Donor Data Collected

Standard data – HLA, IDM, work-up, collection, short-term follow-up

Acute adverse events

Donor self-reported long-term events

Data derived from research samples

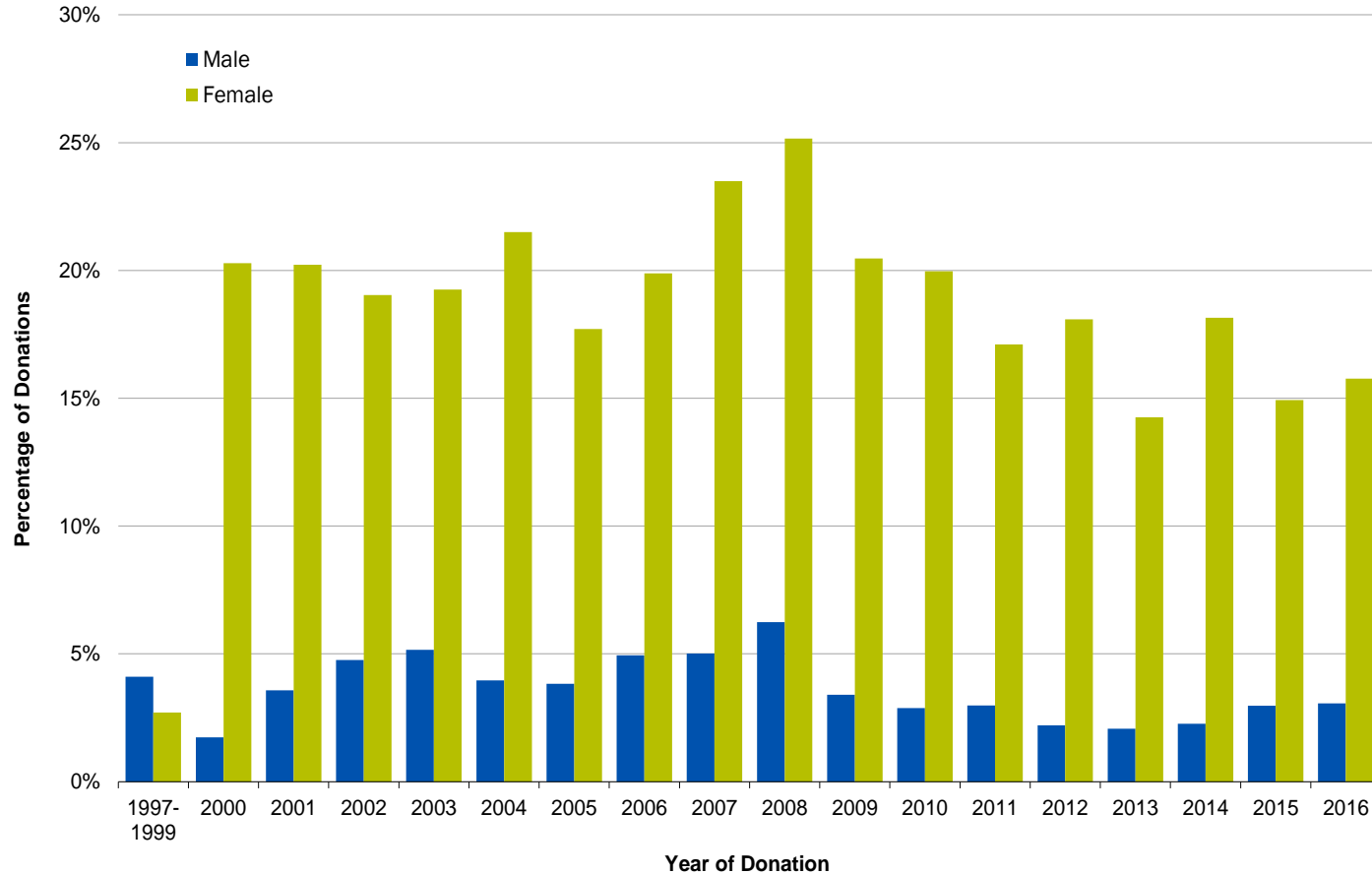
# Primary Uses of Donor Data

- Donor safety
  - DPSP
  - FDA Annual Report
  - Internal and external information requests
  - Quality Assurance activities and reports
- Research
  - Donor focused
  - Recipient focused

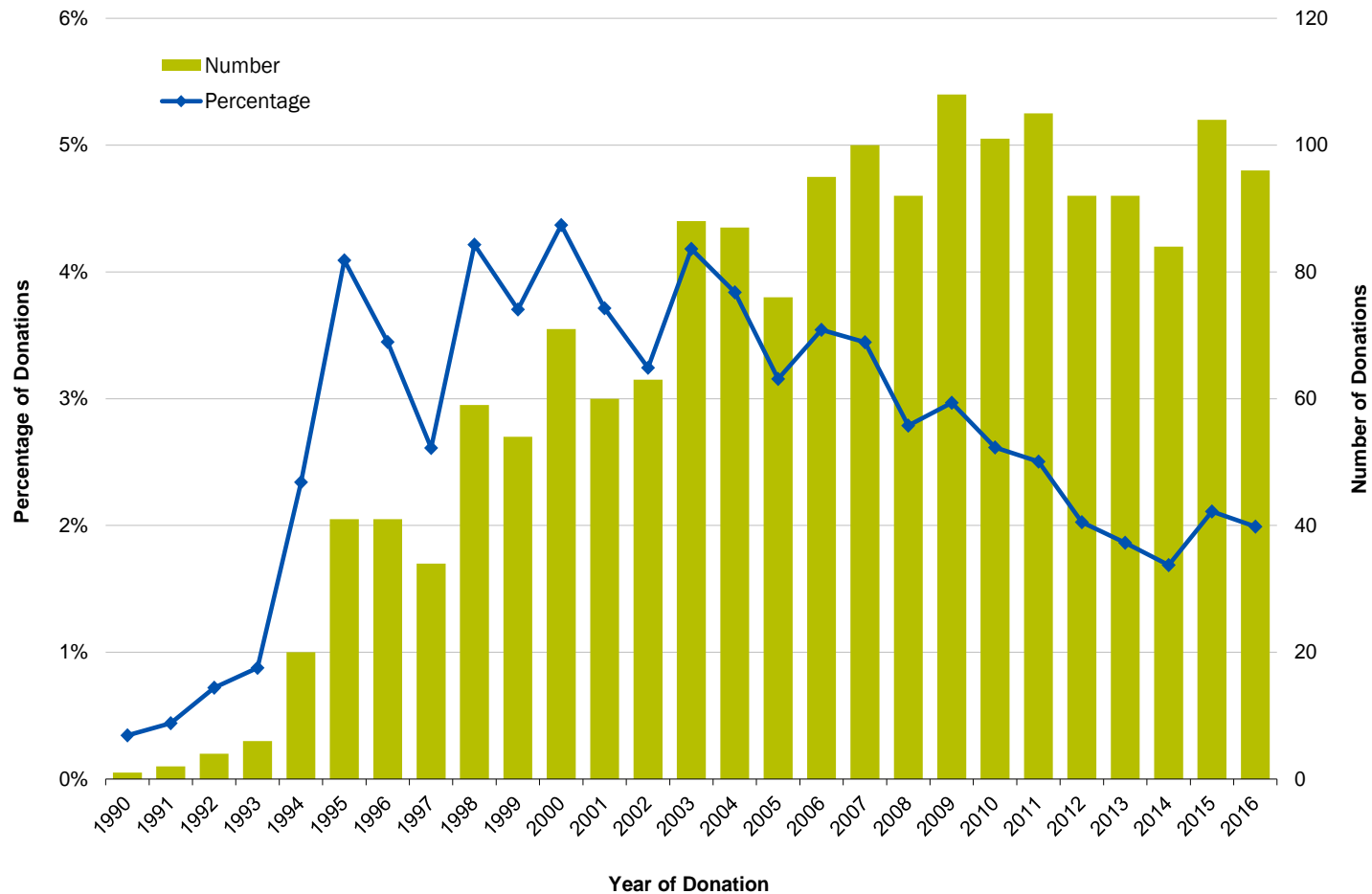
# Donor Safety - DPSM

- Donor and Patient Safety Monitoring (DPSM) Advisory Group to NMDP Board of Directors
- Advises the NMDP on safety issues for donors and patients
- Reviews and responds to annual monitoring report
  - Program activity data
  - Trended outcome data for recipients and donors
  - Product integrity data

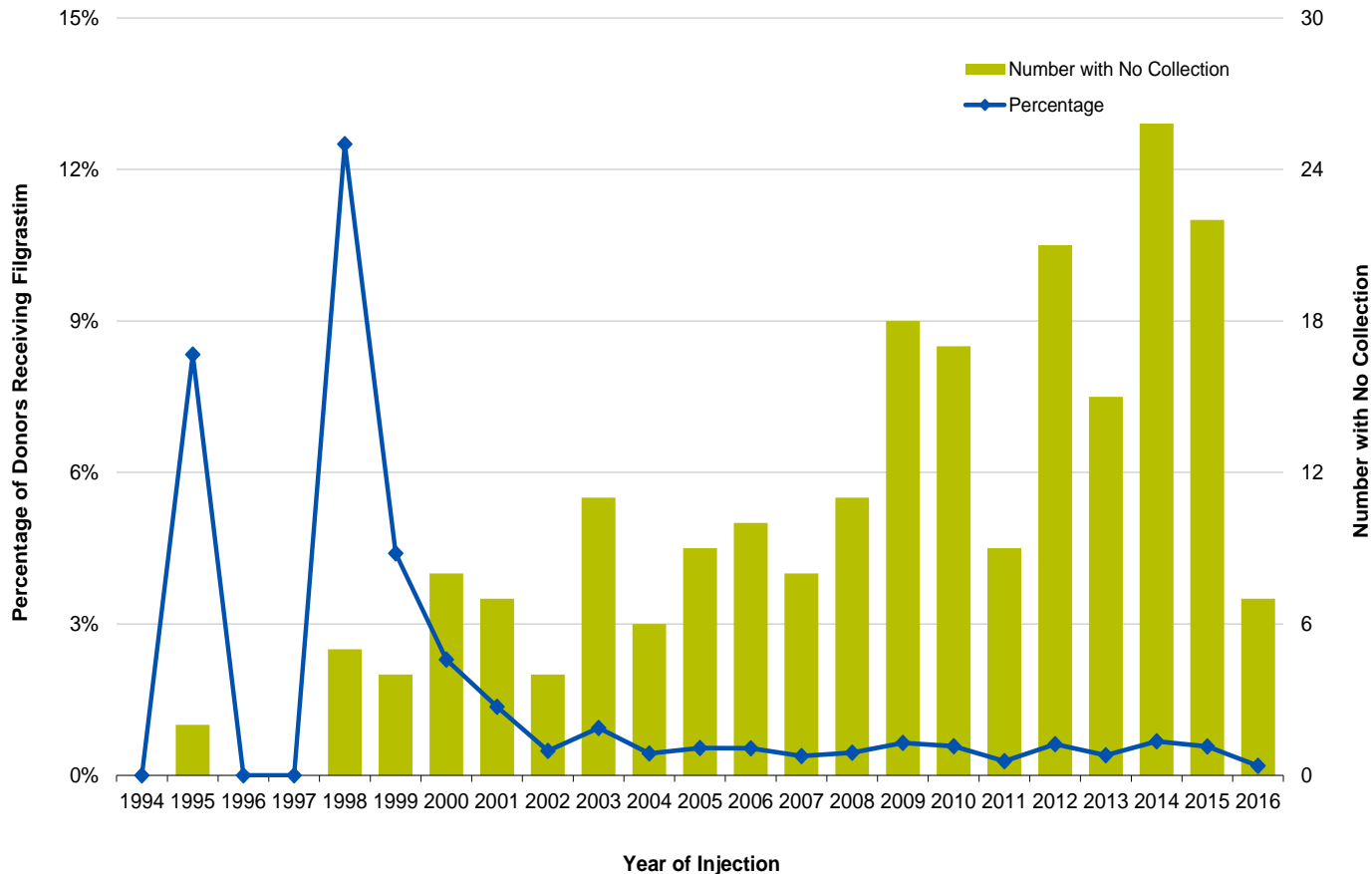
# Percentage of Donations Requiring Central Line Placement on Either Collection Day



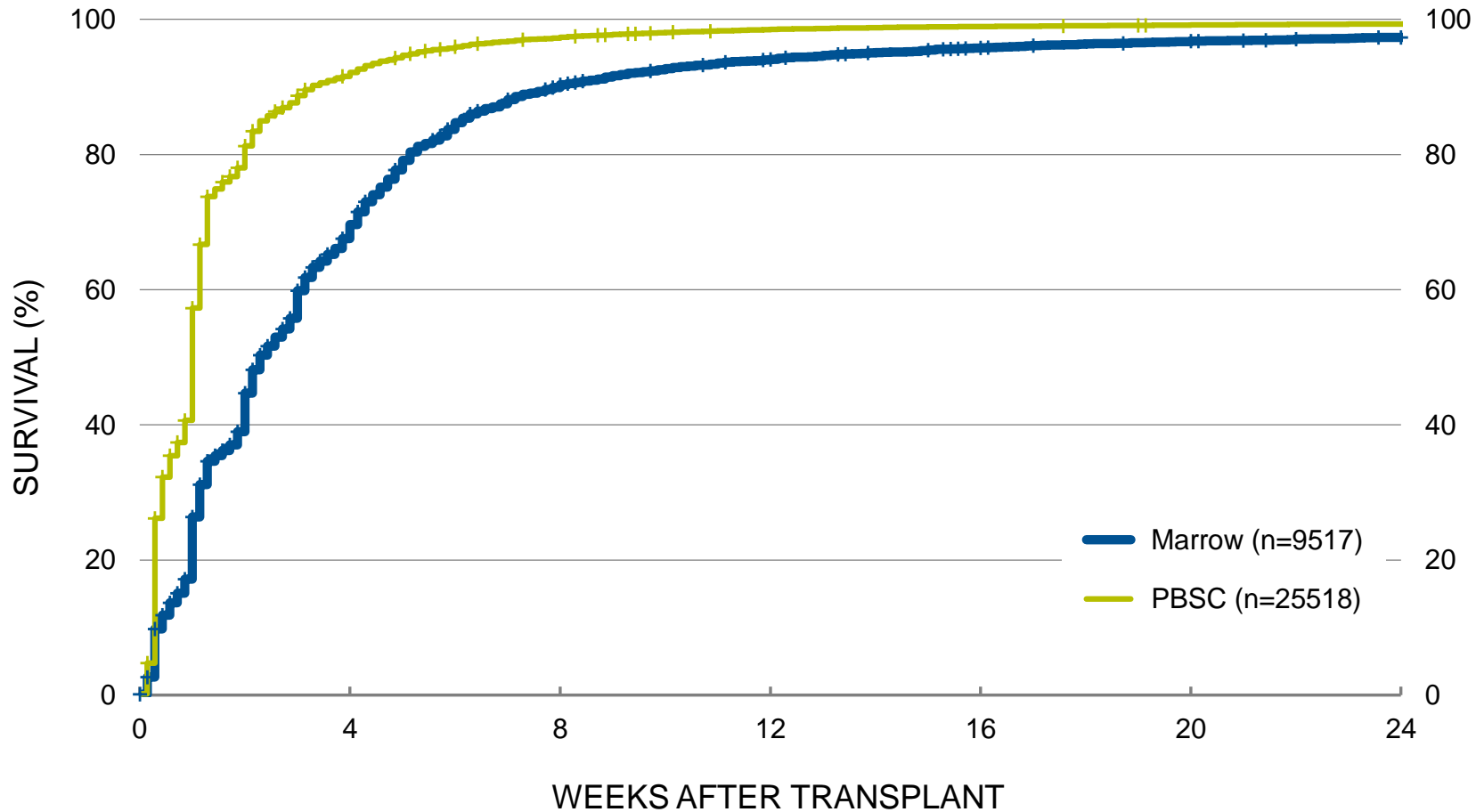
# Subsequent Donations for the Same Recipient



# Filgrastim Injections with No PBSC Product Collection



# Time to Recovery after First Donation



# Donor Safety - PBSC Clinical Trial

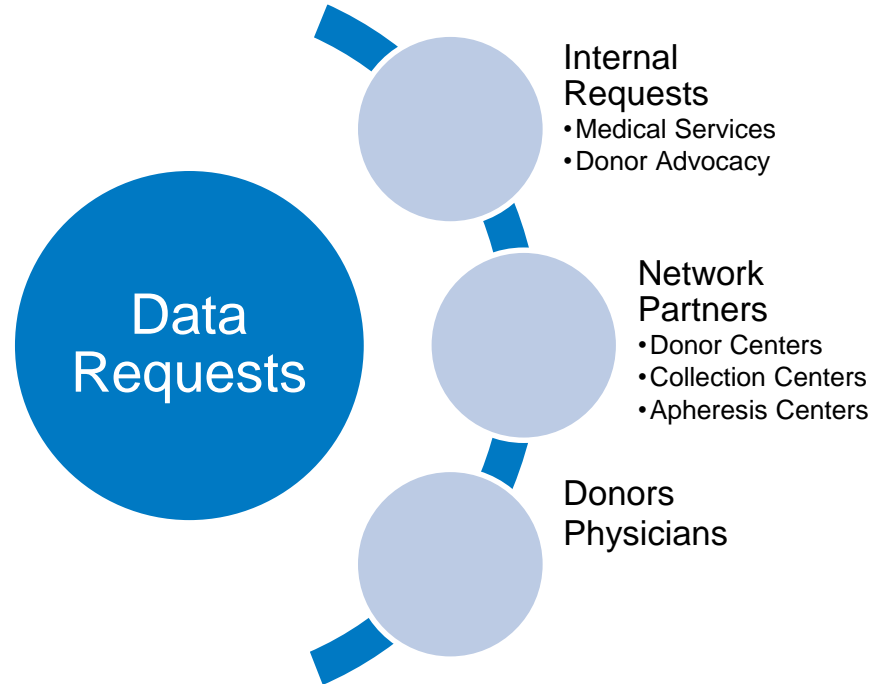
- All PBSC collections done under FDA IND
- Principle Investigator: John Miller, MD, PhD
- Data Collected:
  - Work-up procedures
  - Product collections
  - Product Characteristics
  - Similar types of data collected for marrow donors



# Donor Safety – FDA Annual Report

- Required to submit annual report to FDA for PBSC collections
- Report includes:
  - Donor demographics
  - Donor symptoms and pain assessment
  - Reported adverse events
  - Central line collections

# Donor Safety – Data Requests



# Internal Data Requests

- Requests about the product collections
  - Product TNCs for products collected at a specific center
  - CD34+ counts and liters processed from a specific donor collection
- Requests used for financial projections
  - Number of donors receiving filgrastim broken down by male/female

# Network Partners Data Requests

- Requests about donor collections
  - How many donors received filgrastim but transplant cancelled prior to collection?
- Requests used for IRB renewals
  - Number of donors who consented to the Research Database or Research Repository
- Request about the collection process
  - Average blood volume processed for one-day apheresis collection

# Donor or Physician Data Requests

- Donor diagnosis of specific conditions after donation
  - How many donors have been diagnosed with sarcoidosis
  - Recipient survival status if donor diagnosed with hematologic malignancy
- Questions about recipient engraftment
  - For specific time period, for our donors who donated, did their recipients engraft?

# Quality Assurance



# Quality Assurance - Reports



## Annual Performance Report

- NMDP

## Quarterly Quality Reports

- CIBMTR

# CIBMTR Research

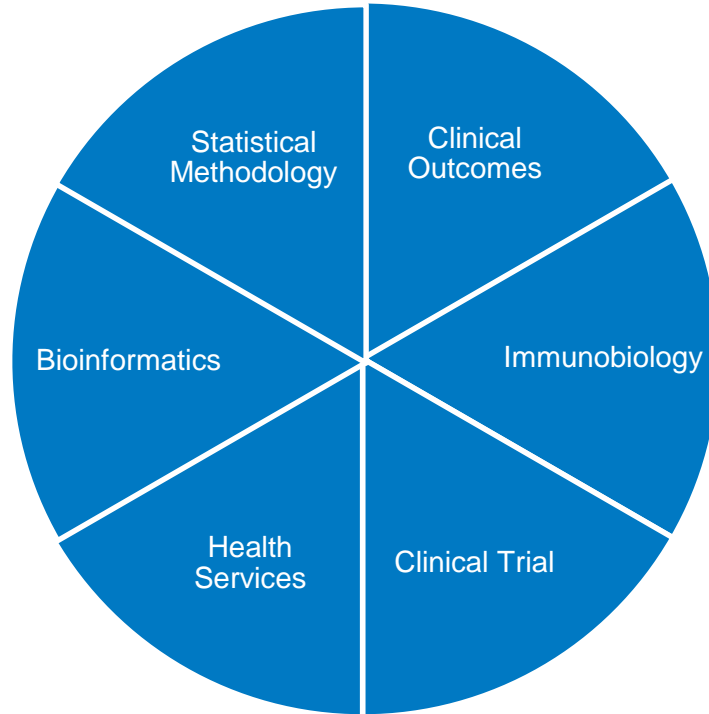


# CIBMTR Mission



- Collaborate with the global scientific community to advance hematopoietic cell transplantation (HCT) and cellular therapy worldwide to increase survival and enrich quality of life for patients.
- Facilitate critical observational and interventional research through scientific and statistical expertise, a large network of transplant centers, and a unique and extensive clinical outcomes database.

# Scientific Programs

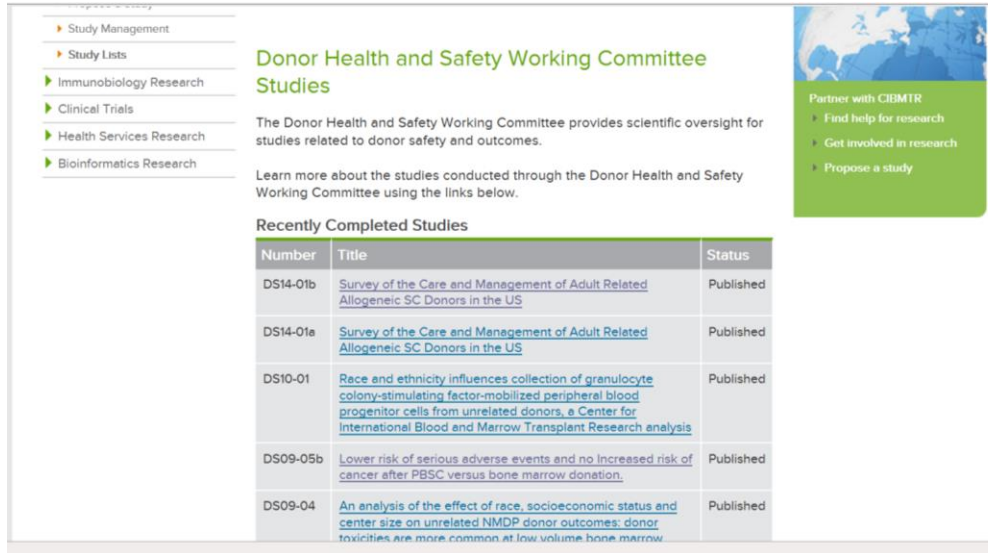


# Donor Focused Research

- Donor Health and Safety CIBMTR Working Committee
  - Provides scientific oversight for studies related to donor safety and outcomes
- Co-Chairs
  - Galen Switzer, PhD, Michael Pulsipher, MD, Nirali Shah, MD, MHSc
- CIBMTR Scientific Director
  - Bronwen Shaw, MBChB, MRCP, PhD
- Ex Officio Senior Advisor
  - Dennis Confer, MD



# CIBMTR Website



The screenshot displays the CIBMTR website interface. On the left is a navigation menu with links: Study Management, Study Lists, Immunobiology Research, Clinical Trials, Health Services Research, and Bioinformatics Research. The main content area is titled "Donor Health and Safety Working Committee Studies". Below the title, a paragraph states: "The Donor Health and Safety Working Committee provides scientific oversight for studies related to donor safety and outcomes. Learn more about the studies conducted through the Donor Health and Safety Working Committee using the links below." Below this text is a section titled "Recently Completed Studies" which contains a table with three columns: Number, Title, and Status. The table lists five studies, all with a status of "Published". To the right of the main content is a green sidebar with the heading "Partner with CIBMTR" and three bullet points: "Find help for research", "Get involved in research", and "Propose a study".

**Donor Health and Safety Working Committee Studies**

The Donor Health and Safety Working Committee provides scientific oversight for studies related to donor safety and outcomes.

Learn more about the studies conducted through the Donor Health and Safety Working Committee using the links below.

**Recently Completed Studies**

Number	Title	Status
DS14-01b	<a href="#">Survey of the Care and Management of Adult Related Allogeneic SC Donors in the US</a>	Published
DS14-01a	<a href="#">Survey of the Care and Management of Adult Related Allogeneic SC Donors in the US</a>	Published
DS10-01	<a href="#">Race and ethnicity influences collection of granulocyte colony-stimulating factor-mobilized peripheral blood progenitor cells from unrelated donors, a Center for International Blood and Marrow Transplant Research analysis</a>	Published
DS09-05b	<a href="#">Lower risk of serious adverse events and no increased risk of cancer after PBSC versus bone marrow donation</a>	Published
DS09-04	<a href="#">An analysis of the effect of race, socioeconomic status and center size on unrelated NMDP donor outcomes: donor toxicities are more common at low volume bone marrow</a>	Published

**Partner with CIBMTR**

- Find help for research
- Get involved in research
- Propose a study

<https://www.cibmtr.org/Studies/Observational/StudyLists/Pages/ObservationalStudies.aspx?OSTID=a0IE00000059llyMAA>

[Biol Blood Marrow Transplant.](#) 2017 Sep 25. pii: S1083-8791(17)30724-3. doi: 10.1016/j.bbmt.2017.09.013. [Epub ahead of print]

## **Donor Experiences of Second Marrow or Peripheral Blood Stem Cell Collection Mirror the First, but CD34+ Yields Are Less.**

[Stroncek DF](#)<sup>1</sup>, [Shaw BE](#)<sup>2</sup>, [Logan BR](#)<sup>3</sup>, [Kiefer DM](#)<sup>4</sup>, [Savani BN](#)<sup>5</sup>, [Anderlini P](#)<sup>6</sup>, [Bredeson CN](#)<sup>7</sup>, [Hematti P](#)<sup>8</sup>, [Ganguly S](#)<sup>9</sup>, [Diaz MA](#)<sup>10</sup>, [Abdel-Azim H](#)<sup>11</sup>, [Ahmed I](#)<sup>12</sup>, [Maharaj D](#)<sup>13</sup>, [Seftel M](#)<sup>14</sup>, [Beitinjaneh A](#)<sup>15</sup>, [Seo S](#)<sup>16</sup>, [Yared JA](#)<sup>17</sup>, [Halter J](#)<sup>18</sup>, [O'Donnell PV](#)<sup>19</sup>, [Hale GA](#)<sup>20</sup>, [Defilipp Z](#)<sup>19</sup>, [Lazarus H](#)<sup>21</sup>, [Liesveld JL](#)<sup>22</sup>, [Zhou Z](#)<sup>23</sup>, [Munshi P](#)<sup>24</sup>, [Olsson RF](#)<sup>25</sup>, [Kasow KA](#)<sup>26</sup>, [Szer J](#)<sup>27</sup>, [Switzer GE](#)<sup>28</sup>, [Chitphakdithai P](#)<sup>4</sup>, [Shah N](#)<sup>29</sup>, [Confer DL](#)<sup>4</sup>, [Pulsipher MA](#)<sup>11</sup>.

# Study Objective

- Evaluate the experiences of NMDP unrelated donors making a second marrow or PBSC donation through 2004 and 2013

# Study Conclusion

- For most donors second donation experiences were similar to first donation experiences, but CD34<sup>+</sup> yields were less.

# Lower risk for serious adverse events and no increased risk for cancer after PBSC vs BM donation

Blood 2014 123:3655-3663; doi: <https://doi.org/10.1182/blood-2013-12-542464>

- We compared serious early and late events experienced by 2726 bone marrow (BM) and 6768 peripheral blood stem cell (PBSC) donors who underwent collection of PBSC or BM between 2004 and 2009 as part of a prospective study through the National Marrow Donor Program. Standardized FDA definitions for serious adverse events (SAEs) were used, and all events were reviewed by an independent physician panel. BM donors had an increased risk for SAEs (2.38% for BM vs 0.56% for PBSC; odds ratio [OR], 4.13;  $P < .001$ ), and women were twice as likely to experience an SAE (OR for men, 0.50;  $P = .005$ ). Restricting the analysis to life-threatening, unexpected, or chronic/disabling events, BM donors maintained an increased risk for SAEs (0.99% for BM vs 0.31% for PBSC; OR, 3.20;  $P < .001$ ). Notably, the incidence of cancer, autoimmune illness, and thrombosis after donation was similar in BM vs PBSC donors. In addition, cancer incidence in PBSC donors was less than that reported in the general population (Surveillance, Epidemiology, and End Results Program database). In conclusion, SAEs after donation are rare but more often occurred in BM donors and women. In addition, there was no evidence of increased risk for cancer, autoimmune illness, and stroke in donors receiving granulocyte colony-stimulating factor during this period of observation.
- [Pulsipher MA](#)<sup>1</sup>, [Chitphakdithai P](#)<sup>2</sup>, [Logan BR](#)<sup>3</sup>, [Navarro WH](#)<sup>4</sup>, [Levine JE](#)<sup>5</sup>, [Miller JP](#)<sup>6</sup>, [Shaw BE](#)<sup>7</sup>, [O'Donnell PV](#)<sup>8</sup>, [Majhail NS](#)<sup>9</sup>, [Confer DL](#)<sup>4</sup>.

# Study Objectives

- Compare the incidence of serious adverse events (SAEs) by donation method (marrow vs peripheral blood).
- Analyze the incidence of hematologic malignancies as well as other cancers in BM donors who were not treated with G-CSF compared with G-CSF-treated PBSC donors.
- Compare both of these groups with expected incidences based on Surveillance, Epidemiology, and End Results (SEER) data.
- Address the concern raised in the literature that G-CSF use in PBSC donation might be associated with autoimmunity or thrombosis.

# Study Conclusions

- BM donors have a threefold higher risk for life-threatening, serious unexpected, or chronic adverse events vs PBSC donors (0.99% vs 0.31%).
- Donors receiving granulocyte colony-stimulating factor for PBSC collection had no evidence of increased risk for cancer, autoimmune illness, and stroke.

# Long-term Donor Follow-up Study

- Primary goal
  - Evaluate if incidence of targeted malignant, thrombotic and autoimmune disorders after unrelated HSC donation are similar between unstimulated BM and Filgrastim-mobilized PBSC
- Phone assessments conducted with donors at one year post-donation; every two years thereafter
- Enrollment initiated October 2010; completed September 2015.
  - As of December 2016, just over 21,500 donors are enrolled and participating
  - Follow up assessment data collection also began in October 2010 and continues through September 30, 2020.

# Donor Focused Studies in Progress

- Comparison between one and two day apheresis in unrelated donors
- Impact of pre-operative collection of auto blood for BM harvest on donor health and outcome

# Recipient Focused Research



### TRANSPLANTATION

## **The effect of donor characteristics on survival after unrelated donor transplantation for hematologic malignancy**

Craig Kollman,<sup>1</sup> Stephen R. Spellman,<sup>2</sup> Mei-Jie Zhang,<sup>3,4</sup> Anna Hassebroek,<sup>2</sup> Claudio Anasetti,<sup>5</sup> Joseph H. Antin,<sup>6</sup> Richard E. Champlin,<sup>7</sup> Dennis L. Confer,<sup>2</sup> John F. DiPersio,<sup>8</sup> Marcelo Fernandez-Viña,<sup>9</sup> Robert J. Hartzman,<sup>10</sup> Mary M. Horowitz,<sup>3</sup> Carolyn K. Hurley,<sup>11</sup> Chatchada Karanes,<sup>12</sup> Martin Maiers,<sup>13</sup> Carlheinz R. Mueller,<sup>14</sup> Miguel-Angel Perales,<sup>15</sup> Michelle Setterholm,<sup>13</sup> Ann E. Woolfrey,<sup>16</sup> Neng Yu,<sup>17</sup> and Mary Eapen<sup>3,18</sup>

Blood 2016 127:260-267;

*On behalf of the CIBMTR Graft Sources Working Committee*

# Study Background

- Searches of unrelated donor registries often identify multiple suitably HLA-matched volunteers
- Various criteria typically used to select a donor
- Conflicting results in the literature on the association of donor characteristics with transplant outcome

# Methods

- Analysis considered the following donor factors:
  - Age
  - Gender/parity
  - CMV serostatus
  - ABO compatibility
  - HLA-A, B, C, DRB1 allele level matching
  - Race/ethnicity

# Study Conclusions

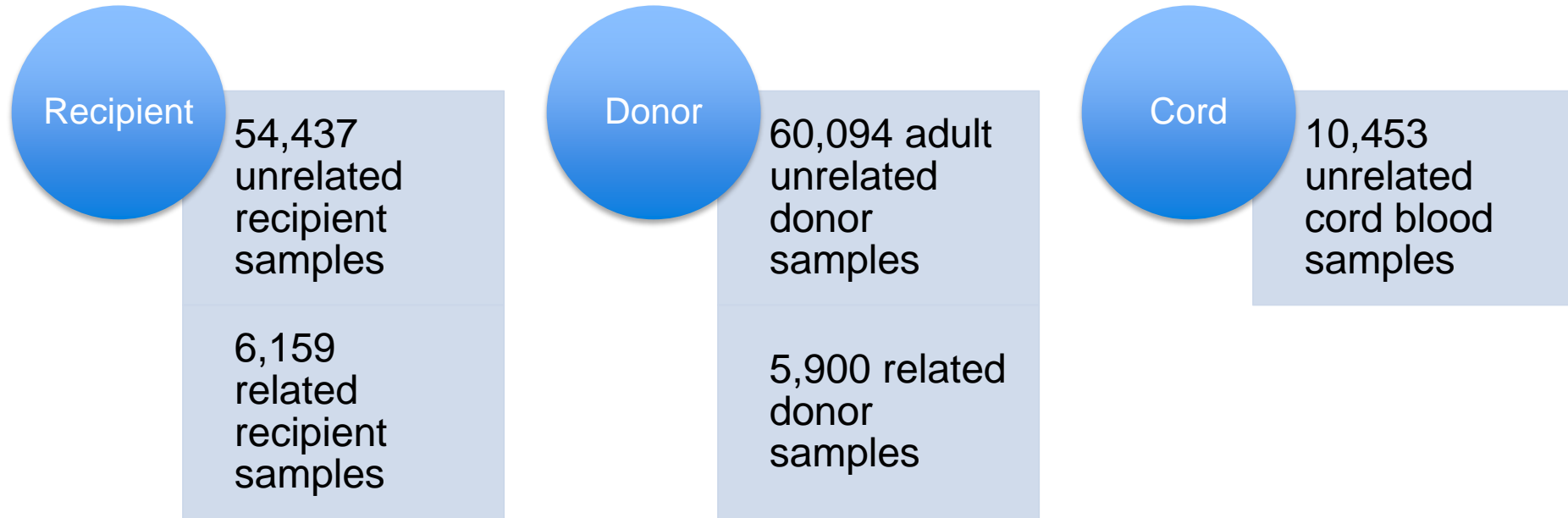
- Age should be considered when selecting among comparably HLA-matched adult unrelated donors
- The effect of ABO matching on survival is modest and must be studied further before definitive recommendations can be offered
- However, a search should not be delayed waiting for the ideal donor to come along

# Research Blood Samples

- Blood collected either just before the marrow or PBSC collection or sometime after the collection
- Cell lines established for research studies
- High Resolution Typing Project



# Research Repository



# 2016 Research Activity Using Research Samples

- Published 7 manuscripts and 2 letters to the editor in peer-reviewed journals
- Presented 9 abstracts at national and international conferences
- Reviewed and accepted 3 new project proposals
- Distributed 15,919 research samples to investigators
- Completed HLA and killer-cell immunoglobulin-like receptor (KIR) typing on >3,000 donor / recipient research sample pairs
- Curated samples from 12,731 participants in the Research Repository (137,044 overall)

# Donor-Recipient Pair Project

- Started in 1994 with funding from U.S. Office of Naval Research
- Goals:
  - Generate data to determine the impact of allele level matching of HLA-A ,B and DRB1 on HCT outcomes
  - Determine the contribution of matching at other loci (HLA-C, DPA1, DPB1, DQA1, and DQB1)
- Unanswered questions:
  - What is the importance of matching alleles?
  - If an allele level match is not possible, what is the next best alternative?
  - Are some loci more important than others to match?

# blood

2004 104: 1923-1930  
Prepublished online June 10, 2004;  
doi:10.1182/blood-2004-03-0803

## **Impact of HLA class I and class II high-resolution matching on outcomes of unrelated donor bone marrow transplantation: HLA-C mismatching is associated with a strong adverse effect on transplantation outcome**

Neal Flomenberg, Lee Ann Baxter-Lowe, Dennis Confer, Marcelo Fernandez-Vina, Alexandra Filipovich, Mary Horowitz, Carolyn Hurley, Craig Kollman, Claudio Anasetti, Harriet Noreen, Ann Begovich, William Hildebrand, Effie Petersdorf, Barbara Schmeckpeper, Michelle Setterholm, Elizabeth Trachtenberg, Thomas Williams, Edmond Yunis and Daniel Weisdorf

# blood

2007 110: 4576-4583  
Prepublished online September 4, 2007;  
doi:10.1182/blood-2007-06-097386

## **High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation**

Stephanie J. Lee, John Klein, Michael Haagenson, Lee Ann Baxter-Lowe, Dennis L. Confer, Mary Eapen, Marcelo Fernandez-Vina, Neal Flomenberg, Mary Horowitz, Carolyn K. Hurley, Harriet Noreen, Machteld Oudshoorn, Effie Petersdorf, Michelle Setterholm, Stephen Spellman, Daniel Weisdorf, Thomas M. Williams and Claudio Anasetti

## **A perspective on the selection of unrelated donors and cord blood units for transplantation**

Stephen R. Spellman, Mary Eapen, Brent R. Logan, Carlheinz Mueller, Pablo Rubinstein, Michelle I. Setterholm, Ann E. Woolfrey, Mary M. Horowitz, Dennis L. Confer and Carolyn K. Hurley

- Incorporated recommendations on:
  - **Role of anti-HLA antibodies** (Spellman et al. Blood 2010)
  - **PBSC transplantation** (Woolfrey et al. BBMT 2011)
  - **HLA-C matching in UCB HCT**(Eapen et al. Lancet Oncology 2011)
  - **Transplantation for non-malignant disease** (Horan et al. Blood 2012)
  - **Matching at low expression loci** (Fernandez-Vina et al. Blood 2013)
- \*Revision incorporating data through 2017 in process

# Donor-Recipient Pair Project

- Answered critical questions about matching
- Changed clinical practice
- Impacted survival outcome for recipients
- Continues to be important as the role of other non-HLA genes in HCT are examined



# Evaluation Reminder

Please complete the Council Meeting 2017 evaluation in order to receive continuing education credits and to provide suggestions for future topics.

We appreciate your feedback!