

# REPORT DOCUMENTATION PAGE

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1. <u>Contingency Preparedness</u> : Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.					
2. <u>Rapid Identification of Matched Donors</u> : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.					
3. <u>Immunogenetic Studies</u> : Increase understanding of the immunologic factors important in HSC transplantation.					
4. <u>Clinical Research in Transplantation</u> : Create a platform that facilitates multicenter collaboration and data management.					
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FOR  
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Office of Naval Research

And

The National Marrow Donor Program  
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## QUARTER PROGRESS REPORT

### Development of Medical Technology for Contingency Response to Marrow Toxic Agents

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**II.A. Contingency Preparedness – Hypothesis 1:** Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

#### Period 8 Activity:

**Aim A.1.1:** Secure Interest of Transplant Physicians

#### Funding provided by both 0859 and 0704 contracts this quarter:

- Conducted physician education seminar titled: Medical and Organizational Challenges Resulting from a Radiological/Nuclear Emergency Seminar Radiological/Nuclear Emergency.
  - Seminar was held on September 25, 2007 in Bethesda, MD.
  - The Medical College of Wisconsin provided 6 CME credits for attendees
  - 132 people advance registered to attend, and 17 people registered the day of the seminar
  - Topics and key speakers include:
    - Threat Assessment : Brooke Buddemeier, C.H.P. - Lawrence Livermore National Laboratory
    - A Possible Scenario for Nuclear Casualties: Carl Curling, Sc.D. - Institute for Defense Analysis
    - Lessons from the Past: Chernobyl: Alla Shapiro, M.D. - Food and Drug Administration
    - Mass Casualty Event Case Studies:
      - David Rutstein, M.D. - Health and Human Services
      - Nelson Valverde, M.D. - State University of Rio de Janeiro
    - Introduction to Radiation Biology: Michael Robbins, Ph.D. - Wake Forest University School of Medicine
    - Biodosimetry: Albert Wiley, M.D. - REAC/TS & WHO Collaborating Center at Oak Ridge
    - ARS Skin syndrome: Viktor Meienke, M.D. - Bundeswehr Institute of Radiobiology
    - ARS Hematologic syndrome: Theodor Fliedner, M.D. – Ulm University
    - ARS Gastrointestinal syndrome: Martin Hauer-Jensen, M.D. - University of Arkansas for Medical Sciences
    - Radiation-induced Brain Injury: Michael Robbins, Ph.D. - Wake Forest University School of Medicine
    - Multi-organ Failure : Marc Benderitter, M.D. - Institut De Radioprotection et de Surete Nucleaire

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	<ul style="list-style-type: none"> <li>▪ National Response Process - the HHS "Playbook": C. Norman Coleman, M.D. - National Institute of Health</li> <li>▪ New Approaches to Therapy Next Generation Medical Countermeasures: Nelson Chao, M.D. - Duke University</li> </ul>
<b>Aim A.1.2:</b> GCSF in Radiation Exposure	<b>Period 8 Activity:</b> This task is closed.
<b>Aim A.1.3:</b> Patient Assessment Guidelines	<b>Period 8 Activity:</b> This task is closed.
<b>Aim A.1.4:</b> National Data Collection Model	<b>Period 8 Activity:</b> This task is closed.
<b>II.A. Contingency Preparedness – Hypothesis 2:</b> Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
<b>Aim A.2.1:</b> Contingency Response Network	<p><b>Period 8 Activity:</b></p> <p><b>Funding provided by both 0859 and 0704 grants this quarter:</b></p> <p><b>RITN development:</b></p> <ul style="list-style-type: none"> <li>• Completed the signing of 53 centers to participate in RITN: <ul style="list-style-type: none"> <li>○ 37 transplant centers</li> <li>○ 9 donor centers</li> <li>○ 7 cord blood banks</li> </ul> </li> </ul> <p><b>Period 8 Activity:</b> This task is closed.</p>
<b>Aim A.2.2:</b> Sibling Typing Standard Operating Procedures	<b>Period 8 Activity:</b> This task is closed.
<b>II.A. Contingency Preparedness – Hypothesis 3:</b> NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
<b>Aim A.3.1:</b> I.S. Disaster Recovery / Business Continuity Planning	<b>Period 8 Activity:</b> This task is closed.

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<p><b>II.B. Rapid Identification of Matched Donors – Hypothesis 1:</b> Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.</p>	
Aim B.1.1: Increase Registry Diversity	Period 8 Activity: This task is closed.
Aim B.1.2: Evaluate HLA-DRB1 High Res typing	Period 8 Activity: This task is closed.
Aim B.1.3: Evaluate HLA-C Typing of Donors	<p>Period 8 Activity: <b>Impact of HLA-C typing on HR/CT/WU rates and time to transplant</b></p> <ul style="list-style-type: none"> <li>• Abstract accepted for ASHI 2007 annual meeting.</li> <li>• Final report in progress.</li> </ul>
Aim B.1.4: Evaluate Buccal Swabs	Period 8 Activity: This task is closed.
<p><b>II.B. Rapid Identification of Matched Donors – Hypothesis 2:</b> Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.</p>	
Aim B.2.1: Collection of Primary Data	Period 8 Activity: This task is closed.
Aim B.2.2: Validation of Logic of Primary Data	Period 8 Activity: This task is closed.
Aim B.2.3: Reinterpretation of Primary Data	Period 8 Activity: This task is closed.
Aim B.2.4: Genotype Lists & Matching Algorithm	Period 8 Activity: This task is closed.
<p><b>II.B. Rapid Identification of Matched Donors – Hypothesis 3:</b> Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.</p>	
Aim B.3.1: Phase I of EM Haplotype Logic	Period 8 Activity: This task is closed.
Aim B.3.2: Enhancement of EM Algorithm	Period 8 Activity: This task is closed.
Aim B.3.3: Optimal Registry Size Analysis	Period 8 Activity: This task is closed.
Aim B.3.4: Target Under-represented Phenotypes	Period 8 Activity: This task is closed.
Aim B.3.5: Bioinformatics Web Site	Period 8 Activity: This task is closed.

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<p><b>Aim B.3.6:</b> Maximize software using consultant data</p>	<p><b>Period 8 Activity:</b>  An informational PI meeting was held at NMDP for the internal and external reviewers involved in the Search Strategy Advice program. Updates included: operational efficiencies, new research data, standardized report format, new haplotype/allele data, cord blood matching (single and double cords) information, introduction of Haplogic II, Antigen Recognition Site matching and new applications (HaploStats and MatchView).  The NMDP HLA Search Strategy Advisors provided 409 search strategy reviews to 87 transplant centers during the quarter. External advisors wrote 256 search reviews for 70 centers with an average turnaround time of 4.4 days. Internal advisors completed 153 reports for 58 centers with a turnaround time average of 2.6 days. Average turnaround time for all 409 reviews was 3.7 days.</p>
<p><b>II.B. Rapid Identification of Matched Donors – Hypothesis 4:</b> Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>Aim B.4.1:</b> Expand Network Communications</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>Aim B.4.2:</b> Central Contingency Management</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>II.C. Immunogenetic Studies – Hypothesis 1:</b> HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>Aim C.1.1:</b> Donor Recipient Pair Project</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>

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<p><b>II.C. Immunogenetic Studies – Hypothesis 2:</b> Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.</p>	
<p><b>Aim C.2.1:</b> Analysis of non-HLA loci</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>Aim C.2.2:</b> Related Pairs Research Repository</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>II.D. Clinical Research in Transplantation – Hypothesis 1:</b> Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.</p>	
<p><b>Aim D.1.1:</b> Observational Research, Clinical Trials and NIH Transplant Center</p>	<p><b>Period 8 Activity:</b></p> <ul style="list-style-type: none"> <li>• Renal Cell Carcinoma trial accrual status; 13 total screened since initiation of trial, 1 remains in screening stage, 2 enrolled and transplanted. One patient did die of disease progression which was determined to be unrelated to study participation.</li> <li>• Adult Double Cord trial officially opened on August 8<sup>th</sup>. At the end of this quarter a total of 3 sites are open for enrollment. Sites currently identifying potential patients.</li> <li>• At the end of this quarter 332 patient/donor pairs were enrolled in the PBSC vs Marrow trial. Enrollment and work-ups continue to be strong.</li> <li>• Staff continues to work on various observational studies. CIBMTR submitted 18 abstracts to the ASH meetings of which 2 were from the Immunobiology Working Committee and 4 from the GVHD</li> </ul>
<p><b>Aim D.1.2:</b> Research with NMDP Donors</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>
<p><b>Aim D.1.3:</b> Expand Immunobiology Research</p>	<p><b>Period 8 Activity:</b> This task is closed.</p>

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**ACRONYM LIST**

AABB	American Association of Blood Banks	ICRHER	International Consortium for Research on Health Effects of Radiation
AML	Acute Myelogenous Leukemia	IS	Information Services
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IT	Information Technology
ASBMT	American Society for Blood and Marrow Transplantation	IRB	Institutional Review Board
ASHI	American Society for Histocompatibility and Immunogenetics	KIR	Killer Immunoglobulin-like Receptor
B-LCLs	B-Lymphoblastoid Cell Lines	NCI	National Cancer Institute
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MHC	Major Histocompatibility Complex
C&A	Certification and Accreditation	MICA	MHC Class I-Like Molecule, Chain A
CBMTG	Canadian Blood and Marrow Transplant Group	MICB	MHC Class I-Like Molecule, Chain B
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NCBM	National Conference of Black Mayors
CBS	Canadian Blood Service	NIH	National Institutes of Health
CBU	Cord Blood Unit	NIMS	National Incident Management System
CHTC	Certified Hematopoietic Transplant Coordinator	NK	Natural Killer
CIBMTR	Center for International Blood & Marrow Transplant Research	NMDP	National Marrow Donor Program
CLIA	Clinical Laboratory Improvement Amendment	NRP	National Response Plan
CME	Continuing Medical Education	NST	Non-myceloablative Allogeneic Stem Cell Transplantation
CREG	Cross Reactive Groups	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget
DIY	Do it yourself	ONR	Office of Naval Research
DKMS	Deutsche Knochenmarkspenderdatei	PBMC	Peripheral Blood Mononuclear Cells

