Department of RESEARCH PROGAMS at Walter Reed National Military Medical Center

VOLUME 1, ISSUE 2 | *What I Do Matters!* | APRIL 2014

Welcome to the Department of Research Programs' April 2014 newsletter!

DRP is happy to announce finalists for the Annual Research and Innovation Competition. To view finalists for the Bailey K. Ashford (BKA) and Robert A. Phillips (RAP) awards, please visit the DRP Intranet News page. Winners of these awards will be announced in our May 2014 newsletter.

In this month's newsletter input is provided from each our sections, including welcoming of three new scientists to the Biomedical Research Laboratory (BRL), staff updates for the Center for Nursing Science & Clinical Inquiry (CNSCI), Q&A provided by DRP's Institutional Review Board (IRB) Operations Office, a feature story from Research Protocol Development, a What's new? section highlighting the monthly Reach Out event in the America Building, an Awards Ceremony honoring SSG Jullian Hodges and SPC Robert Martinez, and a list of February 2014 WRNMMC publications.

Please enjoy this month's newsletter and we welcome feedback, recommendations, and requests for further information. Please email our technical editor **gregory.g.greer.ctr@health.mil** with your comments, suggestions, and requests for follow-up information. Remember also that our Intranet site provides a wealth of resources for investigators conducting research.

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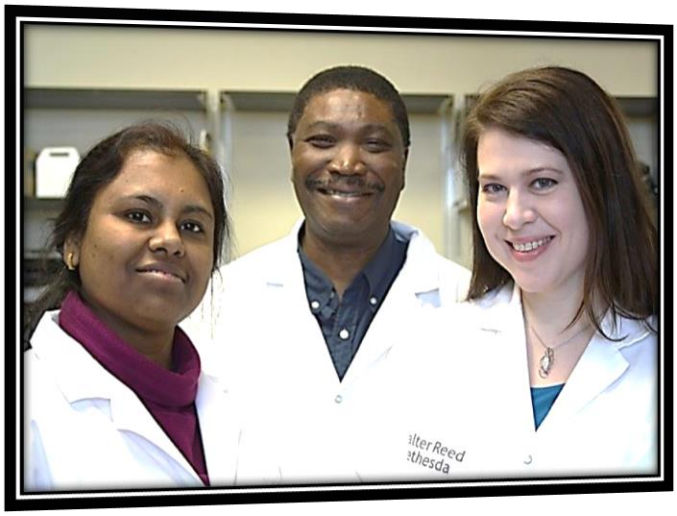
Message from the Chief

I'm happy to report that all of the hard work the Department of Research Programs and WRNMMC investigators and their research teams have done in preparation for the 10-14 March 2014 Army Human Research Protections Office (AHRPO) audit has paid off! The preliminary assessment results produced no significant findings, and the audit team left DRP leadership with valuable feedback on ways we can strengthen our Human Research Protections Program. I am so proud of the many dedicated people who represent the WRNMMC Research Pillar. DRP members, Principal Investigators and study team members, Graduate Medical Education research mentors, and Institutional Review Board and Scientific Review committee members, and others strive every day to ensure the conduct of safe, rigorous research that ensures the protection of human subjects and contributes to military medicine. This audit was a testament to everyone's dedication and represents a job well done.

This was the largest audit ever conducted of a military treatment facility clinical investigation program. The audit included a team of auditors from the Office of the Undersecretary of Defense for Personnel & Readiness (OUSD P&R), Research Regulatory Oversight Office (R2O2), Army Human Research Protections Office (AHRPO), Medical Research and Materiel Command (MRMC), Office of Research Protections (ORP), Clinical Investigations Regulatory Office (CIRO), and the Defense Health Agency Privacy Office. In all, there were a total of 55 protocols audited over a one-week period. In addition, the auditors attended a convened full board Institutional Review Board (IRB) meeting, held a town hall meeting for WRNMMC Principal Investigators and their research teams, and met with the IRB members and Chairpersons, the Scientific Review Committee, and the Office of Research and Technology Applications (ORTA).

The work doesn't stop there. By mid-May, we hope to have the AHRPO final audit report. In the weeks that follow, we will be compiling the auditors' recommendations, updating our WRNMMC Investigator's Guide and solidifying some processes through written Standard Operating Procedures (SOPs). We will be highlighting these changes during our Research Roundtables, Outreach Events, and through daily education offerings provided by DRP staff. See our education calendar on our Internet site for the topics, times, and locations of these offerings. Also, please stay up to date on the latest version of our WRNMMC Investigator's Guide and SOPs through our Intranet site and IRBNet. By the end of summer, the WRNMMC Assurance will be officially transitioned for a three-year period from AHRPO to the OUSD P&R, R2O2, reflecting the alignment of the National Capital Region-Medical Directorate (NCR-MD) under the Defense Health Agency.

Biomedical Research Laboratory (BRL)



The BRL Welcomes New Scientists

Sumana Mukherjee Dey, PhD, (left) is a biochemist. She graduated her PhD from Jadavpur University, India, in 2002, and served as a Research Associate at the Indian Institute of Biology from 2002 to 2003, Post-Doctoral Visiting Fellow at the National Institutes of Health (NIH) from 2003 to 2004, Visiting Fellow at Johns Hopkins University School of Medicine from 2004 to 2005, and in several advanced fellowship and research positions at NIH's National Cancer Institute from 2006 through 2012.

Robert Taylor, PhD, (center) graduated with his PhD in Physiology from Kent State University. His post-doctoral work at the National Jewish Medical and Research Center focused on the Immunological alteration in *M. avium*-infected mice. Dr. Taylor currently serves as a Research Scientist specializing in Immunology/Microbiology.

Cristina Caplinger (right) holds a Master of Science in Biotechnology from Johns Hopkins University. She currently serves as a Research Scientist in the BRL. Previously, she served as a Research Associate at Battelle National Biodefense Institute, an Agricultural Laboratory Scientist at the Maryland Department of Agriculture, and as a Research Assistant at University of Maryland Baltimore Campus (UMBC).

Molecular Biology Short Course

The BRL's Molecular Biology Short Course was held with tremendous success on each of three Wednesdays (i.e., 12, 19, and 26 March) from 1300-1700. Part of the course was a lecture—the rest was held in the Molecular Biology Lab. Sixteen students participated.

Q&A

Can specimens be temporarily stored in the minus 80 degree Celsius freezers if I do not have an IRB-approved protocol? If so, are there any fees associated with the storage?

Yes, samples can be stored based on availability of space. The BRL has a freezer request form (available from the BRL Laboratory Operations Officer by calling 295-8282) that is required to be filled out and assessed based on several criteria: how long will the samples need to be stored, how often might someone need access to the samples, etc. The BRL will start charging fees for freezer storage soon.

Can a Principal Investigator (PI) and Associate Investigator (AI) bring chemicals into the BRL that are to be used for an IRB-approved protocol?

If the PI/AI/lab technician wants to bring chemicals into the BRL they must first request permission from the Laboratory Operations Officer because the chemicals will need to be added to the Authorized User List (AUL), which is a mechanism to track chemical inventories. There are some restrictions on which types of chemicals that can be brought into and/or stored in the lab; for example, Environmental Protection Agency (EPA) Listed Resource Conservation and Recovery Act (RCRA) category P agents (40 CFR §261.33) are restricted.

Center for Nursing Science & Clinical Inquiry (CNSCI)

Staff Updates

MAJ Kyong Hyatt (left) was selected by Sigma Theta Tau International for a podium presentation at the 25th International Nursing Research Congress in Hong Kong this July. This is a very prestigious honor and it brings great credit to the research she has conducted related to reintegration of military personnel with traumatic brain injury (TBI) for married couples.

COL Jeffrey Ashley (right) was the invited speaker for Quality Rocks, the WRNMMC PI Course, relating to his expertise in distinguishing between the differences of research, quality improvement, and evidence-based practice.

CDR Michele Kane has transferred to the new Department of Health Affairs in Washington, DC, as the Executive Assistant to the Commanding General.

COL Ashley is now the CNSCI Chief.

Institutional Review Board (IRB) Operations Office

Q: Where can I get a copy of the IRB Handbook?

The IRB Handbook (table of contents and chapters) can be accessed through IRBNet. Please access the "Forms and Templates" link and choose "WRNMMC Department of Research Programs (DRP) – Documents for Committee Members" to access the handbook.

Q: When are the IRB Meeting dates?

In IRBNet choose the "Forms and Templates" link. Choose "WRNMMC Department of Research Programs (DRP) – Documents for Researchers" and access the document "WRNMMC IRB 2014 Meeting schedule."

Q: Can I still continue my research study after my IRB approval has expired?

Research that continues after IRB approval expires is considered research conducted without IRB approval. All research-related activities, including, but not limited to, recruitment, enrollment, follow-up procedures, and data collection/analysis, must cease once IRB approval has expired.

No further research-related activity may take place until you receive notification that your research study has been granted IRB approval to continue.

If you believe that ceasing research activities places subjects at risk, then you must request that research activities continue in the best interest of enrolled subjects. Please contact the WRNMMC Department of Research Programs (295-8239) immediately to speak with Mary Kelleher, Human Protections Administrator, or Debbie Dasgupta, Director of IRB Operations.

Research Administration

Determining Research Related Costs and Securing Necessary Impact Statements

Significant debate is found in the regulatory community regarding who should bear the cost of the regulatory review process. Within the Department of Defense (DoD), it is recognized that use of Federal monies to support research and to support local infrastructure (including the OIRB) constitutes a commitment from DoD in support of the regulatory enterprise. For commercially sponsored research, however, support of the research is less well defined. Therefore, WRNNMC has established a requirement that Principal Investigators (PI) clearly define all research-related costs above standard of care services that will be incurred in the performance of a research protocol.

For extramurally funded research studies, the WRNMMC IRB requires the research team to submit a budget that clearly outlines research-related costs for services delivered to study participants that are above and beyond what would be considered standard of care. Moreover, the PI must secure an impact statement from any department or clinical service (i.e., Laboratory, Radiology, Pharmacy, Nursing, etc.) whose services or personnel are necessary for support of the conduct of the proposed clinical research study. This impact statement documents the department or clinical services' recognition of, willingness, and capacity to support the services requested in support of the research protocol. Any extramurally funded research that will utilize the services of DRP will be expected to provide reimbursement for IRB-related costs.

This will not be applied to Oncology or Graduate Medical Education studies. In instances of extramural small grant funding, investigators may submit a request to DRP to waive IRB-related fees along with a detailed budget and justification for an exception to this policy.

The Human Protections Administrator (HPA) and/or Director of the IRB (DOIRB) will refer investigators to the Research Protocol Development section, DRP, for questions regarding completing the form "Research Visits Costs Calculator (Extramural)," as well as for securing all applicable Impact Statements.

Assessment and Collection of Fees; Completion of Impact Statements

Research costs above the standard of care will be clearly defined by the research team in the form "Research Visits Cost Calculator (Extramural)," which is available in the IRBNet Forms Library.

Impact Statements will be completed by the research team and submitted for approval by the department/clinical service providing the proposed service. Instructions regarding completion of the Impact Statements as well as appropriate points of contact are available in the IRBNet Forms Library in the document "Resource Impact Statement Instructions WRNMMC."

Collection of fees will be performed by the Research Administration section, DRP.

Regulatory review will proceed while payment is confirmed. Failure of the PI (or the PI's sponsor) to provide payment by the time of the next regulatory action (e.g., failing to provide payment at initial review by the time of the first continuing review), may result in a local suspension of the protocol pending receipt. Local suspension may only be lifted once receipt of the fee is confirmed.

The WRNNMC IRB fee will be reviewed periodically and updated as deemed appropriate by the DRP Chief, OIRB staff, and IRB members.

Use of Collected Fees

Collected research fees will be used to reimburse those services that provided assistance in the performance of research.

Use of all fees is subject to applicable hospital regulations and concurrence of the DRP Chief.

An itemized accounting of all disbursements will be provided by the Research Administration section, DRP, at the time of reporting of receipts.

Research Protocol Development

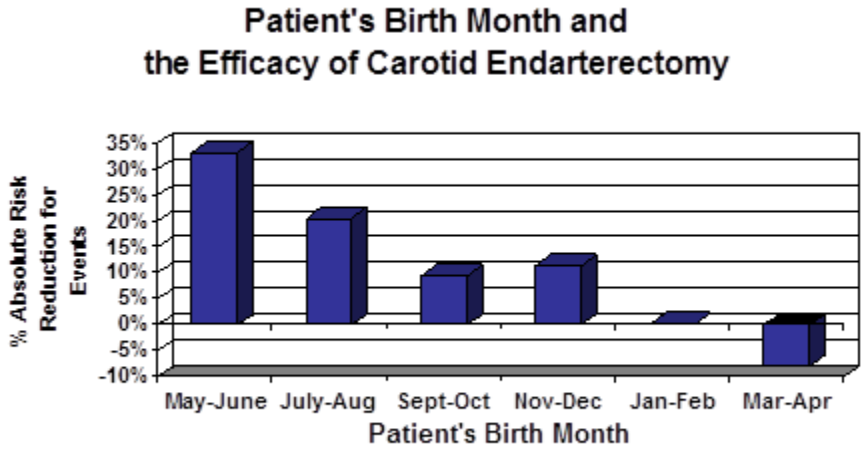
The Perils of Sub-Group Analyses

A patient comes into your office and announces, "Now that I'm 50 years old, I would like every possible lab test and I'm glad to pay for them myself if necessary." You diplomatically explain that this is not possible. You have been trained to understand that the more tests completed on a single patient, the more likely you will find an abnormal result due to chance (rather than due to some underlying disease).

In research, this problem of "too many clinical tests" has a counterpart called "multiple comparisons." This occurs when a researcher examines 10, 20, or 30 different outcomes. Or the investigator will study six different doses of a drug and compare A to B, A to C, A to D…over 20 possible pairwise comparisons between the different doses.

To avoid this problem of multiple comparisons, the researcher should specify one or two **primary** response variables. Additional outcomes may be examined, but the results should not be presented as confirmatory, but rather as exploratory results that warrant further research. If the researcher must examine many outcomes, the sample size can be increased appropriately, and the P value that is used to determine significance should be adjusted based on the number of outcomes studied.

An article in *The Lancet*[1] provides numerous historical examples of clinically important subgroup comparisons in the literature, which have been subsequently shown to be false. The author provides guidelines for the planning, analysis and reporting of subgroup analyses. For example, consider the following data from this article:



Who would have guessed? Based on this subgroup analysis, endarterectomy for severe carotid stenosis is very beneficial for patients born in May-June, but may be harmful for patients born in March through April.

Be wary of presenting too many outcomes or making too many comparisons in your research. Just as you do not want to provide a patient with a false positive test result, you should not send articles with false conclusions to your medical journals.

[1] Rothwell PM. Treating individuals 2. Subgroup analysis in randomised controlled trials: importance, indications, and interpretation. *Lancet*. Jan 8-14 2005;365(9454):176-186

Research Oversight and Compliance Office (ROCO)

What is a protocol deviation and when do I report it?

ALL major deviations must be reported within 24 hours of the event using the Reportable Event Submission Form. The IRB criteria for defining major deviations include any of the following:

1. The deviation has harmed or posed a significant risk of substantive harm to research subjects;
2. The deviation compromised the completeness, accuracy, and reliability of the study data;
3. There is evidence of willful or knowing professional misconduct on the part of an investigator or study staff;
4. The deviation involves serious or continuing non-compliance with Federal, state, or local research regulations or flouting of ethical principles.

What are examples of deviations?

In general, anything outside of the normal protocol is a deviation. To be more specific here are some instances (but not limited to and depending on your individual study):

1. Protocol-required procedures such as labs were not completed (minor)
2. Subject is out of window (minor)
3. Study medication/investigational device is lost (major)
4. Patient did not sign informed consent or signed an expired consent (major)
5. Wrong investigational medicine was given to the subject (major)
6. After subject enrolled, it was found that they did not meet inclusion/exclusion criteria (major)
7. Enrolled subject who did not meet inclusion/exclusion criteria (major)
8. Site over-enrollment (minor)
9. Copy of consent form not given to subject during informed consent process (minor)
10. Subject did not return diary (minor)

Where do I find more information?

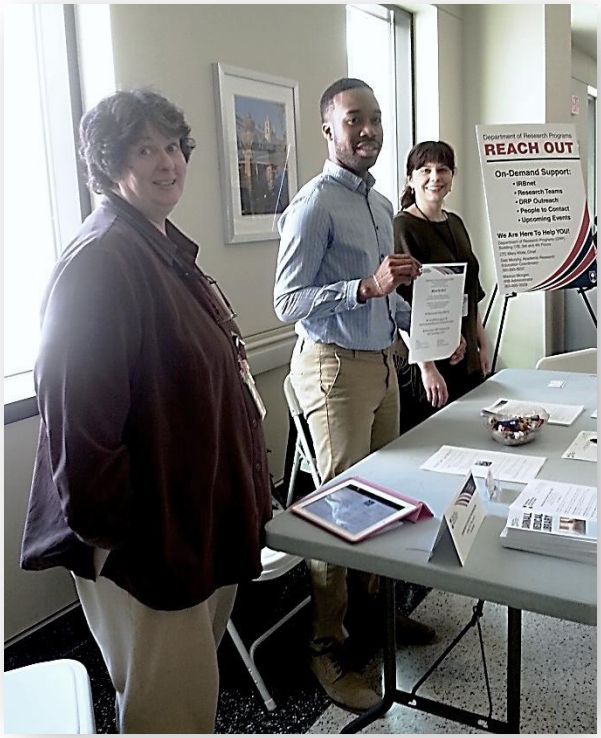
The IRB Handbook offers guidance and policies and can be accessed using this link:

https://www.wrnmmc.intranet.capmed.mil/EducationTrainingResearch/ResearchProgramsDepartment/IBR Member Support/Handbook/IRB Handbook.pdf

What's New?

DRP Monthly Reach Out

As the DRP Academic Research Education Coordinator, Dr. Murphy (above) is frequently asked about how users can access training and certifications, register for research courses, and get support for submitting publication clearance requests.



Ann Holman (left), Biomedical Learning Resource Center Librarian, Marcus Morgan (center), IRB Manager, and Angela Quispe (right), IRB Manager, host DRP monthly Reach Out in the America Building.

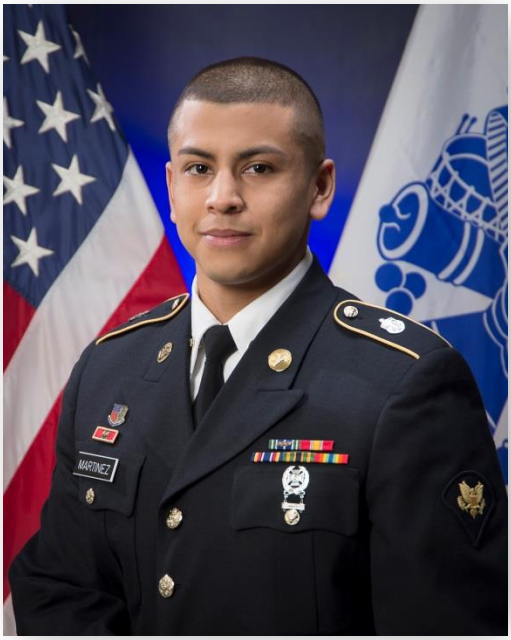
Many other requests find their way to Dr. Murphy. In answer, Dr. Murphy is now offering a curriculum of 20- to 30-minute classes once a day, including weekly morning classes held in the DRP Conference Room 3083 on the 3rd Floor, monthly department orientation to newcomers, a Research Roundtable for key research personnel, and a the monthly Reach Out for on-demand IRBNet support.

To register for these events, please contact Mr. Daniel Rosen who maintains the registration and email distribution lists. Daniel may be contacted at 295-8258 or **daniel.g.rosen.civ@health.mil**.

Awards

Mr. Marcus Morgan receives a Certificate of Achievement for being the outstanding team player of the month for the Department of Research Programs

CPT Raymond Casteline receives an Army Achievement Medal for his hard work in writing the new policies and procedures for the Biomedical Research Lab



SPC Robert Martinez wins the Soldier of the Year for the U.S. Army Element North Troop Command and receives two Army Achievement Medals

SGT Jullian Hodges is promoted to Staff Sergeant as of 1 March 2014 and receives two Army Achievement Medals

February 2014 WRNMMC Publications

Bebu I, Tate J, Rimland D, et al. The VACS Index predicts mortality in a young, healthy HIV population starting highly active antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2014;65:226-30.

Burch HB, Burman KD, Cooper DS, Hennessey JV. A 2013 Survey of clinical practice patterns in the management of primary hypothyroidism.*J Clin Endocrinol Metab*. 2014 Feb 14. [Epub ahead of print]

Caruso AM, Camacho M Jr, Brietzke S. Recurrent auricular perichondritis in a child as the initial manifestation of insulin-dependent diabetes mellitus: a case report. *Ear Nose Throat J*. 2014;93:E4-5.

Dietsch AM, Solomon NP, Steele CM, Pelletier CA. The effect of barium on perceptions of taste intensity and palatability. *Dysphagia*. 2014;29:96-108.

Eickhoff C, Mei JM, Martinez J, Little D. Idiopathic renal infarction in a previously healthy active duty soldier. *Mil Med*. 2014 Feb;179:e259-62.

George S, Hanson J, Jackson JL. Physician, heal thyself: a qualitative study of physician health behaviors. *Acad Psychiatry*. 2014;38:19-25.

Hohenforst-Schmidt W, Banckwitz R, Zarogoulidis P, et al. Radiation exposure of patients by cone beam CT during endobronchial navigation - a phantom study. *J Cancer*. 2014;5:192-202.

Lam ST, Johnson ML, Kwok RM, Bassett JT. Spontaneous bacterial empyema: not your average empyema. *Am J Med*. 2014 Feb 13. [Epub ahead of print]

Lande RG. Sleep problems, posttraumatic stress, and mood disorders among active-duty service members. *J Am Osteopath Assoc*. 2014;114:83-9.

Leitzen KP, Brietzke SE, Lindsay RW. Correlation between nasal anatomy and objective obstructive sleep apnea severity. *Otolaryngol Head Neck Surg*. 2014;150:325-31.

Mikals SJ, Brigger MT. Adenoidectomy as an adjuvant to primary tympanostomy tube placement: a systematic review and meta-analysis. *JAMA Otolaryngol Head Neck Surg*. 2014;140:95-101.

Miletta N1, Miller ME, Lam T, Chung KK, Hivnor C. The management of pemphigus vulgaris in a burn intensive care unit: a case report and treatment review. *J Burn Care Res*. 2014 Feb 25. [Epub ahead of print]

Min JK, Labounty TM, Gomez MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk prediction of major adverse cardiac events in asymptomatic diabetic individuals. *Atherosclerosis*. 2014;232:298-304.

Moawad FJ, Horwhat JD. Cryotherapy for treatment of radiation proctitis. *Gastrointest Endosc*. 2014;79:209-10.

Radowsky JS, Howard RS, Burch HB, Stojadinovic A. Impact of degree of extrathyroidal extension of disease on papillary thyroid cancer outcome. *Thyroid*. 2014;24:241-4.

Stokes TA, Watson KL, Boss RD. Teaching antenatal counseling skills to neonatal providers. *Semin Perinatol*. 2014;38:47-51.

Trinca KD, Cox TC, Pearl JP, Ritter EM. Validity evidence for the Simulated Colonoscopy Objective Performance Evaluation scoring system. *Am J Surg*. 2014;207:218-25.

van Ryn M, Phelan SM, Arora NK, et al. Patient-reported quality of supportive care among patients with colorectal cancer in the Veterans Affairs Health Care System. *J Clin Oncol*. 2014 Feb 3. [Epub ahead of print]

Waterman BR, Burns TC, McCriskin B, Kilcoyne K, Cameron KL, Owens BD. Outcomes after bankart repair in a military population: predictors for surgical revision and long-term disability. *Arthroscopy*. 2014;30:172-7.

Yeung E, Krantz MJ, Schuller JL, Dale RA, Haigney MC. Ranolazine for the suppression of ventricular arrhythmia: a case series. *Ann Noninvasive Electrocardiol*. 2014 Feb 17. [Epub ahead of print]