

Inquiring Minds

*News and notes from the Department of Clinical Investigation, WRAMC
September/October, 1999*

MAJ Catherine A. Dinauer, MC, to come on board as Assistant Chief, DCI

The Department of Clinical Investigation (DCI), WRAMC is pleased to announce the addition of MAJ Catherine A. Dinauer, MC, effective 01 October 1999. MAJ Dinauer will serve as Assistant Chief, DCI, and as Chief, Clinical Studies Service, DCI.

MAJ Dinauer comes to DCI from the Department of Pediatrics, WRAMC, where she served as a staff pediatric Endocrinologist, fellow, chief resident, and resident, from 1991 through 1999. MAJ Dinauer was a recipient of the General Erskine B. Graves Award for being the outstanding graduating fellow at Walter Reed in 1998.

MAJ Dinauer's primary research interest has been thyroid cancer in children. For her research efforts, she received the Fellow Clinical Research Award of the Society for Pediatric Research. Additionally, during her time at WRAMC, MAJ Dinauer was a semi-finalist for the Bailey K. Ashford Clinical Research Award in 1994 and a finalist for the Bailey K. Ashford Award in 1998.

IRB Calendar

The following Institutional Review Board (IRB) meetings will be held in the months of October, November, and December, 1999:

CLINICAL INVESTIGATION COMMITTEE (CIC):

05 October
12 October
02 November
(The second November CIC meeting is being rescheduled)
07 December

HUMAN USE COMMITTEE (HUC):

19 October
26 October
16 November
23 November
14 December

All meetings will begin at 1300 and will be held in the fourth floor conference room, Building 6, WRAMC.

WRAMC Research Course held on 9 September; over 120 attendees receive training on how to conduct research at WRAMC

DCI presented the WRAMC Research Course on 9 September 1999 at the Holiday Inn Silver Spring on Georgia Avenue. Completion of the Research Course is required for all personnel who wish to serve as a Principal Investigator (PI) on a research project at WRAMC.

Over 120 current and potential investigators attended the course, enduring less than ideal weather and severe traffic congestion to make it to the course on time. The first speaker was MAJ Lisa Moores, MC, Pulmonary Service, who spoke on the topic of developing a research protocol. Next, Dr. David Cruess of USUHS gave attendees an overview of research study design, and stressed the importance of sound study design in producing a solid research effort.

After a short break, Ms. Corinne Maydonovitch of DCI gave a talk entitled, "Protocol Processing from Beginning to Completion", which described the protocol process as it pertains to DCI. This talk gave the attendees step-by-step instructions on how to proceed through the protocol creation and review process. Ms.

Maydonovitch was followed by Ms. Robin Howard of DCI, who gave a talk on how to avoid making common mistakes in protocol design, as well as in research data analysis.

After a lunch break, the program continued with a talk by Dr. Dale Vander Hamm, formerly of the Human Use Regulatory Affairs office in Ft. Detrick, spoke on the current application of human use protection regulations. Dr. Vander Hamm was followed by COL Carl Alving of WRAIR, whose talk entitled, "How Science Works" stressed the importance of inquisitiveness and imagination in research investigations. The last two speakers for the day were COL Thomas Beam of the Borden Institute, who spoke on research ethics, and COL (Ret.) Louis Diehl, currently of Johns Hopkins, who gave a history of the pertinent research regulations in military medicine.

The WRAMC Research Course will next be given early in calendar year 2000; watch CHCS e-mail for an announcement of the next date!

Important news regarding TDY funding through DCI

By the Research Administration Service, DCI

As part of its services to investigators, DCI provides funding on intramurally-funded protocols to allow a Principal Investigator (PI) on a protocol to go on TDY in order to present their research. The following are some guidelines to remember for investigators who wish to access this funding. For additional questions, please call Mr. Ed Garcia, Chief, Research Administration Service, DCI, at (202) 782-7859.

-- Only the Principal Investigator (PI) on a protocol may travel using the travel funding allocated in the protocol budget. Associate investigators, etc. are not eligible.

-- DCI funding to support TDY may be accessed only once during the life of the protocol.

-- Presentations must be cleared and approved by the traveler's service Chief, department Chief, the Public Affairs office, and by the Chief, DCI. The clearance forms can be accessed at the DCI Web site (see below) and in DCI. For assistance in the clearance process, contact MAJ Andrea Stahl at (202) 782-7823. With the clearance form, please submit a copy of the abstract for the publication.

-- DCI is limited to providing one thousand dollars (\$1,000) of financial support to facilitate PI travel. In our experience, this equates to CONUS airfare and three or four days' worth of per diem expenses, depending on the destination. For OCONUS travel, or for CONUS trips which may cost more than \$1,000, investigators are urged to seek funding from their department or service to provide for their travel.

-- To request access to DCI travel funding, an investigator must complete a DCI TDY request form. These forms are available on the DCI site on the World Wide Web at:
(<http://www.wramc.amedd.army.mil/departments/dci>)
Please provide DCI a copy of the schedule of events and registration fee requirements. DCI will prepare the travel orders (DD 1610) and notify the PI for distribution.

-- A completed Travel Voucher (DD1351-2) and supporting documents must be submitted to DCI within 5 working days upon return from TDY. After approval, the voucher is then sent to DFAS in San Antonio for reimbursement via direct deposit to your checking or savings account. A copy of the actual computation and payments will be received through the mail. Please provide DCI a copy of this payment computation.

Research protocol audits: their importance in maintaining research integrity and their processing in DCI

By the Research Review Service and Clinical Studies Service, DCI

(1) Purpose: The Department of Clinical Investigation (DCI) conducts periodic audits on approved WRAMC research protocols in order to ensure "good clinical practice" and to enhance the quality of the research.

(2) Criteria for Audits: Selection of protocols for auditing is based on the following criteria:

- (a) High risk or invasive procedures
- (b) High volume subject enrollment
- (c) Adverse events-Absence of reporting or unexpected number of events
- (d) Multi-center trials
- (e) Identification of significant problems during review of annual reports
- (f) Random selection

(3) Notification: Once a protocol has been selected for an audit, the principal investigator (PI) will be contacted by the Chief of the Clinical Studies Service (CSS) or the Clinical Research Associate. The PI will be provided with written notification confirming the date, and time of the audit. An Investigator's Checklist for DCI Audit with the critical elements required is provided to assist him or her in preparing for the audit.

(4) Audit Procedure: The audit is conducted by the Clinical Studies Service auditor and at least one other individual selected from DCI. In most cases, the Chief, Clinical Studies Service, participates in the audit. If she is unavailable then another experienced member of the CIC or HUC participates in the audit. The administrative record as well as the PI's study records should be made available for auditing purposes. The auditors will review the administrative file and the study records and then complete the clinical studies checklist for DCI audit by assessing the completeness and adequacy of the required critical elements.

(5) Reporting: Once the audit has been completed, the CSS auditors will conduct an exit interview with the PI to review the audit findings and clarify any issues that arose during the audit. A report of the audit findings is prepared by the Clinical Research Associate and reviewed by the Chief, Clinical Studies Service. Recommendations/actions, are recorded. The report of findings is then submitted to the Chief, DCI, the Human Use Committee, and the PI.

Recently- approved protocols at WRAMC

Congratulations to the following principal investigators on their recently approved protocols.

Department of Medicine

Cardiology Service

1221-99 Atrial Fibrillation and Mode-Switching Pacemakers Study: Overdrive Pacing in the Prevention of Paroxysmal Atrial Fibrillation in Patients with Automatic Mode Switching Pacemakers

Wiley, Thomas A., LTC, MC 8/16/99

Hematology-Oncology Service

1520-99CALGB 9863: Phase I Study of Irenotecan (CPT-11) in Patients with Abnormal Liver or Renal Function or with Prior Pelvic Radiation Therapy

Byrd, John C., MAJ, MC 8/6/99

1626-99 A Phase III, Open-Labelled, Nonrandomized, Controlled, Multi-Center Trial to Evaluate the Efficacy and Safety of IDEC-Y2B8 Radioimmunotherapy in Patients with B-Cell Non-Hodgkin's Lymphoma

Byrd, John C., MAJ, MC 8/5/99

1628-99 Phase I Trial of Humanized 1D10 Monoclonal Antibody (Hu1D10) in Patients with Relapsed Non-Hodgkin's Lymphoma

Byrd, John C., MAJ, MC 8/26/99

Nephrology Service

1197-99 The Impact of Therapeutic Plasma Exchange on the Medications Used in Transplantation

Stiles, Kevin, CPT, MC 8/31/99

Department of Obstetrics and Gynecology

4415-99 A Prospective Assessment of Antral Follicle Number and Ovarian Volume to Predict Ovarian Responsiveness in In Vitro Fertilization

Frattarelli, John L., CPT, MC 5/11/99

4416-99 Process of Care Review of Benign Hysterectomy: A Quality Outcomes Management Protocol and the Clinical Value Compass Quality Assessment Model

Fisk, Daniel R., MAJ, MC 9/10/99

4417-99 Evaluation of Metabolic Products of Embryo Culture and their Correlation with Morphologic Appearance and Pregnancy Outcome

Alvero, Ruben, LTC, MC 7/19/99

Department of Nursing

7578-99Development and Evaluation of the Military Nursing Moral Distress Scale

Harris, Janet R., COL, AN 8/23/99

7579-99 Nurses' Influence on Patient Outcomes in US Army Hospitals

Harris, Janet R., COL, AN 8/23/99

Department of Pediatrics

6428-99 Significance of ret/PTC mRNA in Peripheral Blood of Subjects with Diseases of the Thyroid

Fenton, Cydney L., MAJ, MC 5/10/99

6429-99Bone Mineral Density in Survivors of Childhood Thyroid Cancer

Dinauer, Catherine A., MAJ, MC 7/26/99

Department of Surgery

Otolaryngology-Head & Neck Service

2584-99 A New Treatment for Xerostomia in Post-irradiated Head and Neck Cancer Patients

Criswell, Mark A., CPT, MC 5/21/99

2588-99Variations in Orofacial Reflexes with Stuttering Severity

McClean, Michael, PhD., DAC 8/6/99

2589-99 Treatment of Snoring with Palatal Stiffening Injection Sclerotherapy Using Sotradecol- A Pilot Study

Mair, Eric, MC, USAF 8/12/99

Peripheral Vascular Surgery Service

2132-99Candidates for Reconstruction

Hadro, Neal C., MAJ, MC 7/28/99

Urology Service

2885-99An Open-Label Trial of Vasomax™ (Oral Phentolamine) in Patients with Mild to Moderate Erectile Dysfunction Who Have Undergone Bilateral Nerve Sparing Radical Prostatectomy

McLeod, David G., COL, MC 7/28/99

2886-99 Prostate Cancer: A Patient Education Intervention

Moul, Judd W., LTC, MC 7/22/99

2887-99 ALZA Overactive Bladder Registry Design Document

Zorn, Burkhardt H., LTC, MC 9/23/99

2894-99 Database of Urinary Stone Patients

Schenkman, Noah S., LTC, MC 9/24/99

Welcome to the following new DCI employees:

Dr. Gregory Fant, PhD (Biostatistician)--

Biometrics Section,
Research Review Service

Norman Gardner (HMJF administrator)--

Research Administration Service/
Research Review Service

Kim Toppin (Admin coordinator)--

Research Administration Service

Inquiring Minds is published six times a year by the Department of Clinical Investigation, WRAMC, as a service to DCI employees and the WRAMC research community.

Any submissions or questions about content should be directed to the editors:

Mr. William Woodcock, (202) 782-7829

MAJ Andrea Stahl, (202) 782-7823

We want your input!

We try to make the *Inquiring Minds* which DCI communicates to the greater WRAMC community regarding issues pertaining to military medical research in general and WRAMC medical research in particular. From time to time, we would like to know what you, our readership, think about the job we are doing in attempting to achieve that goal. Also, we would appreciate your input as to research issues you would like to see us address.

Please take a moment to complete the questions below (anonymity is preferred) and either send to Mr. Bill Woodcock, co-editor, via distribution, or fax it to (202) 782-3881.

1. Through reading this newsletter, I have a better appreciation of WRAMC's research mission:

(Circle) Agree Disagree

2. I read the lists of newly-approved protocols and recent WRAMC publications which appear in the newsletter:

(Circle) Agree Disagree

3. I feel the length of the newsletter is:

(Circle) Too long Too short About right

BMAR Calendar for October, November, and December, 1999

BMAR will be held on the following dates in October, November, and December, 1999. BMAR is held from 0730-1200 in the Joel Auditorium, Building 2:

7 October
21 October
18 November
9 December

The following DCI personnel have birthdays in the months of October, November, and December:

Eleanor Bicknell
Ed Garcia
MAJ Stahl
Audrey Franklin
Janet Jamison
Wilfred Shelton
Barbara Solomon
Richard Terrell
Yvonne Lukes

Happy Birthday, but please don't forget to attend your BMAR training!!

4. I feel that this newsletter provides a useful service to the WRA MC community and to DCI personnel:

(Circle) Agree Disagree

5. Please indicate what parts of the newsletter you find most useful:

6. Please indicate what parts of the newsletter you find least useful:

7. Please indicate any issues regarding research at WRAMC you would like the newsletter to address in the future:

Recent WRAMC Publications

Congratulations to the following WRAMC investigators on their recently published papers. The list was compiled from a recent MEDLINE search of the literature. Listed articles have been cleared through DCI and the WRAMC Public Affairs Office. If you have recently published, and we have not included your publication, please let us know so we may list your publication in the next issue of the newsletter.

Allen PJ, Shriver, CD. Desmoid tumors of the chest wall. *Semin Thorac Cardiovasc Surg* 264-9, 1999.

Bauer JJ, JT Bishoff, RG Moore, RN Chen, AJ Iverson, LR Kavoussi. Laparoscopic versus open pyeloplasty: assessment of objective and subjective outcome. *J Urol* 162:692-5, 1999.

Byrd JC, C Shinn, R Ravi, CR Willis, JK Waselenko, IW Flinn, N Dawson, MR Grever. Depsipeptide (Fr901228): a novel therapeutic agent with selective, in vitro activity against human B-cell chronic lymphocytic leukemia cells. *Blood* 94:101-8, 1999.

Fenton CL, PM Clemons, GL Francis. How do the results of the diabetes control and complications trial relate to the practice of pediatrics: who should have intensive management? *Pediatrics* 104:1999.

Fincher RK, ED Christensen, AM Tsuchida. Ampullary somatostatinoma in a patient with Merkel cell carcinoma. *Am J Gastroenterol* 1955-7, 1999.

Fincher RK, EM Osgard, JL Jackson, JS Strong, RK Wong. A comparison of bowel preparation for flexible sigmoidoscopy: oral magnesium citrate combined with oral bisacodyl, one hypertonic phosphate enema, or to hypertonic phosphate enemas. *Am J Gastroenterol* 2122-7, 1999.

Goeckeritz BE, M Fillora, K Witherspoon, Q Vos, A Lees, GJ Dennis, DS Pisetsky, DM Klinman, CM Snapper, JJ Mond. Multivalent cross-linking of membrane Ig sensitizes murine B cells to a broader spectrum of CpG-containing oligodeoxynucleotide motifs, including their methylated counterparts, for stimulation of proliferation and Ig secretion. *J Immunol* 1693-1700, 1999.

Hsu DP, AJ Folstad. Resident's column: diabetes mellitus: a challenge for pediatricians of the new millennium. *Pediatr* 104:1999.

Klem C, EA Mair. Four-duct ligation: a simple and effective treatment for chronic aspiration from sialorrhea. *Arch Otolaryngol Head Neck Surg* 125: 796-800, 1999.

McLeod DG, PF Schellhammer, NJ Vogelzang, MS Soloway, R Sharifi, NL Block, PM Venner, AL Patterson, MF Sarosdy, RP Kelley, GJ Kolvenbag. Exploratory analysis on the effect of race on clinical outcome in patients with advanced prostate cancer receiving bicalutamide or flutamide, each in combination with LHRH analogues. The Casodex Combination Study Group. *Cancer* 84:24, 1999.

Moul JW. Rising PSA after local therapy failure: immediate vs deferred treatment. *Oncology (Huntingt)* 13: 985-90, 993; discussion 993-5, 999, 1999.

Stelzle RC, EN Squire. Oral desensitization to 5-aminosalicylic acid medications. *Ann Allergy Asthma Immunol* 83: 23-4, 1999.

Teyhen DS. Physical therapy in a peacekeeping operation: Operation Joint Endeavor/Operation Joint Guard. *Mil Med* 168:4, 1999.

Walden BE, RK Surr, MT Cord, CV Pavlovic. A clinical trial of the ReSound Ic4 hearing device. *Am J Audiol* 8: 65-78, 1999.

DCI Passes FDA Inspection

Throughout August, 1999, inspectors from the Food and Drug Administration visited DCI and inspected the state of the WRAMC research program, including DCI records and files. No deficiencies were noted.

This is again a testament not only to the vigilance of the DCI staff, but an indication of the commitment shown by the entire WRAMC research community towards keeping WRAMC's mission strong. Let's keep up the great work!

CRDA FAQ, part 2

In the last issue of the newsletter we discussed Cooperative Research and Development Agreements (CRDAs), which serve to permit the transfer of resources between the federal government and the private sector. We use CRDAs in cases where private firms wish to sponsor medical research at WRAMC. In most cases, an intermediary organization (HMJF, TRUE, Geneva, FACT, etc.) works with the sponsor, DCI, and the federal physician in order to obtain approval for the CRDA document and to act as a repository for the sponsor's funding.

The last issue's column dealt with why a CRDA is needed, and the CRDA approval process. This column deals with some specific issues relevant to doing research under a CRDA. If you would like a copy of last issue's article, please call (202) 782-7829 and we will send or fax one to you.

More questions frequently asked about CRDAs:

I would like to use my CRDA funds to travel. My CRDA does authorize me funds for travel. I am using an intermediary to manage my funds. Does the intermediary do my travel orders?

No, the travel orders may be done by DCI or by your service. Please keep in mind the guidelines regarding having your travel orders done by DCI, which can be found in this newsletter. The intermediary will be responsible for issuing you a "travel proffer" letter (also known as a Payment of Travel from a Nonfederal Source [PTNS] letter) which will outline which travel expenses will be drawn from your CRDA account. This letter is attached to your travel orders, and the package is sent to DRM for their signature.

My CRDA funding allows me up to \$5,000 for supplies, but I know I'm going to need more. What should I do?

First, you will need to work with your intermediary to determine if the extra funding is available. If so, then the intermediary will need to submit to DCI an amendment to the CRDA, describing whatever changes are desired to be made. The amendment is approved at both WRAMC and CIRO before it may take effect.

I have a CRDA account with an intermediary, but I am leaving the service. Can I take my funding with me?

No, those funds remain property of the intermediary organization. We advise investigators who are leaving the service (or who are leaving for another duty station) to make the proper arrangements as soon as possible with the intermediary to have another investigator assume responsibility for that account. Of course, you will also need to notify DCI under a separate memo of a change in Principal Investigator for that protocol.

I would like to start a multi-center, multi-phase study. Do I need a CRDA for each phase of my protocol (Phase I, Phase II, Phase III?)

The preferred method of handling this issue would be to do a "blanket" CRDA, which would encompass all phases, or parts, of your protocol. Doing so would require that the intermediary (or whoever is authoring your CRDA) would need to get all financial data from the sponsor up front. This data would then be incorporated into the blanket CRDA. So, even though the protocol may be approved by phase, it would be possible to only have to submit one CRDA which would cover all phases of your project.

A drug company has approached me about a project. They have given me an "investigator's agreement" to sign, on behalf of WRAMC, so I can work on their project. I asked the company if they do CRDAs, and they told me that they always have used these agreements. Is it OK just to sign the agreement and forgo the CRDA?

No, in any case in which a federal physician, civilian or military, is being asked to represent WRAMC in an agreement with a private company which involves the sharing of resources and/or information between the two parties, appropriate documents must be prepared and signed by representatives of the institution after legal review.

A CRDA is straightforward to put together, and can be approved along with the protocol. If a sponsor has no experience in designing a CRDA, an intermediary or DCI staff will be happy to assist them.

There are some cases where no resources are being exchanged and the investigator can sign such an agreement. However, to be on the safe side, DO NOT SIGN IT!! Please send it to DCI for our staff to work to decide whether or not the agreement is appropriate for signature.

I have completed my project which was funded through a CRDA. There are leftover funds from the project. Can I use them for something else?

No, you can not. CRDA funding is designed in such a way so that no funds should be left in a CRDA account when the project is complete. Any funds which are left over are not property of the Government, but are property of the intermediary. To this end, we advise that you determine your project length in such a way that you allow ample time for the collection and analysis of data, preparation of publications, and attendance at scientific meetings to present your work.

*Frequently Asked Questions (FAQ)
Regarding CRDAs, Part 1*

