Naval Medical Research Unit Dayton
Wright-Patterson AFB, Ohio

Science Update

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NAMRU-D MISSION:

To maximize warfighter performance and survivability through premier aeromedical and environmental health research- delivering solutions to the field, the Fleet, and for the future.

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Generation of Lab Data to Test Key Assumptions for Making Casualty Estimates: A Case Study with HCN

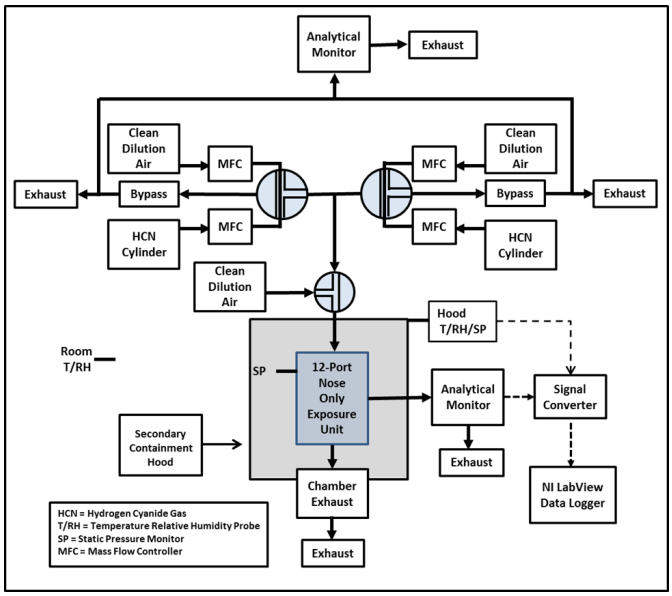
Dr. Lisa M. Sweeney

An accurate understanding of the potential acute vapor/gas lethality of chemical warfare agents (CWAs) and toxic industrial chemicals (TICs) is needed for a variety of applications including military operational risk management and civilian consequence management. The hazard posed by inhalation of CWAs/TICs (from either accidental or deliberate releases) is a function of the manner of the dispersion and transport of the compound to the exposed personnel, the intensity and duration of that exposure, and the toxicological properties of the given chemical. Typically, laboratory animals are exposed for a specified duration to a constant concentration of the compound of concern, effects are observed, and these results guide estimates of human lethality.

Various modeling approaches are applied to address the need for predictive acute toxicity parameters that allow for casualty estimation and planning. The U.S. Department of Defense (DOD) currently uses the toxic load model (TLM; $C^n \times t$ = constant toxicity) to estimate the time-dependency of (military) chemical and biological agents' human toxicity (DOD, 2005). A key assumption in the human risk estimation is that all human exposures that yield the same cumulative exposure, regardless of the concentration-time profile, will produce the same outcome. The validity of this assumption has not been experimentally tested.

Nose-only exposure chamber system

There were no known acute inhalation animal studies that systematically investigated non-constant concentration-time profiles, so the Defense Threat Reduction Agency (DTRA) has funded laboratory studies to fill this information gap (Sweeney et al., 2013). NAMRU-D has conducted such studies and their researchers are collaborating with the Army's Edgewood Chemical Biological Center (Aberdeen Proving Ground, MD) and the Science Applications International Corporation (SAIC) to analyze the data. Historically, typical whole-body exposure chambers could not adequately generate such profiles. However, it is possible with current technology to generate such profiles using nose-only exposure systems. Hydrogen cyanide (HCN) was selected based on previously observed relationships among exposure concentration, exposure duration, and toxicity in rats. To better reflect reality, this study sought to demonstrate the quantitative relationship between non-constant concentration-time profiles and standard fixed concentration-time profiles that have been the historical norm in laboratory toxicity studies. The study design employed at NAMRU-D tests both baseline exposure profiles (i.e., constant concentration exposures) and non-constant exposures that permit the evaluation of specific factors that might influence lethality. For the non-constant exposures, a C × t profile with two pulses of unequal concentration (higher concentration followed by a lower concentration) was used.



Representation of HCN Exposure System

Story continues on bottom of page 2.

Time Course to Recovery of Performance Following Hypoxic Exposure

Dr. Matthew Funke & Dr. Leslie Drummond

Flight safety continues to be a top priority within the NAMRU-D Aeromedical Directorate. Over the past decade, in-flight hypoxic events have increased leading to four Class-A mishaps that cost the U.S. Military over $300 million in aircraft and the lives of four pilots. For the past several years, a significant portion of NAMRU-D's research has focused on the cognitive deficits experienced by pilots and aircrew when presented with hypoxic stress, and how that type of stressor affects flight performance. Previous work at the Naval Aerospace Medical Research Lab (NAMRL), Pensacola, FL and at NAMRU-D has established that participants' cognitive and perceptual performance does not return to baseline levels for up to 24 hours after hypoxic exposure and that these processes are affected much earlier than the Time of Useful Consciousness table suggests.

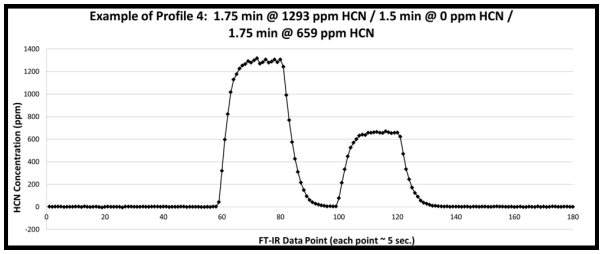
NAMRU-D researcher tests the X-Plane flight simulator used during hypoxic exposure.

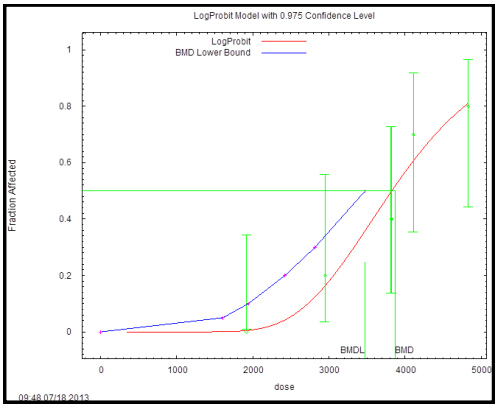
To date, it is unknown how much time is needed for normal cognitive functioning to recover from such an exposure. Current practice and treatment in flight assumes that when physiological recovery (e.g., blood oxygenation, heart rate, etc.) is complete, cognitive functioning also returns to normal. However, previous research conducted at NAMRU-D indicated that is likely not the case. Therefore, the latest experiment will follow participants for significantly longer after exposure to pinpoint when cognitive functioning returns to baseline levels. Participants will be exposed to varying simulated altitudes while performing several iterations of reaction time and perceptual tasks, and will continue to be monitored and tested for the ensuing four hours.

This study will also examine the effect that a five minute treatment with 100% oxygen has on the protracted recovery periods observed in prior studies. If results show that participants' performance levels remain impaired after breathing 100% oxygen, it would imply that following hypoxia exposure, operators remain significantly impaired throughout the remainder of the flight. In such a case, the current practice of treating hypoxia after symptoms present themselves should be abandoned in favor of an approach that detects and mitigates hypoxia prior to symptom onset. Improving aviation safety through hypoxia mitigation continues to be a goal of the research program at NAMRU-D and our researchers are investigating this and other factors related to hypoxia daily."

A Case Study with HCN (cont.)

In Phase 1 of the TLM project (Sweeney et al., 2013), three factors were considered: exposure duration, pulse concentration ratio, and the presence or absence of a gap between pulses. Using a factorial study design, eight exposure profiles were developed to test these three factors ($2^3 = 8$). An additional baseline exposure (15 minutes) was tested to aid in the estimation of the toxic load exponent ("n" in $C^n \times t$). Thus, a total of 11 C × t profiles (3 baseline, 8, nonconstant) were evaluated in Phase 1. An example trace of a concentration vs. profile is provided. The median lethal concentrations were determined for each of the 11 profiles using U.S. EPA's Benchmark Dose Software. In this case study, the TLM was found to be applicable under the tested conditions, with the exception of very brief (<5 minutes), high concentration, discontinuous exposures. Results from this study can aid the DOD and the Department of Homeland Security in identifying the circumstances within which traditional laboratory data can be used to reliably estimate military and civilian casualties from inadvertent environmental releases or hostile use of TICs.





Profile 1 (5 minutes, constant concentration) dose-response relationship (Log probit model, p = 0.872). X axis indicates dose in ppm-minutes.

For further investigation please refer to these two documents:

Department of Defense (DOD). (2005). Potential Military Chemical/Biological Agents and Compounds. Army Field Manual 3-11.9, Marine Corps Reference Publication 3-37.1B, Navy Tactical Reference Publication 3-11.32, Air Force Tactics, Techniques, and Procedures (Instruction) 3-2.55.

Sweeney, L.M., Sharits, B., Gargas, N.M., Doyle, T., Wong, B.A., and James, R.A. (2013). Acute lethality of inhaled hydrogen cyanide in the laboratory rat: Impact of concentration × time profile and evaluation of the predictivity of "toxic load" models. Technical Report NAMRU-D-13-35. Naval Medical Research Unit Dayton, Wright-Patterson Air Force Base, Ohio. < http://www.dtic.mil/dtic/tr/fulltext/us/a579551.pdf.>.

Developing Night Vision Goggle and Rotary-Wing Hands-On Simulation for the U.S. Navy Spatial Disorientation Countermeasures Training System

CDR Richard Folga

As reported previously in Science Update, NAMRU-D's ongoing work to address the persistent and often deadly threat of aviation spatial disorientation (SD) has thus far involved development of an alternative paradigm, firmly grounded in validated sensory-spatial reflexes and emerging definitions of pilot spatial strategies. With a better understanding of the fundamental causes of SD, NAMRU-D scientists have generated unique training concepts for classroom instruction, as well as a low-cost fixed-wing flight simulator to apply these concepts with hands-on training. Both the classroom and simulator approaches address the cognitive processes and spatial strategies that pilots develop and use to deal with the challenges of maintaining spatial orientation in flight. Results from these efforts have led to the creation of innovative methods for identifying SD problems and proposing SD training solutions. NAMRU-D has produced new training applications to help fixed-wing pilots utilize specific cockpit spatial strategies for SD avoidance and recovery. We have recently been charged to begin the initial steps in adapting and extending these new fixed-wing SD simulator training methods to the rotary-wing world, where SD presents the same (if not greater) threat. This effort involves developing a low-cost, medium-fidelity TH-57C Bell Jet Ranger simulator cockpit and Instructor-Operator Station that is compatible with existing off-the-shelf simulation software (Laminar X-Plane). This cockpit will be constructed with off-the-shelf components and will be designed for use in at least one of our existing visual display systems. The end product will be an affordable fixed-base flight simulation system that can be used to develop and validate helicopter SD countermeasure training programs.

The NAVAIR ROBD-SD simulator cockpit, currently installed at NAMRU-D, will be used to assess night vision device stimulation for SD training.

Building on early successes, NAMRU-D has acquired an additional fixed wing aircraft simulator system developed by NAVAIR to deliver both aircraft-specific hypoxia recognition and recovery training (via the Reduced Oxygen Breathing Device) and hands-on SD familiarization. The very first SD scenarios used in the NAVAIR simulator will be those developed for the U.S. Navy and Marine Corps Spatial Disorientation Countermeasures Training System by NAMRU-D researchers. In partnership with PMA-205 (Aviation Training Systems), NAWC-TSD Orlando and Renaissance Sciences Corporation, we will also develop and test the first non-motion SD simulator with authentic Night Vision Goggles (NVG). The first unaided (night time, no NVGs) scenarios to be tested will include the Black Hole Illusion and the Autokinesis illusion. The Black Hole illusion is a common visual-spatial misperception that sometimes results in unintentionally low flight paths during night landing approaches with sparse depth cues and/or limited outside visibility. The Autokinesis illusion, which involves the apparent motion of fixed or relatively fixed light sources against a non-descript, dark, horizon-less background, is also a common problem that may lead to mild or even severe SD. These same two scenarios will be developed and tested using authentic Aviators Night Vision Systems NVGs. It is hypothesized that the NVG condition may be equally as challenging as the unaided condition due to complex sensory-spatial interactions with important changes in the presentation of pilot's spatial cues. System engineering is underway, with data collection scheduled for FY14. This effort is led by CDR Rich Folga, Dr. Fred Patterson and Dr. Hank Williams with critical technical support of Mr. Robbie Powell.

A screen shot of a courseware support product for SD night vision device interaction training as developed by NAMRU-D researchers.

Continued Participation in Consortium Leads to R&D Jointness

NAMRU-D Public Affairs

A meeting of the Tri-Service Toxicology Consortium (TSTC) was hosted 13-14 August, 2013 by the Army Public Health Command at Aberdeen Proving Ground, MD. Among others, NAMRU-D attended via teleconference. During the meeting each laboratory gave updates regarding on-going research and proposed research. NAMRU-D's Environmental Health Effects Research directorate staff members provided six presentations that described collaborative efforts with the US Air Force and US Army. The Center for Environmental Health Research, the Engineering Research and Development Center and the Edgewood Chemical Biological Center represented the US Army. A representative from the office of Mr. John Seibert, Assistant for Safety, health and Fire, Office of the Under Secretary of Defense (Installation and Environment) was present to hear of the TSTC's progress on developing an updated safe blood lead (Pb) level for possible use in evaluating exposure criteria for our personnel working at small arms firing ranges. Joint initiatives such as this are integral in he Charter of the TSTC.

> *The TSTC will participate in technical reviews, interagency organizations, and evaluate various techniques and methodologies for toxicological assessments, with the goal of focusing the science of toxicology towards the pressing needs of the DoD; to minimize duplication and enhance mission capabilities.*
>
> - From TSTC Charter

NAMRU-D Environmental Health Effects scientists who attended the TSTC via teleconference.

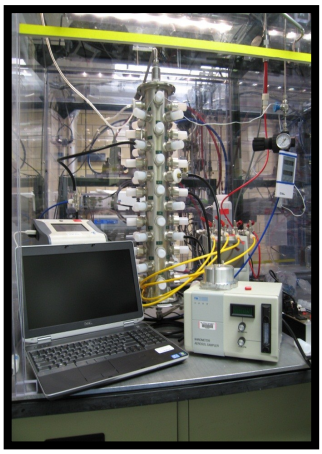
Back left to right: Mr. Arden James, Dr. Michael Gargas, CDR Bill Howard, Dr. Brian Wong. *Front left to right:* Dr. Vivian Vralsted, Dr. Karen Mumy, and Dr. Lisa Sweeney.

Aluminum Nano Particles Research at NAMRU - Dayton

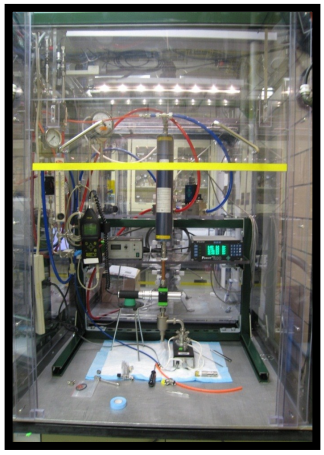
Mr. R. Arden James & Dr. Brian Wong

Engineered Nano materials (ENM), objects that measure 1 to 100 nm, have many unique physical and chemical properties because of their dimensions. ENM are increasingly being used in commercial products such as food, sunscreen and electronic components. These unique properties have led to nano-particles being developed for military-related uses. Aluminum (Al) nano particles are of particular interest to the Department of Defense as either intentionally produced engineered nano materials (ENM) or as by-products, incidental nano materials (INM). ENM are manufactured by chemical processes and have been used to produce reactive accelerants, light weight substitutes for steel, and more durable protective coatings. INM are produced as a by-product of a process such as grinding, milling, abrasive blasting or from arc welding aluminum materials. There are currently few studies of the health effects of breathing airborne aluminum nano materials, either engineered or incidental.

Since the most likely route of exposure for aluminum nano particles is inhalation, collaborative studies have been proposed with the 711 HPW in which NAMRU-D would conduct inhalation exposures to Al ENM. Dr. Saber Hussein of the USAF 711 HPW Molecular Bioeffects Branch/RHDJ, co-located with NAMRU-D at Wright-Patterson AFB, has conducted experimental *in vitro* studies of the mechanisms of aluminum nano particles toxicity based on physical characteristics of size, crystal structure, coating and impurities. At NAMRU-D an *in vivo* inhalation system was constructed using a dry powder generator to aerosolize aluminum nano material into an air stream that was delivered to a nose only exposure unit. The test atmosphere in the exposure unit was monitored for concentration and particle size distribution using sensitive analytical equipment. Proof-of-principle experiments were completed demonstrating a system that can be used for future *in vivo* nanoparticle research. The ultimate result of this testing will be studies that increase the knowledge data base of the health effects of aluminum nano particles in support of military personnel.



Inhalation exposure system showing the nose only exposure unit, an aerosol sampler and a nano particle counter. Mr. Gary Labance, NAMRU-D Aeromedical Program Manager assisted construction of the device.



Aluminum nano particle generation system showing a dry powder generator, an aerosol monitor, an aerosol neutralizer and air flow control devices.

NAMRU - Dayton Visits U.S. Army Aeromedical Research Laboratory, Ft. Rucker, AL

Dr. Richard Arnold

Captain Jeffrey Andrews, Commanding Officer, Naval Medical Research Unit Dayton, and Dr. Richard Arnold, Aeromedical Research director, NAMRU-D visited U.S. Army Aeromedical Research Laboratory (USAARL), Ft. Rucker, AL on September 18, 2013. The purpose of the visit was to enhance alignment of joint aeromedical research initiatives and identify opportunities for greater collaboration. USAARL showcased their capabilities in the areas of en route care, whole body vibration, acceleration, spatial orientation, vision science, and hearing protection.

Dr. Ben Lawson of USAARL presented motion sickness research conducted at USAARL in addition to demonstrating the Tactile Situation Awareness System (TSAS) Lite to Dr. Arnold and the applications in balance disorders and rehabilitation medicine.

NAMRU-D hopes to host a reciprocal visit where they are a tenant command at Wright-Patterson AFB in the near future.

NAMRU-D meets USAARL. Left to right: Tom Harding, Dr. Barazanji, Dr. Lattimore, Col Smyrski III, CAPT Andrews, Dr. Arnold, Dr. Crowley, Dr. Lawson, Arthur Estrada.

Chief Pilot, John Ramiccio, USAARL, demonstrated cutting edge spatial disorientation research to CAPT Andrews while flying with the Tactile Situation Awareness (TSAS) Lite in the H-60 simulator.

Dr. Ben Lawson of USAARL demonstrates the Tactile Situation Awareness System (TSAS) Lite to Dr. Arnold and describes its application to balance disorders and rehabilitation medicine.

NAMRU-D Products & Presentations

Howard, W.R., Wong, B.A., Okolica, M., Bynum, K.S. James, R.A. (July 2013). *The Prenatal Development Effects of Carbon Dioxide (CO2) Exposure in Rats (Rattus Norvegicus).* Retrieved from http://www.dtic.mil/get-tr-doc/pdf?AD=ADA583166.

Sweeney, L.M., Sharits, B., Gargas, N.M., Doyle, T., Wong, B.A, James, R.A. (July 2013). *Acute Lethality of Inhaled Hydrogen Cyanide in the Laboratory Rat: Impact of Concentration x Time Profile and Evaluation of the Predictivity of Toxic Load Models.* Retrieved from http://www.dtic.mil/get-tr-doc/pdf?AD=ADA579551.

Naval Medical Research Unit Dayton Change of Command Ceremony

NAMRU-D Public Affairs

Naval Medical Research Unit Dayton Change of Command was held 22 August 2013 at Wright-Patterson Air Force Base.

CAPT Doug Forcino, previous CO of NAMRU-D, turned the command over to CAPT Jeffrey Andrews, previous XO of NAMRU-D. The ceremony's presiding officer and guest speaker, CO of Naval Medical Research Center (NMRC), CAPT John Sanders applauded CAPT Forcino for his outstanding leadership and overall tour of duty while in command of NAMRU-D.

CAPT Forcino will fulfill his new role representing the Navy at the Army's Medical Research and Development Headquarters and to manage the Army's Military Operational Medicine Research Program as well as the joint Military Operational Medicine research program that is funded by the Defense Health Program.

CAPT Andrews, CO of NAMRU-D is piped ashore.

CAPT Forcino and CAPT Andrews shake hands, as is military tradition, before CAPT Sanders gives them his blessing.

CAPT Sanders presented the Legion of Merit award to CAPT Forcino, "CAPT. Forcino's superb leadership and vision were critical to the growth of new state of the science capabilities and world class laboratory facilities in support of our joint warfighters." Upon receiving the award CAPT Forcino said, "I love NAMRU-D, the people who work here, and my job. But in this business, change is the only constant, and my obligation is to go where the Navy needs me to go." He acknowledged that "being a military spouse is the toughest job in the military – and that applies equally to Navy, Marine Corps, Army and Air Force spouses."

CAPT Forcino thanked the wardroom, government civilians and contract staff of NAMRU-D. "Together, we faced some rather extraordinary challenges" and "in spite of these challenges you have maintained a focus on mission of NAMRU-D and have even expanded our capabilities to serve the needs of the joint warfighter." He identified each science directorate for their "truly remarkable" dedication to the NAMRU-D mission.

As CAPT Andrews assumed command of NAMRU-D, "I am honored and privileged to be given the opportunity to lead you," he thanked CAPT Forcino "for the wise counsel and the many lessons learned… [his] constant guidance, support, and friendship."

Since NAMRU-D's activation date, October 6 2010, the command has experience a good deal of leadership changeover due to the base realignment and closure decisions made in the nation's 2005 BRAC round. The two Navy medical R&D laboratories that merged to form NAMRU-D, "have succeeded in making an organization where the whole is greater than the sum of its parts," said CAPT Forcino.

Following CAPT Andrews speech he presented CAPT Forcino with a binnacle. The Master of Ceremonies and current NAMRU-D XO, CDR Michael Reddix, briefly explained the history of the unique compass, "It protected the ship's compass… had an oil lamp to enable the helmsman to check his course at night. You may have heard of the term 'binnacle list' which gets its name from the old nautical practice of the ship's surgeon tacking the 'Sick-In-Quarters' (SIQ) list on the binnacle each morning so the Captain could view it and get an idea of the health of his crew; very important, especially for a warship that needed every able-bodied sailor to man the decks in battle."

CAPT Andrews presents CAPT Forcino with a binnacle while CDR Reddix explains the traditional meaning of this nautical item.

Prior to the departing of the official party and the boatswain piping the side boys CAPT Andrews said, "Remember and know that each of you makes a difference and your efforts impact operational readiness of our joint warfighters. I challenge you to stay focused, keep motivated, and continue to climb and maintain the NAMRU-D tradition of excellence!"

Commanding Officer's Corner

CAPT Jeffrey Andrews.

Captain Jeffrey M. Andrews, MSC, USN
Commanding Officer

I am honored and privileged to be given the opportunity to lead NAMRU - Dayton into the beginning of its 4th year as Navy Medicine's world class, global aeromedical and toxicology research leader. Our efforts and innovative products continue to be aligned with operational requirements to solve the naval and joint warfighter challenges of the future. As the XO for one year and current CO of nine weeks, I remain impressed with the unmatched professionalism, dedication, and expertise of the NAMRU - Dayton team. I extend my sincere appreciation and gratitude to all of the command staff and to a special leader, CAPT Doug Forcino, who was short toured due to his selection to direct funding across joint R&D programs.

Despite fiscal uncertainty across the DoD and the many challenges facing Research and Development, I am confident in the skills and experience of our team to produce unique capabilities and solutions that will make a difference in warfighter performance and survivability. Our Toxicology capabilities include cutting edge In Vitro Programs, Nano Particle research, and one-of-a kind inhalation facilities, all with applications to real world threats. NAMRU-D's most recent research results with Chemical Warfare Agents and Toxic Industrial Chemicals could prove beneficial in aiding high level decision makers in casualty estimates following toxic exposures of chemicals and/or agents. Our Aeromedical capabilities include state of the art research in Spatial Disorientation, Hypoxia, Fatigue, and Visual Science. Our hypoxia research revealed that longer recovery periods are indicated after hypoxia events compared to historically accepted recovery recommendations. Also, proposals are in work to investigate Night Vision Device stimulation for Spatial Disorientation training, a new concept that has far reaching implications in the way we train and fight.

Even in these difficult times, NAMRU-D is developing innovative methods to expand capabilities and deliver high quality products on time and on target. The pursuit of jointness is becoming more of a reality in our mission. A recent visit to the U.S. Army Aeromedical Research Laboratory (USAARL) was very productive and resulted in a valuable exchange of ideas and potential leveraging of each command's capabilities. Another joint endeavor is NAMRU-D's continued active participation in the Tri-Service Toxicology Consortium which was hosted by the Army in August of this year. In addition, the colocation with the Air Force 711th Human Performance Wing and School of Aerospace Medicine is a tremendous opportunity for joint research and sharing of resources and talent. Reorganization efforts are currently underway in Navy Medicine with the goal of streamlining processes, combining resources, and future R&D joint operations. NAMRU-D will continue to CLIMB, ROLL, and BOOM into the future.

Taking the Helm of Navy Medicine's Aeromedical & Environmental Health Research

NAMRU - Dayton

Commanding Officer
CAPT Jeffrey Andrews, MSC, USN

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