

U.S. Army Medical Materiel Development Activity

USAMMDA



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Commander's Message



My dear colleagues,

It is my pleasure to be able to bring you the USAMMDA Annual Report for calendar year 2003. In last year's report, I told you that we had begun preparing to support Operation Enduring Freedom (which evolved into Operation Iraqi Freedom (OIF) that year). I am proud to tell you that during 2003 we successfully implemented that support.

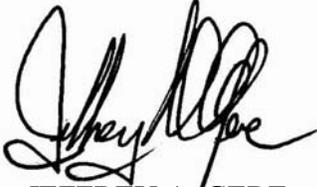
In February, the FDA approved our New Drug Application (NDA) for pyridostigmine bromide (PB – nerve agent pretreatment) and we were able to field it to OIF as a licensed drug. A tremendous amount of work went into this NDA; great thanks are due the dedicated

professionals at USAMMDA, Chem-Bio Medical Systems (CBMS), the U.S. Army Medical Research Institute for Chemical Defense (ICD), and the 18th MEDCOM (Korea) who released COL Jerry Pierson to come back and spearhead this magnificent effort. Fortunately, PB was not needed during OIF. During February we also deployed a Special Medical Augmentation Response Team – Investigational New Drugs (SMART-IND). This team of 10 people task organized from our laboratories, provided direct support to the deployed troops by administering botulism countermeasures (vaccines and drugs) that are under IND. USAMMDA and HQ, MRMC personnel provided the logistical and administrative support that enabled this mission. We also deployed a team to train the troops in the use of hemostatic countermeasures (fibrin and chitosan dressings). These products are designed to stop severe, potentially fatal bleeding, and reports from the field are that several lives have been saved through use of these products. We provided additional support to OIF warfighters by printing and shipping over 250,000 multiple page Post Deployment Health Assessment forms, which were a critical component of redeployment preparations. It is indeed gratifying that we were able to make a difference; this was only possible through a team effort. Many thanks are due MRMC Headquarters, the U.S. Army Institute of Surgical Research (ISR), Walter Reed Army Institute of Research (WRAIR), the U.S. Army Research Institute of Infectious Diseases (RIID), and ICD all of whom contributed personnel to these efforts.

In addition to our support to OIF, we continued our many developmental programs which will ultimately bring new products to the soldier. I invite you to read the descriptions on the following pages that detail some of the great work our people are doing. In October we conducted a Milestone C review on the Dental Field Treatment and Operating System (DEFTOS). This new dental set has now been thoroughly field tested, including evaluation by some OEF/OIF units, and it is now being integrated throughout the military dental support services. Our new, portable, lightweight oxygen generating systems are in prototype and soon will replace the current system of having to transport multiple heavy, unwieldy and dangerous oxygen cylinders to the field.

As always we continue to provide regulatory support to the many clinical trials being conducted throughout the Command. Please visit us at our website, www.usammda.army.mil, or contact us at any time that we can be of service to you.

This will be my final annual report to you as Commander of USAMMDA. It has been a great pleasure to serve you and to be the coach and leader of such a dedicated team of professionals. I wish you all the best in the future.



JEFFREY A. GERE
COL, MS
Commanding

Our Mission

To protect and preserve the lives of America's sons and daughters by developing new drugs, vaccines and medical devices that enhance readiness, ensure the provision of the highest quality medical care to Department of Defense (DoD), and maximize survival of medical casualties on the battlefield.

Our Vision

Military operations of the 21st Century will be more survivable because of USAMMDA initiatives.

- New drugs and vaccines that we developed will protect our personnel from the threats of infectious disease and chemical attack.
- Casualties will be evacuated in vehicles we developed.
- Our combat casualty care products will enhance far-forward medical care.

Lives that otherwise would be lost, will be saved because of the vision and dedication of USAMMDA employees.

Our Personnel

Organizational Chart at Appendix A.

The year 2003 brought many personnel changes to USAMMDA. Due to PCS orders, four officers left, while three were newly assigned. USAMMDA welcomed seven new civilian employees and said farewell to two. Through the various personnel changes our total actual strength has increased by four since last year. Several civilian positions were realigned to more accurately reflect the duties and responsibilities of the position.

A most noteworthy accomplishment of 2003 was the establishment and deployment of the Special Medical Augmentation Response Team (SMART)-Investigational New Drug (IND) Team, on which our Deputy Commander played an important role. When the SMART-IND Team returned from the deployment in Kuwait, our Deputy Commander remained there for over a year and returned after having also served in Baghdad. Two of our other officers were sent on Temporary Duty in support of Operation Iraqi Freedom/Operation Enduring Freedom.

USAMMDA has continued to provide matrixed support to other organizations through Memoranda of Agreement between U.S. Army Medical Research and Materiel Command (USAMRMC) and the parent organizations. Five civilians are matrixed to the PM, Chemical-Biological Medical Systems (CBMS) one civilian and two officers to the PM-MC4, Enterprise Information Systems, two officers to the Telemedicine and Advanced

Technology Research Center (TATRC), and three civilians to the Headquarters, USAMRMC

The following table presents a comparison between 2002 and 2003 personnel strength. Overall, USAMMDA strength varied between 56 and 62.

| 2002 PERSONNEL PROFILE | | |
|-------------------------------|------------|--------|
| Required | Authorized | Actual |
| 75 | 38 | 66 |

| 2003 PERSONNEL PROFILE | | |
|-------------------------------|------------|--------|
| Required | Authorized | Actual |
| 75 | 38 | 60 |

STRENGTH: As of 31 December 2002

| | Military | Civilian | Contractors | Total |
|------------|----------|----------|-------------|-------|
| Required | 18 | 47 | 10 | 75 |
| Authorized | 11 | 27 | 0 | 38 |
| Actual | 17 | 34 | 15 | 66 |

STRENGTH: As of 31 December 2003

| | Military | Civilian | Contractors | Total |
|------------|----------|----------|-------------|-------|
| Required | 18 | 47 | 10 | 75 |
| Authorized | 11 | 27 | 0 | 38 |
| Actual | 14 | 39 | 7 | 60 |

Key Personnel are listed at Appendix B.

Fiscal Performance 2003

In-House: In FY03, USAMMDA's in-house fiscal execution of direct funds exceeded the USAMRMC obligation target by five percent and the disbursement target by 14 percent. The FY03 in-house direct funds included technology-base funds received for quality assurance monitoring, and DHP funds for HIV and Adenovirus support.

| | <u>In-House (Direct)</u> | | |
|-----------------------------|--------------------------|--------------------|----------------------|
| | <u>Allotment</u> | <u>Obligations</u> | <u>Disbursements</u> |
| Fiscal 2003 Dollars (\$000) | 3,925 | 3,920 | 2,760 |
| Target (%) | | 95 | 56 |
| Actual (%) | | 100 | 70 |

In addition, USAMMDA in-house managed \$4.9M in reimbursable funds in FY03. This included funds from the CBMS and PM-MC4 offices for matrix support personnel, from the Marine Corps, and from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and Walter Reed Army Institute of Research (WRAIR) for various task order services.

Program Wide: (Total direct, Congressional and reimbursable) Obligations for the FY03 laboratory and extramural programs exceeded the established target by four to five percent. The laboratory programs exceeded the disbursement target by 16 percent, and the extramural program fell below the target by ten percent. Performance in the total Command-wide development program was five percent above the obligation and disbursement targets. In addition, FY03 total program direct funds reflect a \$12M decrease from FY02 funding. Total program execution exceeded the FY02 actual disbursements by ten percent, and the obligation level by one percent. Fiscal execution performance at the project level is provided on the next page.

| | <u>Program-Wide (Direct)</u> | | |
|-----------------------------|------------------------------|--------------------|----------------------|
| | <u>Allotment</u> | <u>Obligations</u> | <u>Disbursements</u> |
| Fiscal 2003 Dollars (\$000) | 22,591 | 22,570 | 13751 |
| Target (%) | | 95 | 56 |
| Actual (%) | | 100 | 61 |

In FY03, USAMMDA also managed \$13.1M of Congressional funds. FY03 Congressional funds were received for Future Medical Shelter System (FMSS), Life Support for Trauma And Transport (LSTAT), Hemorrhage Control Dressings, Combat Support Hospital (CSH)/Mobile Surgical Unit, Cartledge Infuser, and Hemoglobin Based Oxygen Carrier (HBOC). In total, including direct, reimbursable, and Congressional funding, USAMMDA managed \$40.6M of funds in FY03.

Fiscal 2003 Program Execution Table

| DIRECT – ADVANCED DEVELOPMENT | | | | | | | | | |
|--------------------------------------|------------------|-----------------|-------------|------------|-------------|-------------------|-------------|--------------|-------------|
| | | PERCENT | | | | | | | |
| | Allotment | In-House | | Lab | | Extramural | | Total | |
| Project | (\$000) | OBL | DISB | OBL | DISB | OBL | DISB | OBL | DISB |
| 808 | 4779 | 100 | 87 | 100 | 62 | 100 | 57 | 100 | 64 |
| 836 | 3599 | 100 | 82 | 100 | 75 | 100 | 72 | 100 | 75 |
| 837 | 840 | 100 | 61 | 100 | 100 | 100 | 6 | 100 | 37 |
| Total 6.4 | 9,218 | 100 | 83 | 100 | 67 | 100 | 58 | 100 | 66 |
| 832 | 9041 | 100 | 67 | 100 | 99 | 100 | 53 | 100 | 61 |
| 834 | 731 | 100 | 84 | 100 | 99 | 100 | 58 | 100 | 84 |
| 849 | 3152 | 100 | 55 | 99 | 12 | 100 | 45 | 100 | 44 |
| Total 6.5 | 12,924 | 100 | 65 | 100 | 85 | 100 | 51 | 100 | 58 |
| Total Adv Dev | 22,142 | 100 | 75 | 100 | 74 | 100 | 54 | 100 | 61 |
| Tech Base | 99 | 98 | 72 | 0 | 0 | 0 | 0 | 98 | 72 |
| DHP | 350 | 100 | 29 | 0 | 0 | 0 | 0 | 100 | 29 |
| Congressional | 13070 | 97 | 16 | 63 | 0 | 97 | 36 | 95 | 31 |
| Total Direct | 35,661 | 99 | 45 | 96 | 72 | 99 | 46 | 98 | 50 |
| REIMBURSABLE | | | | | | | | | |
| | | PERCENT | | | | | | | |
| | Allotment | In-House | | Lab | | Extramural | | Total | |
| Project | (\$000) | OBL | DISB | OBL | DISB | OBL | DISB | OBL | DISB |
| CBMS | 1317 | 100 | 44 | 0 | 0 | 0 | 0 | 100 | 44 |
| Other Reimb | 3557 | 100 | 55 | 0 | 0 | 0 | 0 | 100 | 55 |
| Total Reimb. | 4874 | 100 | 52 | 0 | 0 | 0 | 0 | 100 | 52 |
| TOTAL PROGRAM MANAGED | | | | | | | | | |
| | | PERCENT | | | | | | | |
| | Allotment | In-House | | Lab | | Extramural | | Total | |
| Project | (\$000) | OBL | DISB | OBL | DISB | OBL | DISB | OBL | DISB |
| Total Program | 40,535 | 99 | 48 | 96 | 72 | 99 | 46 | 99 | 50 |

Applied Medical Systems Project Management Division

Introduction

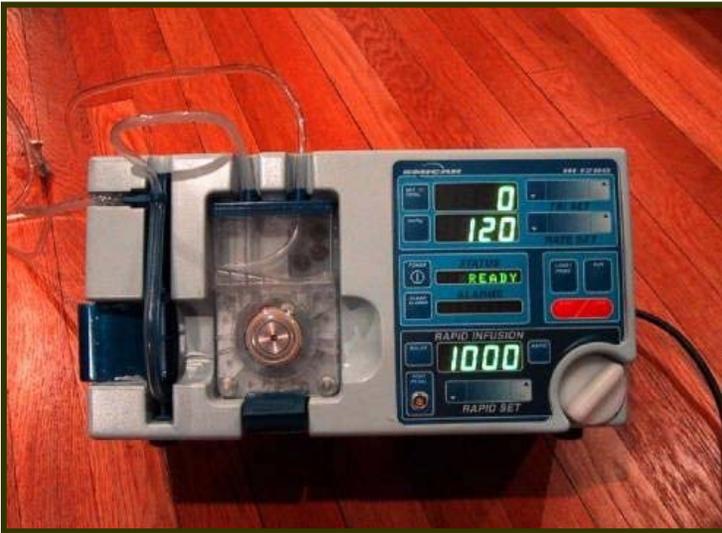
The Applied Medical Systems Project Management Division (AMSPMD) is a multidisciplinary team with broad mission capabilities for the advanced development of medical products used to sustain and support the warfighters. The team consists of both product managers and model makers, who have expertise in project management, engineering, fabrication, and technical testing. The product managers analyze functional requirements, conduct market investigations, and develop and execute technical and program strategies and plans for all acquisition program phases from pre-Milestone A through Full Rate Production. The product managers also direct program resources, and defend program content and structure during science and acquisition forums. The focus for the Division is an early involvement with products that are within the technology base, resulting in streamlined development efforts by combining Milestones and transitioning medical products rapidly to the logistician for procurement and fielding. As a result of this emphasis, product managers are busy with many products either developing and executing broad acquisition strategies or monitoring technology base research efforts. Examples of active products include: Ceramic Oxygen Generator; Dental Field Treatment and Operating System; Future Medical Shelter System; Future Combat Systems – Medical Variants; Hemostatic Dressing; Thawed Blood Processing System; and One-Handed Tourniquet.

Military Relevance

The AMSPMD designs, develops, and tests field medical equipment in support of battlefield combat casualties. The AMSPMD specializes in developing new and innovative breakthrough technology as well as adapting and hardening commercial-off-the-shelf (COTS) systems for joint military applications. For example, AMSPMD personnel were intimately involved with the Navy in the development of a Thawed Blood Processing System for far forward deglycerolization of frozen blood on board Naval ships which will extend the post-wash shelf-life from the current 1-day to 14 days. This will have a dramatic effect on the storage, logistics, and flexibility of processing and utilizing frozen blood.

Cartledge Infuser

The Cartledge Infuser (CI) is intended to allow a physician to normalize a patient's hemodynamic status. The CI is a variable rate infusion pump that allows a physician to replace blood volume at volume rates ranging from 20 milliliters (ml) per hour up to 1200 ml per minute. A blood warming system is incorporated into the design and provides optimal blood warming at any flow rate. The CI operates on standard alternating electrical power, and is capable of battery operation for up to one hour. It



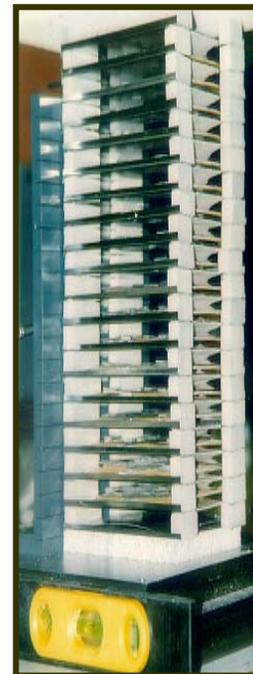
weighs approximately 18 pounds, and is 14 inches wide, 8 inches high, and 8 inches deep.

Design efforts are ongoing and Smisson-Cartledge, the contractor, selected Spartan, Inc., of Deland, FL, to finalize the design and produce the prototype system. A design review meeting at Spartan's facilities was held in August 2003.

Ceramic Oxygen Generator

The Ceramic Oxygen Generator (COG) project is developing leading edge technology for the production of high purity, medical grade oxygen. This type of oxygen generator has an advantage over conventional methods such as pressure swing adsorption by generating very high purity oxygen without using any moving parts. This system uses a metal/ceramic membrane matrix to avoid the cracking and sealing problems that have been experienced by other developers attempting to commercialize COGs.

This past year has further demonstrated the long-term stability of the cells. Improvements to the cell electrodes have produced a five-fold reduction in the power required to produce oxygen. The elimination of high cost electrode materials has greatly lowered the raw materials cost and simplified the manufacturing process. New cells with two active surfaces per cell have been tested and have worked without problems. This design has cut the size and weight of the oxygen generator in half. A lightweight heat



exchanger made of Inconel was fabricated this year. It recovers the heat from the exhaust stream and returns it to the input air stream. The recovered heat nearly doubles the efficiency of the generator.

Critical Care System for Trauma and Transport

The requirement for a Critical Care System for Trauma and Transport (CSTAT) describes a single-patient, intensive care capability that will be used to maintain life support and stabilization of battlefield casualties during evacuation. The CSTAT requires incorporation of a defibrillator, ventilator, vital signs monitor, infusion pumps for fluid resuscitation and administration of medications, suction unit, and self-contained oxygen supply in a unit that attaches to a standard North Atlantic Treaty Organization (NATO) litter. The most recent CSTAT Analysis of Alternatives identified the Life Support for Trauma and Transport (LSTAT) as the lead CSTAT candidate. The LSTAT, which was cleared for marketing by the Food and Drug Administration (FDA), satisfies the majority of the CSTAT requirements. The contractor is currently modifying the LSTAT to fully satisfy those requirements.

The White House Medical Unit (WHMU) continues to employ an LSTAT in its operations. An LSTAT was also deployed to the Joint Trauma Training Center (JTTC) in Miami, FL. Another LSTAT was deployed with a surgical SMART (SMART) out of Tripler Army Medical Center. This SMART is currently providing humanitarian surgical care in Cambodia where it is using the LSTAT as a surgical platform. The WRAIR continues to use an earlier version LSTAT system for research, demonstration, and training purposes.

In February 2003, the U.S. Central Command (CENTCOM) Surgeon requested the deployment of additional LSTAT systems to support medical operations. In response, all fielded LSTAT systems, with the exception of the WHMU, JTTC, and WRAIR systems were recalled for subsequent CENTCOM deployment. A total of 10 LSTAT systems (including the one currently deployed to Cambodia) were deployed in response



to this order. Examples of deployed medical units that have utilized the LSTAT include: the 86th CSH, the 115th CSH, the 865th CSH, the 801st CSH, the 47th CSH, and the USS Tarawa.

Sixteen LSTAT systems have been manufactured and fielded under a cooperative agreement, which is now being closed out. Nine more systems are being fabricated under a contract through the U.S. Army Medical Materiel Agency (USAMMA). Currently four of the nine LSTAT systems have been fabricated under a contract through USAMMA. The remaining five systems will be manufactured and delivered by 30 July 2004.

Upgrade modifications of the LSTAT include a new vital signs monitor, infusion pump, and defibrillator. Explosion safety validation has been successfully completed, and air-worthiness validation at China Lake, scheduled for 1QFY04, will complete testing.

Dental Field Treatment and Operating System

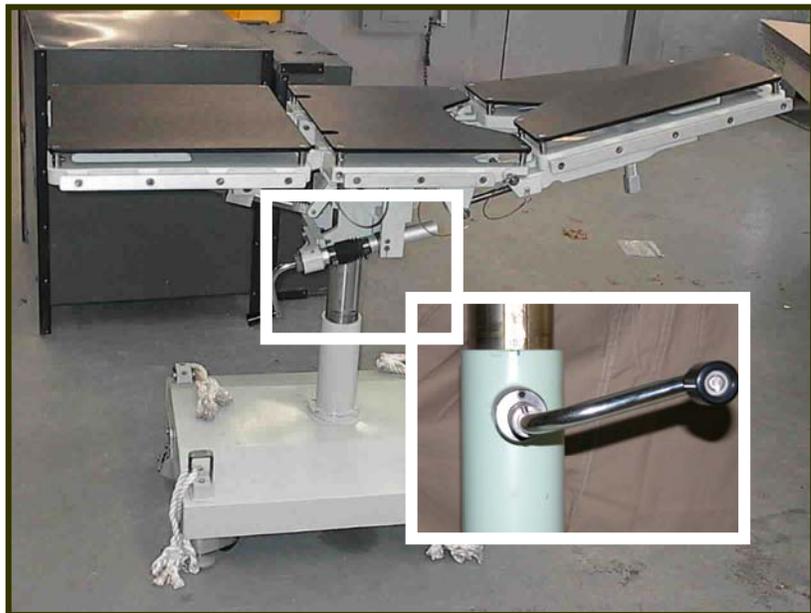


The Dental Field Treatment and Operating System (DEFTOS) incorporates the latest technology to provide a modern, lightweight dental system for field operations. It reduces the need for compressed air and thus large power generator capacity in the field. The unit incorporates an electric hand piece, which produces superior torque compared to previous systems.

During CY03, worldwide user evaluation was conducted of 20 units. The evaluation results showed a user approval rate of 85 percent. There were several changes recommended by the users, including 110-220 VAC, 50/60 Hz operations, improved vacuum, and a more comfortable foot switch. The 20 units were modified to incorporate suggested changes and sent back to the users for long-term evaluation.

The U.S. Army Training and Doctrine Command (TRADOC) has approved the Operational Requirements Document (ORD), and an Integrated Product Team (IPT) meeting was held in September 2003 recommending transition of the product for procurement. A Milestone C was approved.

Field Operating Table Improvement



The column lock on the field-operating table has never been secure enough to keep the table from being able to rotate slightly. A new column lock was developed that securely locked the table in position. This will make the table that the Army developed and already owns suitable for use in field hospitals. A commercial table, which weighs 500

pounds more than the Army table, is being used in the Deployable Medical Systems (DEPMEDS) hospitals. The drawings and other information for the column lock have been sent to the National Maintenance Point (NMP) for procurement from a contract machine shop.

Field Sterilizer Improvement Device

The field sterilizer currently in use is a well-proven piece of equipment. One of the shortcomings has been its high water consumption; it uses 2½ -gallons of water every time it sterilizes a load of materials. A water recovery device was being developed before Operation Desert Storm. To meet the immediate need, the prototype was put into production before completely optimizing the design. There is a need to complete the engineering development process to improve the manufacturability and maintainability and to get it fully incorporated into the field hospital equipment set. The new version will need testing to verify its performance and ruggedness.

This project is being coordinated with USAMMA, as well as the combat developer, who has written the ORD and sent it to TRADOC for approval. The current plan is to incorporate the Field Sterilizer Improvement Device (FSID) into the new hospital sets as they are built at the depot; the FSID would be added to the Unit Assemblage (UA) for the Central Medical Supply to equip existing hospitals. The addition to the UA requires a request from USAMMA, and the concurrence of the Directorate of Combat and Doctrine Development.

Future Combat Systems – Medical Variants

The Future Combat System (FCS) – Medical Vehicle-Evacuation (MV-E) and Medical Vehicle-Treatment (MV-T) will function as the ground medical evacuation and treatment assets in the Unit of Action (UA). Medical capability will include an automated litter lift system, on-board oxygen generation, suction, storage space for essential medical items and equipment, automated data management, plus the capacity to carry four litter patients or six ambulatory patients and a crew of three (MV-E), or provide interior space for the treatment of two patients and a crew of four (MV-T).

The Joint Requirements Oversight Committee approved the ORD on 14 April 2003. A Milestone B review was held on 15 May 2003; the system was transitioned to the next phase of development. United Defense, the FCS vehicle manufacturer, has produced several iterations of potential designs (Design Excursions 3 and 4) and is now working on the Best Technical Approach (BTA) for vehicle design. The PM-FCS conducted a Manned Ground Vehicle (MGV) In-Process Review (IPR), and confirmed that the FCS contract does include one MV prototype to be delivered in FY08 in line with the other MGV prototypes. The ORD requirements have been reviewed and all suggested changes have been forwarded to TRADOC for inclusion in the next iteration of the ORD, for anticipated issue in 4QFY04.

Future Medical Shelter System

The Future Medical Shelter System (FMSS) is a multifaceted program, which leverages Congressional funding to explore advanced rigid and soft-walled shelters for forward deployed healthcare providers. The objectives of the FMSS program are (1) to develop a self-contained emergency response package for use by



During a demonstration of the FMSS, Dr. Donald Caldwell, Project Manager, and Mr. Steve Reichard, Deputy Project Manager of the AMSPMD, discuss the benefits of the shelter with Ms. Amy Leighton, NATICK, MA, Mr. Lee Bzorgi, Mr. Terry Bowman, and Mr. Duane Bias, of The ORNL.

Forward Surgical Teams (FST), and (2) to develop a replacement for the DEPMEDS operating room shelter, which has reduced weight and enhanced transportability and deployability. These efforts consist of chemically/biologically-hardened International Standards Organization (ISO) shelter with quick erect/strike times and integrated electrical, water, and medical packages, and provide 1200 square feet of soft tentage as patient care wards. Three development efforts are underway:

The Oak Ridge National Laboratory (ORNL) prototype was displayed at the November 2003 Association of Military Surgeons of the United States (AMSUS) Conference in San Antonio, TX. Conference attendee response was overwhelmingly favorable. Additionally, the Congressional sponsor, Representative Zach Wamp, R-TN, participated in a media day at the ORNL facilities and pledged to seek an additional \$10M in FY05 Research, Development, Testing and Engineering (RDT&E) funds for a next generation prototype effort. This sixty-foot airbeam tentage developed by ORNL, in conjunction with Natick Laboratories and Vertigo, Inc., was demonstrated by Vertigo, Inc., and accepted by USAMMDA in October 2003.

The Mobile Medical International Corporation (MMIC) fabrication is ongoing. Prototype delivery is scheduled for 4QFY04. MMIC will deliver a 3:1 expandable ISO shelter with an integrated environmental control unit and generator, as well as sixty feet of airbeam tentage. MMIC is seeking approximately \$9M in FY05 Congressional appropriations.

The company of EADS-Dornier plans to develop schematic plans for the 3:1 expandable ISO shelter configured as an operating room. Insufficient funds exist for the development of airbeam tentage or fabrication of any prototypes. EADS-Dornier is seeking approximately \$8M in FY05 Congressional funding.

Hemorrhage Control Dressing



The Hemorrhage Control Dressing (Chitosan Dressing [CD]) is intended to provide a revolutionary improvement in the control of severe life-threatening hemorrhage. The CD is manufactured from chitosan; a natural biomaterial derived from shrimp shells. It is intended for use by the combat medic/combat lifesaver and other medical personnel on the battlefield.

The U.S. Food and Drug Administration (FDA) cleared the CD for marketing on 4 November 2002. On 19 June 2003, the FDA gave the manufacturer clearance to market the CD with an Over-the-Counter (OTC) indication. The indicated use for the OTC product is for local management of bleeding from lacerations and other minor bleeding. The prescription label remains in effect for external temporary control of severely bleeding wounds.



This is a simulation of the Chitosan Bandage when used on a severely bleeding lower leg wound. The training mannequin depicts the bandage application when the patient is prepared for transport.

Approximately 3000 CDs were shipped in support of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). Reports of use in OIF indicated the CD worked “amazingly well.”

Requests for CDs were received from the U.S. Southern Command Surgeon; Air Force Special Operations Command Surgeon; U.S. Army Special Operations Command Surgeon; U.S. Special Operations Command (USSOCOM) Surgeon; and the Brigade Surgeon, 1st Brigade, 1st Infantry Division (Mechanized). USAMMDA coordinated with USAMMA to fulfill these requests. An inquiry was also received from the U.S. Pacific Command Surgeon.

With the withdrawal of the Hemostatic Dressing (HD) Investigational New Drug (IND) Battlefield Protocol, USSOCOM instituted a policy of replacing IND HDs one-for-one with FDA-approved CDs.

The Directorate for Combat and Doctrine Development, U.S. Army Medical Department Center and School, approved a Basis of Issue (BOI) for the CD on 3 April 2003. The BOI calls for one CD per Combat Life Saver and five CDs per medic.

The CD was subjected to operational testing by the U.S. Air Force Medical Evaluation Support Activity (AFMESA). The report recommended that specific training materials be developed to support CD field use. A poll of the evaluation team showed that 89% of the respondents rated the CD as either excellent or good.

Hemostatic Dressing

The Hemostatic Dressing (HD) is intended to provide a revolutionary improvement in the control of severe life-threatening hemorrhage. The HD is manufactured from human blood clotting proteins, fibrinogen and thrombin, obtained from expired blood plasma. It is intended for use by the combat medic/combat lifesaver and other medical personnel on the battlefield.

On 8 March 2003, the Office of the Secretary of Defense approved USSOCOM's request to activate a battlefield IND protocol to use the HD to treat soldiers with serious hemorrhage in the CENTCOM area of responsibility. On 20 August 2003, a soldier received multiple gunshot wounds to both thighs and left shoulder while engaged in military operations in Iraq. Under the IND treatment protocol, the team medic applied an HD to the left thigh wound after he was unable to completely control femoral arterial bleeding with pressure dressing and tourniquet. The femoral wound stopped bleeding after the HD was applied. Adequate hemostasis was achieved in the right thigh and shoulder wounds with application of field dressings. The casualty was evacuated to a CSH for initial surgery and then to a U.S. based medical treatment facility for definitive care where the soldier underwent routine wound care and physical therapy. He made an uneventful recovery and has since returned to duty.

The principal investigator withdrew the battlefield IND protocol on 26 August 2003 due to staffing and funding difficulties.

Non-Contact Respiration Monitor



The Non-Contact Respiration Monitor (NCRM) is a device for use by the medic to monitor the respiration of soldiers in Military Operational Protective Posture (MOPP) gear at a distance. It senses the flow of air entering the gas mask filter canister, and causes red or green light-emitting diodes to signal the state of casualty breathing. This will be a new capability for the medic that will be particularly useful for triage in mass casualty nuclear, biological, and chemical environments. It will be lightweight, totally self-contained, and reliable in high noise and vibration environments such as medical evacuation helicopters.

The NCRM provisional patent was filed on 10 September 2003. A second concept design was developed, and a new electronic circuit board is being designed.

One-Handed Tourniquet



The One-Handed Tourniquet (OHT) is being designed to enable a severely wounded casualty to stop his or her own flow of blood in the field when assistance is not available. The plan for the OHT is to eventually be



issued to individual soldiers. Ten thousand of the cinch-design OHTs have been procured, of which half were provided to the Special Operations Command for user evaluation. Ten thousand additional OHTs are being procured by USAMMA for contingency requirements. Initially, to expedite the availability of the OHT, the Center And School decided that each Combat Medic (91W) would be provided three and each Combat Lifesaver would be provided two. A transportable training package has been developed.

Studies show that the device is 100% effective for upper extremity wounds and lower extremity wounds below the knee. More studies are underway and samples from industry and academia are being evaluated for effectiveness on the upper thigh.

Rotary Valve Pressure Swing Oxygen Generator

The Rotary Valve Pressure Swing Oxygen Generator (RVPSOG) is designed to replace the “D” cylinder for patient care and transport. The RVPSOG is a substantial simplification of existing pressure swing adsorption oxygen generator technology. The use of a rotary valve, driven directly by a small motor, eliminates complex valve and control systems used in conventional oxygen generators. Taking advantage of the reduced complexity reduces the weight and size of the oxygen generator and increases the efficiency of the generation process. This project will develop a portable device to meet the combat developer’s requirements for a portable point-of-use oxygen generator.



The RVPSOG manufacturer built and delivered two different types of prototypes this year. The first prototype delivered used reciprocating air compressors, weighed about 14 pounds each, and used standard lithium ion batteries. These prototypes were each small enough to fit into an airline-size carry-on bag. The second set of prototypes, which are

approaching the objective requirements, are smaller, use a new scroll compressor technology, weigh about 10 pounds, and use a high energy density type of lithium polymer battery. Although the second set of prototypes are a significant improvement over the first, the performance characteristics of the scroll compressor are not well known. For this compressor to be used in a medical device, its failure modes and wear characteristics will have to be well understood; this testing is currently underway. The requirement for oil free operation significantly increases the compressor complexity. A free piston linear compressor is being evaluated as a back-up design.

Special Medical Emergency Evacuation Device

The Special Medical Emergency Evacuation Device (SMEED) is a lightweight platform designed to quickly attach to any standard NATO litter. Designed by SSG Eric Smeed, U.S. Army Institute of Surgical Research (USAISR), for medical evacuation of burn patients, the device is usually mounted over the feet of the patient, although it can be attached anywhere along the length of the litter.



The SMEED platform has various universal fasteners so that it can be configured in several ways, depending on the mission. It is specifically designed to accommodate all of the Patient Movement Items (PMI) in the Army inventory to include vital signs monitor, infusion pump, aspirator, D-cylinder oxygen tank, ventilator, and defibrillator, and has the flexibility to mount other medical devices as required.

Efforts to attain Army Air Worthiness Release (AWR) continue. Impact Instrumentation, in accordance with a Test Plan written by the U.S. Army Aeromedical Research Laboratory (USAARL), conducted a series of vibration tests in an effort to attain an Army AWR. Based on results of these tests, modifications were made to the mounting attachments of several PMI devices. A second series of tests were conducted to verify the efficacy of the modifications. Results of these tests were successful. The USAARL is currently evaluating these test results, along with new modeling for crash worthiness, to make a determination on AWR.

Responding to an urgent request from the Commander of the 28th CSH in Baghdad, 10 SMEEDS were delivered by Impact Instrumentation Inc., directly to the 28th CSH, in support of OIF. That request prompted the U.S. Army Medical Command to expedite a restricted AWR for in-theater use. At the same time, a parallel path of structural analysis will continue in order to obtain an unrestricted AWR.

Stryker – Medical Evacuation Vehicle



The Stryker – Medical Evacuation Vehicle (MEV) functions as the medical evacuation variant of the Stryker Armored Vehicle platform for the Stryker Brigade Combat Team (SBCT). Medical capability includes an automated litter lift system, on-board oxygen, suction, storage space for essential medical items and equipment, plus the capacity to carry four litter patients or six ambulatory patients, and a crew of three.

The Stryker – MEV was fielded to the first SBCT at Fort Lewis, WA, and is currently deployed for duty in OIF. After action reports from Iraq indicate that the Stryker is performing well and that deficiencies are being addressed. Reports on the Stryker MEV indicate that the primary issues involve ordering and receiving spare parts for medical unique items, particularly the litter lifting system. The prime contractor, General Dynamics Land Systems, is working to rectify this situation. Discussions are ongoing between PM-SBCT and General Dynamics to include air conditioning on the fourth and fifth SBCTs.

Thawed Blood Processing System

The Thawed Blood Processing System (TBPS) consists of a blood processor and related components that will replace the existing Haemonetics frozen blood system. The current system does not meet military requirements because it is labor-intensive, limits production to one-blood unit per hour per technician, and limits shelf life of processed thawed blood to only one-day. The new system is an automated, closed-loop sterile blood-processing system capable of increasing thawed blood production and shelf life from the current one-day to 14-days. The TBPS also includes a bar code reader for automated data collection, a printer, a newly designed dry thawing device to reduce thaw time from the current 50 minutes in a conventional water bath to less than 10 minutes, and a new blood bag to eliminate the current 20 to 50 percent leakage rate. The TBPS processing device is a compact, tabletop design.

Approval from the FDA to proceed with clinical trials was obtained in April 2003. Mission Medical Inc. (MMI) has since contracted with three clinical research laboratories well-known to the FDA. They have also developed the clinical protocols and submitted the human use documentation to the Human Subjects Research Review Board (HSRRB)

at Fort Detrick. Comparison testing of the Mission Medical System versus the Haemonetics is currently being conducted at WRAIR. A final report is expected before the end of the calendar year.

Ventilatory Assist Device

The Ventilatory Assist Device (VAD) is an FDA-approved anesthesia delivery system consisting of an anesthesia apparatus, ventilator, and patient ventilator circuit. The VAD will be used to anesthetize patients during surgical procedures with the FST and CSH. The VAD will eliminate the need for the anesthesia provider to hand bag the patient. Manually ventilating a patient is very labor-intensive and reduces the number of surgical procedures that can be performed. The VAD will be compatible with low-pressure oxygen sources such as oxygen concentrators. The use of the VAD will ensure proper patient ventilation during surgery.



The operational assessments conducted at 5 CONUS hospitals were highly successful. Additionally, several VADs were used in Iraq, in both FST and CHS settings. The VAD used in the FST was parachuted in during an airborne assault in northern Iraq. As a result of the evaluations, the manufacturer made several modifications, including a revised packaging design to include a holder for a small oxygen cylinder,

wheels to move the VAD around in the operating room, and compartment labels for the parts and accessories that the operator needs. An evaluation of the modifications was conducted at the Ryder Trauma Center in Miami, FL, with the help of a nurse anesthetist that used the equipment in Iraq. The evaluation was favorable, and an evaluation report will be issued by the Army Medical Department Board (AMEDDBD).

In order to further reduce weight, the manufacturer has initiated plans to integrate a ventilator into the VAD that can be powered by either an electrical or compressed gas source. This will eliminate the current need for a separate air compressor while retaining the versatility of using any standard drive source such as a medical or dental air compressor, bottled air or oxygen, or manual ventilation.

The ORD has been approved by the Army Requirements Oversight Review Council, and is pending review by the Joint Requirements Oversight Council. Preparations are being made to conduct a Milestone C IPR. Manuals for operators and maintainers are being reviewed by USAMMA's NMP, and supportability and maintenance plans are being developed by the manufacturer.

Industrial Services Branch

Introduction

The Industrial Services Branch (ISB) of AMSPMD is a small team of craftsmen model makers, each possessing at least two trade skills, who design concepts, develop drawing packages, and rapidly prototype medical equipment in support of the USAMRMC. The ISB is capable of rapidly prototyping medical devices in a wide range of scales and variety of materials, and can also harden COTS equipment for use in a field environment.

Major Accomplishments

Portable Mini Gas Analyzer

ISB also worked collaboratively with Aberdeen Proving Ground in the development of a unique mini gas analyzer. This technology has the potential for performing real-time analysis of gases such as halogen acid, hydrogen sulfide, hydrogen cyanide, and ammonia with the appropriate ion-selective electrode. The detection and measurement of these gases are important for various Army uses. Currently, this technology is used to troubleshoot leaks, conduct area sampling and measuring of occupational exposure levels of toxic gases in the air. Over the past few months, the Army, Navy, and the National Institute of Standards and Technology (NIST) used this instrument to measure toxic gases produced from fire tests.

The ISB was instrumental in the design and packaging of the portable mini gas analyzer. These efforts include designing, miniaturizing and hardening numerous components. Specialized mounting hardware was fabricated and married with “commercial-off-the-shelf” lab components to enable a compact and user-friendly device. Additionally, the electronic circuitry, including a microprocessor, was designed and utilized to control the pump speed, display, and recording of data. The culmination of design, fabrication and chemistry has provided the Army with a one-of-a-kind, hardened, portable and real time mini gas analyzer. Virtually a “laboratory in a box.”



USUHS Mosquito Test Chamber

The ISB, working in support of the Uniformed Services University of the Health Sciences (USUHS), designed and fabricated two mosquito test chambers. In an effort to reduce the biological and physical side effects of the conventional pesticides/repellants, Dichlorodiphenyltrichloroethane (DDT) and N,N-Diethyl-meta-Toluamide (DEET), USUHS researchers planned to evaluate numerous previously untested chemicals.

Faced with the overwhelming task of evaluating hundreds of chemicals for possible use as repellants, USUHS turned to USAMMDA's ISB team to assist in the development of prototype test chambers. The ISB designed and fabricated two unique mosquito test chambers that quickly assemble and disassemble. The use of the chambers requires no tools in the assembly or disassembly, thereby minimizing the test time required for each chemical. This was accomplished by the utilization of spring loaded ball detents to provide a simple, yet effective, means to snap the chamber's components together. In addition, the overall design of the components was made with the user in mind; all of the parts are interchangeable. Consequently, these chambers will turn a once daunting requirement into a doable project.

Pharmaceutical Systems

Introduction

The Pharmaceutical Systems Project Management Division (PSPMD) centrally manages the development and acquisition of pharmaceutical and biological products (drugs, vaccines, toxoids). These products are fielded as preventive, protective and therapeutic modalities for use against infectious diseases. Product Managers leverage domestic and foreign medical technology to remedy deficiencies identified by the Combat Developer and monitor military, industrial, and university research projects for potential solutions to identified problems.

Military Relevance

U.S. Military Forces must be prepared to serve anywhere in the world against any threat. This could result not only in conventional injuries sustained during combat operations but exposure to chemical and biological warfare agents, as well as exposure to endemic diseases not commonly found in the United States. The development of products against these threats will help save lives, sustain the fighting Force and enhance return to duty.

Adenovirus Vaccine, Types 4 and 7

Adenovirus vaccine has been used exclusively by the military to prevent Adenovirus- related acute respiratory disease (ARD) in soldiers during basic training, while living in barrack-type environments. The vaccine is an orally administered enteric-coated tablet containing live adenovirus serotypes 4 or 7. Prior to the use of vaccines, adenovirus types 4 and 7 accounted for 60 percent of all ARD in military recruits who were hospitalized. Adenoviruses are associated with pharyngitis, conjunctivitis, atypical pneumonia, and rhinitis. A contract to develop and manufacture the type 4 and 7 adenovirus vaccines was awarded in 2001 to Barr Laboratories, Inc. The first phase of the contract requires an IND application and successful completion of Phase 1 clinical trials. The second phase requires completion of all clinical trials and full FDA licensure of the product. The vaccines are expected to be available early in 2008.



Barr completed building construction of the adenovirus manufacturing facility at their Forest, Virginia, laboratory site. All equipment has been installed and qualifications performed. The Phase 1 clinical trial protocol was reviewed by the HSRRB in December

2003. The protocol will be executed by WRAIR under a Cooperative Research and Development Agreement with Barr's subcontractor, VaccGen, at a military training facility. A pre-IND meeting is scheduled in May 2004 to obtain FDA's comments for USAMMDA's manufacturing plans to produce comparable adenovirus vaccines and proposed clinical trial plan.

Dengue Tetravalent Vaccine (DTV)

The dengue tetravalent vaccine (DTV) is a live-attenuated virus vaccine for prevention of dengue fever. The DTV contains all four monovalent serotypes grown in fetal Rhesus lung (FRhL) cell culture.

In CY03, Phase 1 trials were conducted to test the safety and immunogenicity of two different tetravalent vaccine formulations (formulations 17 and 18), and to assess the safety and immunogenicity of an intradermal route of administration. A Phase 1 study to assess the safety and immunogenicity of DTV in Thai school-aged children was begun. The lead laboratories are WRAIR and Armed Forces Institute for Medical Sciences (AFRIMS).

Hepatitis E Virus Vaccine (HEVV)

The HEVV consists of a purified polypeptide produced in insect cells infected with a recombinant baculovirus containing truncated hepatitis E virus (HEV) genomic sequences encoding the viral capsid antigen. The recombinant HEV protein is formulated with an aluminum salt adjuvant. The HEVV is designed to protect DoD personnel and their families from hepatic disease caused by infection with the HEV.

A Phase 2, prospective, randomized, double-blind, placebo-controlled (vaccine placebo 1:1) field efficacy trial of the HEVV was started in Royal Nepal Army personnel in Kathmandu in 2001. The two thousand volunteers received either placebo or 20 micrograms of HEV recombinant protein at 0, 1 and 6 months. The volunteers are being followed for signs and symptoms of hepatitis for 24 months after the first dose. Completion of the trial is expected in late calendar year 2004. The lead laboratory is WRAIR.

Human Immunodeficiency Virus (HIV) Vaccine

The HIV vaccine, currently in advanced development, combines two vaccines: a priming inoculation that is designed to stimulate the cellular immune system, and a boosting inoculation that is designed to stimulate the humoral immune system. The priming inoculation (vCP1521) provides HIV genes that are inserted into a canarypox virus. The boosting inoculation (AIDSVAX B/E) provides purified HIV glycoproteins from two types of HIV virus. The Ministry of Public Health of Thailand has the lead for carrying out the trial. Several agencies are cooperating in this effort, including the

Division of AIDS of the National Institute of Allergy and Infectious Diseases, WRAIR, the Armed Forces Research Institute of Medical Sciences, Mahidol University, Aventis, VaxGen, the Henry M. Jackson Foundation, the Royal Thai Army, Quintiles, MetaSolutions, and EMMES.

The study is designed to determine the ability of the vaccine to protect against HIV infection, and will enroll 16,000 subjects. Half will receive vaccine and half, placebo. Following enrollment and immunization, subjects will be followed for 3.5 years to detect HIV cases that may occur. The study will be completed in 2009.

Leishmania Skin Test



The cutaneous form of the disease can sometimes cause highly mutilating lesions on one's skin/face, wherever an infected sandfly bites. In the city of Kabul, Afghanistan, an estimated 270,000 cases of cutaneous leishmaniasis occurred in 1996 among the less than 2 million inhabitants of the city.

The *Leishmania* Skin Test will be used to screen U.S. Service members who may have been exposed to *Leishmania* species (parasites) after deployment to Leishmania-endemic areas. The skin test for *Leishmania* is made according to the same general principles as the skin test for tuberculosis. The *Leishmania* test is performed by injecting a small amount of purified *Leishmania* proteins under the skin and then measuring any local skin reaction 48-72 hours later. A small bump of 5mm or greater is a positive indication that the individual has been exposed to the *Leishmania* parasite.

The disease leishmaniasis occurs in 88 countries around the world and is caused by protozoan parasites transmitted to humans from the bite of an infected sandfly. More than a million new cases of human leishmaniasis are reported annually in the world. Currently, some 12 million people throughout the world suffer from leishmaniasis

During CY03, due to program reprioritization and outyear funding limitations, our Industry Partner's scope of work was reduced to the submission of an IND to the FDA and performance of a Phase 1 safety trial with their *Leishmania tropica* skin test. Development effort by our Industry Partner will cease by 3QFY2005 unless Congressional-directed funding is secured by the Industry Partner. Lead lab is WRAIR.

Topical Antileishmanial Drug, Paromomycin/Gentamicin

Soldiers who contract cutaneous leishmaniasis are currently evacuated to the Walter Reed Army Medical Center (WRAMC) and treated under an IND protocol with Pentostam®, which is administered intravenously for 28 days. This extended treatment regimen possesses undesirable side effects, requires extended hospitalization, and is expensive. The topical Antileishmanial Drug is a topical ointment made from two aminoglycosidic antibiotics, 15 percent paramomycin sulfate and 0.5 percent gentamicin sulfate in an aquaphilic base. The goal is to replace Pentostam® with this drug for the treatment of the cutaneous form of leishmaniasis.

A Phase 2 clinical trial is now ongoing. This protocol is being performed in cooperation with the Institut Pasteur – Paris and Tunisia against Old World *Leishmania*. This study started in Paris in March 2003, and in Tunisia during September 2003. Presently, this study has 91 subjects enrolled, is to be completed in October 2004, and the blinding code broken in November 2004.

Malaria Rapid Diagnostic Device (MRDD)

The Malaria Rapid Diagnostic Device (MRDD) will be an FDA-approved field deployable, handheld, disposable point-of-care test to rapidly detect the presence of malaria parasites found in the blood samples of patients displaying symptoms of malaria. The MRDD will not require the use of additional equipment to analyze appropriate clinical specimens. The MRDD will facilitate the early diagnosis of malaria infection



The latest MRDD packaging will indicate a positive or negative finding in the test window. Early detection and diagnosis is key in successfully treating this serious, infectious disease.

and prompt medical intervention. Malaria, in its various forms, constitutes a serious infectious disease threat to the U.S. Forces, including operations other than war, in all tropical and sub-tropical regions of the world. The 80,000 malaria cases in Vietnam resulted in a loss of more than a million man-hours. Similarly, in Operation Restore Hope (Somalia) and Operation Uphold Democracy (Haiti), numerous soldiers contracted malaria. Malaria is an acute infection with high morbidity (severe illness) and the potential to rapidly incapacitate large numbers of personnel. Because one type of malaria is often fatal if untreated in non-immune individuals, the diagnosis of malaria must be accomplished for any service member with fever occurring during or after sojourns in a malaria-endemic region. Even though there are MRDDs marketed outside of the United States, U.S. Forces cannot use them until the MRDDs are approved by the FDA for commercial sale in the United States. To that end, for the MRDD, a 510(k) Premarket Notification must be submitted to the FDA. A 510(k) is a scientific,

regulatory document by which the FDA evaluates the safety and effectiveness of medical devices.

During CY03, we prepared an analytical plan which defines the statistical methods planned for the analyses of the 2001 study of WRAIR Protocol 687, a study of the diagnostic accuracy and performance characteristics of the NOW® ICT Malaria *P.f./P.v.* for Whole Blood (ICT) malaria rapid diagnostic device (MRDD). Another analytical plan was also drafted for the 2003 study of WRAIR/AFRIMS Protocol 1036, a “Comparison of Diagnostic Accuracy and Performance of the BINAX NOW® ICT Malaria Test on Specimens Collected by Venous and Fingerstick Sampling.” In CY03 we completed the in-life portion of this Protocol 1036 (Fingerstick trial) and began entering data into a database for follow-on statistical analysis. In CY03 the FDA determined that the MRDD can be submitted as a *de novo* 510(k) Premarket Notification versus the previous requirement that the submission be a Premarket Approval Application (PMA). This change is likely to shorten the FDA’s internal review time of the submission from one year to three months. A final clinical study, called a True-Negative Clinical Protocol, was drafted for study initiation in CY04. Lead lab is WRAIR.

Malaria Recombinant Vaccine With Adjuvant Combinations (RTS,S)



RTS,S vaccine consists of recombinantly engineered immunogenic fractions of the malaria sporozoite surface coat co-expressed with protective epitopes from the hepatitis B surface antigen. During purification, these proteins self-assemble into particles that form the antigenic component of the vaccine. The vaccine is formulated in a liquid emulsion containing potent immunostimulants (designated as AS02A) that dramatically enhance the immune response to the RTS,S particles. The vaccine is delivered by intramuscular injection to protect U.S. Forces from falciparum malaria. The vaccine is manufactured by GlaxoSmithKline Biologicals. Lead laboratory is WRAIR.

In an effort to enhance the immunogenicity and duration of protection, the RTS,S vaccine will be combined with a new, proprietary adjuvant system (AS01B) and evaluated in a Phase 1/2a safety, immunogenicity and preliminary efficacy trial in U.S. volunteers. An IND application to cover this vaccine-adjuvant formulation was filed with the FDA in CY03, with an expected start date of January 2004.

Shigella flexneri Vaccine (SC602)

Shigella flexneri 2a vaccine (SC602) is a live, oral, attenuated vaccine developed at the Institut Pasteur in France and manufactured as a lyophilized product in the WRAIR pilot vaccine production facility under current Good Manufacturing Practices (GMP). The

SC602 strain is attenuated by inactivation of the *icsA* gene in the invasive plasmid and inactivation of the *iuc* (aerobactin) gene in the chromosome. The mutations prevent spread of the organism within the intestinal epithelium and diminish iron-binding capacity, but do not affect immunogenicity.

Due to limited funding at USAMRMC, the advanced development of this vaccine was put on hold in CY03.

ETEC Whole Cell, Recombinant B Subunit Vaccine

The ETEC vaccine is composed of killed whole cell *Escherichia coli* (*E. coli*) plus the B subunit of cholera toxin produced by recombinant technology to protect U.S. Forces deployed worldwide against severe diarrhea and fever caused by enterotoxigenic *E. coli*. SBL Vaccin, a Swedish company, manufactures the vaccine. The lead laboratory is NMRC.

A Phase 2 clinical trial was completed in CY03 assessing vaccine efficacy in 314 Egyptian infants and young children. The adjusted vaccine efficacy estimate was twenty percent in the trial. The principal investigator's conclusion was that "the ETEC/cCTB vaccine failed to elicit significant protection against non-severe ETEC diarrhea in this community-based pediatric setting."

***Campylobacter* Whole Cell (CWC) Vaccine**

The CWC vaccine is an oral, monovalent, killed *Campylobacter jejuni* (strain 81-176) vaccine, combined with a modified *E. coli* heat-labile toxin adjuvant, LT(R192G). The adjuvant is a recombinantly produced, genetically modified, less-toxic form of the *E. coli* heat-labile enterotoxin, that enhances the ability of the vaccine to elicit an immune response at the mucosal surfaces of the intestinal tract. The vaccine has been developed through a Cooperative Research and Development Agreement with Antex Biologics, Inc.

A Phase 1 clinical trial, testing a more highly purified form of the LT(192G) adjuvant, was completed. It concluded that, while there is no universally agreed upon immune correlate of protection for *Campylobacter*, CWC-specific intestinal antibody production and cell mediated immunity of the Th-1 type (as measured by *in vitro* production of IFN- γ) appeared to be associated with protection from illness. This study also defined the upper window of adjuvant dosage, after which diarrhea is a notable side effect.

This vaccine fell below the cut-off levels for continued advanced development at both USAMRMC and the commercial partner, Antex, a company which was purchased by BioPort Corporation in CY03. An IPR was called to address possible product termination in the coming year.

Combined Camouflage Face Paint (CCFP)



The new CCFP is currently packaged in a compact container with a mirror on top and compartments on the bottom to provide for 20 applications of the loam, green, and sand colors, and 10 applications of black and white colors.

Camouflage face paint now offers more than simple concealment. The new Combined Camouflage Face Paint (CCFP) in stick-type dispensers will be a U.S. Environmental Protection Agency registered blend of face paint with DEET insect repellent to provide a minimum of 8 hours of protection against biting insects. Inclusion of insect repellent protection will reduce nuisance factors by repelling insects near the face and help reduce diseases (e.g., malaria and dengue fever) transmitted by biting insects. All CCFP formulations will be used by individual soldiers for protection against biting insects, protection against detection by night vision goggles (the face paint reduces a soldier's near-infrared signature), and for blending into the environment in all military missions.

During CY03, technical issues with performance of temperature storage chambers were identified. Contracted maintenance began to address the re-validation of all three chambers. Preliminary stick formulations underwent technical testing by our Industry Partner. Natick Soldier Center provided a Soldier Market Survey that addresses their “likes” and “dislikes” of the currently fielded two-color camouflage face paint sticks. Lead lab for efficacy is WRAIR. Lead lab for camouflage is Natick Soldier Center.

Antimalarial Drug, Tafenoquine (WR238605)

WR238605 (Tafenoquine) is an 8-aminoquinoline that has demonstrated antimalarial potential in both pre-clinical and clinical studies. While it has demonstrated potential both as a prophylactic and treatment drug, it is being developed first for the prophylaxis indication.



A study carried out from late 2000 to early 2001 compared tafenoquine to mefloquine administered for six months in a double-blind fashion to Australian soldiers deployed to East Timor. A sub-set of these soldiers had an array of ophthalmic examinations performed after their return to Australia that showed that over 90% of the tafenoquine recipients had developed corneal deposits compared to none of the mefloquine recipients. The tafenoquine

IND was then voluntarily suspended in May 2001 so that this phenomenon could be further examined in greater detail. An expert panel of ophthalmology consultants was subsequently convened which felt that tafenoquine was not harmful to vision based on

the test results, and also recommended investigating in a prospective fashion any possible effects of tafenoquine on visual function.

In addition, it was noted that a few of the Australian soldiers had developed mild elevations of creatine during both tafenoquine and mefloquine dosing, which nevertheless, remained within normal limits in the vast majority of cases.

Follow-up of the group that developed corneal deposits revealed complete resolution of these deposits in all soldiers by one year following cessation of tafenoquine dosing. Careful evaluation of those soldiers who had increases in serum creatinine showed continuing normal renal function and no evidence of any kind of kidney disease in either tafenoquine or mefloquine recipients.

In the meantime, the results of long-term rat carcinogenicity studies involving high-dose lifetime exposure to tafenoquine became available. These revealed that a small number of male rats developed renal tumors by the end of the trial. Additional pre-clinical toxicity studies and review of previous data confirmed that the renal toxicity findings were confined solely to male rats. Both female rats and male and female mice were free of tumors when exposed to high doses of tafenoquine for two years. In addition, genotoxicity and lymphocyte studies were repeated and all results of these were negative. Finally, the follow-up of those Australian soldiers who had experienced elevations of creatinine showed no evidence of any renal pathology, including renal tumors.

These additional safety data were presented to the FDA in December 2002, after which the FDA allowed the tafenoquine IND to be re-activated effective 19 January 2003. A Phase 1 safety trial was subsequently initiated in July 2003 at the Uniformed Services University of the Health Sciences in Bethesda, MD, that closely examines normal volunteer subjects in a double-blind, placebo-controlled prospective fashion for any evidence of effects on renal function or visual function due to administration of tafenoquine. A second study site for this trial will open in the United Kingdom in July 2004. If, as expected, these study results show that six-month dosing of tafenoquine in humans is safe, then Phase 3 prospective clinical trials will be initiated to investigate the efficacy and safety of tafenoquine in the prophylaxis of malaria. Unstable political conditions and the world-wide threat of terrorism continue to have an impact on Phase 3 study site availability and access, and alternative sites are being investigated for suitability for these trials. The lead laboratory is WRAIR.

Tick-Borne Encephalitis Virus Vaccine

Tick-borne Encephalitis (TBE) is a viral infection of the central nervous system transmitted to people by infected ticks. This disease is endemic in several European countries, Russia, and China. Transmission is seasonal and occurs between April and November, particularly in forest and rural areas. The incubation period averages 7-14 days, followed by 1-8 days of fever and flu-like symptoms. Encephalitis occurs in up to 30 percent of infected individuals, requiring many weeks of hospitalization and rehabilitation. Mortality is 1-2 percent in general, but can be as high as 23 percent in the

Far East. Once infected, there is no effective curative treatment, only supportive care. However, a TBE virus vaccine has been used in Europe for over 20 years to prevent illness due to TBE virus infection. The vaccine is licensed for use in Europe, but it is not licensed in the U.S.

During CY03, the TBE vaccine effort remained unfunded due to limited availability of development funds and the relatively low priority of TBE against other infectious disease threats. However, an industrial partner submitted an National Institute of Allergy and Infectious Diseases (NIAID) Challenge Grant application that, should it be approved, would support FDA licensure effort.

Quality Assurance

Major Accomplishments

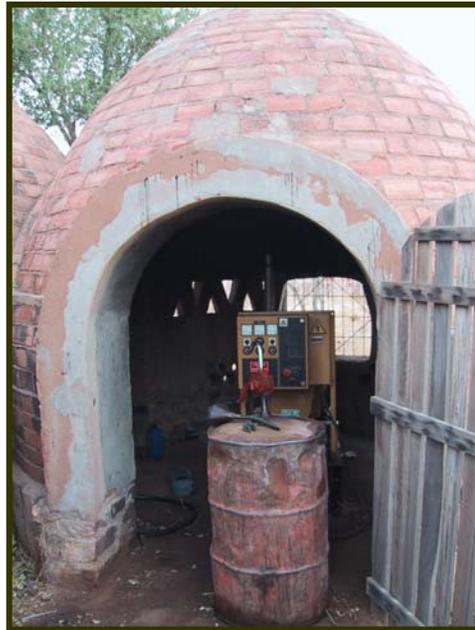
During the calendar year 2003, the Quality Assurance Office was involved in monitoring many clinical trials for protection of our military in the United States and throughout the world.

The Quality Assurance Division (QAD) maintains a brisk, vigilant monitoring program to assure the safety of volunteer subjects and the integrity of scientific data. The QAD has visited extensively in the United States during 2003, including study sites at the WRAIR, and overseas sites in Nepal, Thailand, Australia, Peru, Kenya, France, Tunisia, England and Korea.

The Phase 3 non-pivotal Hepatitis trial in Kathmandu, Nepal with 2000 subjects enrolled is progressing with hope to unblind the data in mid-2004. It is very hopeful the vaccine will show protection for our military and the Nepal people, including children and pregnant women, whom are most vulnerable to the disease. This study has kept the USAMMDA monitors busy with visits every three months.



This Malaria Vaccine Testing site in Africa: Bandiagara, Mali, is designed to represent the traditional building structure. The site was developed to establish research in an endemic community, and to train Malian scientists and physicians in preparation for clinical trials.



After years of planning, the U.S. Army's largest multi-site HIV study, "A Phase 3 Trial of Aventis Pasteur Live Recombinant ALVAC-HIV (vCP1521) Priming With VaxGen gp120 B/E (AIDSVAX B/E) Boosting in HIV-uninfected Thai Adults," began screening and vaccinating in late October 2003. The monitoring of the trial has been contracted to the Quintiles Corporation, and contract compliance is being audited by USAMMDA. The USAMMDA auditors, along with help from the HIV Research auditors of the Henry M. Jackson Foundation in Rockville, MD, are making visits to Thailand every two months. Of the twenty-five thousand subjects projected to be screened, 8,000 will receive the test vaccine, and 8,000 will receive the placebo. The screening and

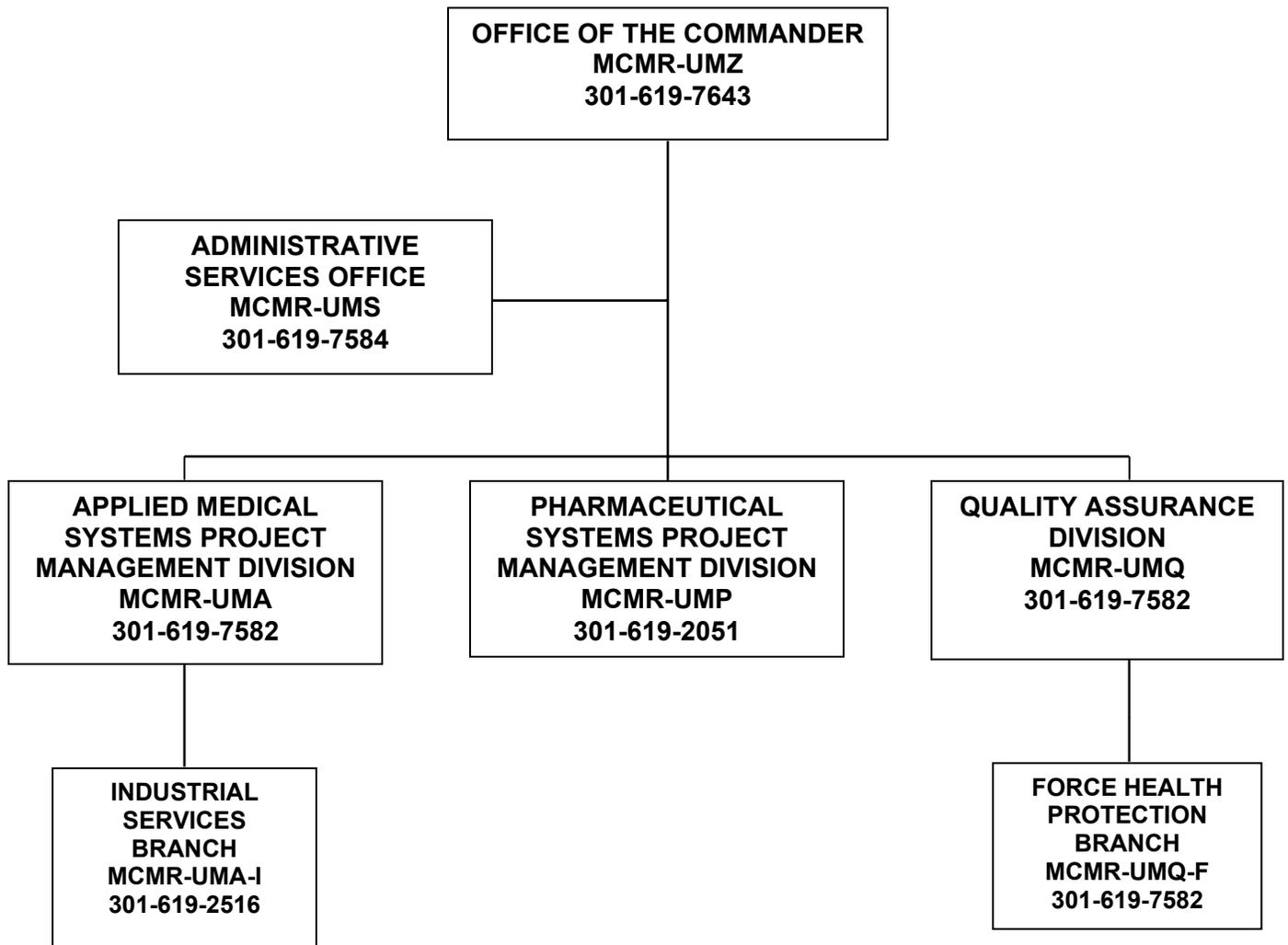
vaccination will be accomplished over a two-year period. The QAD has traveled extensively to Thailand in preparation for the conduct of the study. Many hours of strategic planning went into the development of the infrastructure at study sites, development of source documents, Case Report Forms and the informed consents. HIV causes major morbidity and mortality worldwide. We hope this vaccine will demonstrate protection of the study volunteers and will significantly enhance the arsenal available to fight this disease.

The WRAMC, Department of Infectious Diseases holds the only Army treatment protocol for cutaneous Leishmaniasis using the chemical agent “Pentostam®”. Leishmania has become a threat to our Servicemen and women serving in Iraq and Afghanistan. The QAD has worked closely with the WRAMC’s physicians monitoring the subject’s files and giving professional recommendations.

Additionally, the QAD has been devoted to monitoring the 12 USAMRIID study protection protocols for laboratory workers.

The world is growing smaller and thus making each of us a part of the international community. Malaria and other diseases, that were at one time a disease of a foreign country, are now a reality at home. The USAMMDA’s QAD is ready to monitor and audit clinical trials to protect our U.S. military, U.S. citizens and clinical trials throughout the world.

Appendix A – Organization Chart



Appendix B – Key Personnel

| | | |
|---|--|--|
| Commander | COL Jeffrey A. Gere | 01 Jan 03 to 31 Dec 03 |
| Deputy Commander | LTC Coleen K Martinez LTC Janet Moser (Acting) | 01 Jan 03 to 21 Feb 03 22 Feb 03 to 31 Dec 03 |
| Project Manager, Applied Medical Systems Project Management Division | Dr. Donald W. Caldwell | 01 Jan 03 to 31 Dec 03 |
| Project Manager, Pharmaceutical System Project Management Division | LTC Janet Moser (Acting) Dr. Lawrence K. Lightner | 01 Jan 03 to 22 Mar 03 23 Mar 03 to 31 Dec 03 |
| Chief, Administrative Services Office | Ms. Anna M. Poole | 01 Jan 03 to 31 Dec 03 |
| Chief, Quality Assurance Office | LTC Ann M. Altman | 01 Jan 03 to 31 Dec 03 |
| Administrative Officer | Ms. Crystal Shumaker | 01 Jan 03 to 31 Dec 03 |

