A. INTRODUCTION

1. Definition and Scope

The Biomedical technology area is divided into six technology subareas (Figure VI–1). The program is focused to yield essential technology in support of the DoD mission to provide health support and services to U.S. armed forces. Most national and international medical S&T investment is focused on public health problems of the general population. Military medical S&T is concerned with developing technologies in order to preserve combatants’ health and optimal mission capabilities despite extraordinary battle and nonbattle threats to their well being. Preservation of individual health and well being sustains warfighting capabilities.

The Biomedical Reliance Panel is included within the overarching structure of the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee, which provides joint coordination and cooperation within and among the four primary subareas shown in Figure VI–1, and two additional technology subareas, medical chemical defense and medical biological defense, that are reported in Chapter II.

The ASBREM Committee has overlapping member responsibilities with the Chemical/Biological Defense Panel. ASBREM reviews the four primary technology subareas shown in

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Figure VI–1. Planning Structure: Biomedical Technology Area
Figure VI–1, plus the medical chemical defense and medical biological defense subarea research programs, on an annual basis to ensure synergy across all biomedical programs.

2. **Strategic Goals**

   The strategic goals of the Biomedical technology area include:

   - Providing medical technology to enable a full spectrum of military operations for crisis and conflict resolution.
   - Protecting and sustaining warfighters from battle and nonbattle health threats.
   - Optimizing military performance.
   - Optimizing survival and stabilization of combat casualties.
   - Providing advanced technology to optimize medical support for battle and nonbattle operations at all levels of care and during patient evacuation.

3. **Acquisition/Warfighting Needs**

   Modern warfighting strategy emphasizes preparedness for regional rather than global conflict utilizing continental U.S. (CONUS)-based forces. Joint Staff-defined requirements emphasize preventive medicine to reduce casualties resulting from disease and nonbattle injuries, immediate life-saving treatment, resuscitative care and stabilization, and technologies for rapid evacuation of casualties to definitive-care, CONUS-based facilities. The deployable health service support structure must recognize and overcome logistics and communications constraints in order to reduce its in-theater medical footprint and the lift requirements associated with a forward positioning of medical care assets. Simultaneous full integration of medical communications systems with operational command systems is essential. Capability to enhance individual personnel readiness for joint and combined operations is an identified warfighting need.

   Table VI–1 shows the technology forecast for the military Biomedical area. Development of novel vaccines will protect deployed forces against a number of debilitating and life-threatening infectious diseases to which they are now vulnerable. Life-support systems with enhanced mobility and physiological monitoring capability will be provided to enable in-flight maintenance of patient stabilization, allowing safe long-range evacuation of critically injured service personnel. Scientifically based operational doctrine and ration supplements will improve and better sustain individual operational capabilities. New radioprotective strategies will be developed that provide protection against both prompt and late effects of ionizing radiation.

   Provision of vaccines, protectants, and therapeutics directed against biological and chemical threat agents will deter and constrain proliferation of these weapons while defeating their use.¹

¹ Refer to Chapter II for more complete details regarding the medical chemical defense and medical biological defense subareas.
## Table VI–1. Biomedical Technology Forecast

<table>
<thead>
<tr>
<th>Current Baseline</th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INFECTIOUS DISEASES OF MILITARY IMPORTANCE SUBAREA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs for prevention and treatment of malaria</td>
<td>Additional drugs for multi-drug resistant malaria</td>
<td>Malaria drugs derived from combinatorial chemistry</td>
<td>Drugs derived from analysis of malaria genome</td>
</tr>
<tr>
<td>Pilot lots of vaccines for prevention of malaria</td>
<td>Protein antigen-based malaria vaccines</td>
<td>Multi-antigen malaria vaccines</td>
<td>Combined vaccines for major malaria types (<em>falciparum</em> and <em>vivax</em>)</td>
</tr>
<tr>
<td>Enterotoxigenic <em>E. coli</em> (ETEC) vaccine</td>
<td>Shigella vaccine</td>
<td>Campylobacter, ETEC vaccines</td>
<td>Diarrheal disease vaccine</td>
</tr>
<tr>
<td>Repellent protection against biting vectors of disease transmission</td>
<td>Multivalent dengue vaccine</td>
<td>Norwalk virus vaccine</td>
<td>Handheld device to detect naturally occurring and manmade pathogens</td>
</tr>
<tr>
<td>Diagnostic reference laboratories</td>
<td>Drug for cutaneous leishmaniasis</td>
<td>Multivalent flavivirus vaccine (yellow fever, dengue, Japanese</td>
<td>Vaccines for other bacteria of military importance (strep, staph,</td>
</tr>
<tr>
<td>No protection from Group B. <em>meningococcus</em></td>
<td>Field diagnostic devices for common pathogens</td>
<td>encephalitis, West Nile fever)</td>
<td>pseudomonas)</td>
</tr>
<tr>
<td>Avoidance of unauthorized water sources</td>
<td>Vaccine for Group B. <em>meningococcus</em></td>
<td>Vaccine for leishmaniasis</td>
<td>Combined hepatitis A, B, E vaccine</td>
</tr>
<tr>
<td>Abstinence</td>
<td>Hepatitis E vaccine</td>
<td>Handheld devices to detect common pathogens</td>
<td>Third-generation HIV vaccine</td>
</tr>
<tr>
<td>Avoidance of potential sources of viral agents</td>
<td>HIV vaccine for strains of military relevance</td>
<td>Multivalent hantavirus vaccine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Monovalent hantavirus vaccine</td>
<td>Restored Adenovirus types 4 and 7 vaccine</td>
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<td></td>
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<tr>
<td><strong>COMBAT CASUALTY CARE SUBAREA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuscitation solutions</td>
<td>Improve blood storage</td>
<td>Agents to reduce secondary effects of trauma</td>
<td>“Extensive care” evacuation platform</td>
</tr>
<tr>
<td>Six-week liquid red cell storage</td>
<td>Small volume resuscitation fluids</td>
<td>Intensive care evacuation platform</td>
<td>Metabolic down-regulation</td>
</tr>
<tr>
<td>Frozen platelets in dimethyl sulfoxide</td>
<td>Medical decision-assist devices</td>
<td>Individual O₂ generators</td>
<td>Enhanced agents to reduce secondary effects of trauma</td>
</tr>
<tr>
<td>Pressure dressings</td>
<td>Preclinical trials of fibrin agents</td>
<td>Local hemostatic agents</td>
<td>Freeze-dried blood cells</td>
</tr>
<tr>
<td>Oxygen cylinders</td>
<td></td>
<td>Universal blood reagents</td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td><strong>MILITARY OPERATIONAL MEDICINE SUBAREA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blast standards</td>
<td>Performance-enhancing nutrients</td>
<td>Sleep/alertness enhancers</td>
<td>Physiological status monitors</td>
</tr>
<tr>
<td>Spatial disorientation model</td>
<td>Vigilance/alertness monitor</td>
<td>Spatial awareness incorporation into trainers</td>
<td>Treatments for laser retinal injury</td>
</tr>
<tr>
<td>Vestibular test battery</td>
<td>Electromagnetic radiation standards</td>
<td>Improved injury prevention guidelines</td>
<td>Memory enhancers</td>
</tr>
<tr>
<td></td>
<td>RF radiation dosimeter</td>
<td>Pharmacodynamic model of neurotoxicity</td>
<td>Strength enhancers</td>
</tr>
<tr>
<td></td>
<td>Advanced laser protection</td>
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<td></td>
</tr>
</tbody>
</table>
Table VI–1. Biomedical Technology Forecast (cont’d)

<table>
<thead>
<tr>
<th>Current Baseline</th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunomodulator therapy</td>
<td>Novel radioprotective drugs</td>
<td>Modeling for casualties in NBC environments</td>
<td>Combined injury treatment protocols</td>
</tr>
<tr>
<td>Anti-emetic compounds</td>
<td>Fieldable biodosimetry capability</td>
<td>Mustard bioassay capability</td>
<td>Nontoxic chelators to treat internal contamination</td>
</tr>
<tr>
<td>Reference biodosimetry capability</td>
<td>Depleted uranium risk assessment and treatment analysis</td>
<td>Preventive treatments for late-arising pathologies</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Therapeutic strategies for anthrax and radiation exposure</td>
<td></td>
</tr>
</tbody>
</table>

B. DEFENSE TECHNOLOGY OBJECTIVES

The DTOs applicable to the Biomedical subareas are as follows:

Infectious Diseases of Military Importance

MD.02 Vaccines for Prevention of Malaria
MD.06 Prevention of Diarrheal Diseases
MD.12 Drugs for Prevention and Treatment of Malaria

Combat Casualty Care

MD.03 Far-Forward Hemostasis; Development of Blood Products
MD.09 Advanced Medical Technology—Advanced Field Medical Support in Forward Combat Areas
MD.11 Far-Forward Treatment of Trauma and Its Sequelae

Military Operational Medicine

MD.01 Sustained Operations Enhancement
MD.08 Laser Bioeffects Countermeasures
MD.10 Deployment Toxic Hazard Assessment Tools
MD.19 Optimization of Physical Health and Readiness
MD.23 Radio Frequency Radiation Bioeffects and Countermeasures

Medical Radiological Defense

MD.18 Medical Countermeasures Against Ionizing Radiation
MD.20 Cytogenetic-Based Diagnostic Biodosimetry System
MD.21 Toxicity of Embedded Depleted Uranium
MD.22 Risk Assessment of Combined Exposures to Radiation and Anthrax
C. TECHNOLOGY DESCRIPTIONS

1. Infectious Diseases of Military Importance

   a. Warfighter Needs

   Infectious diseases that are endemic in military deployment areas pose a significant threat to successful completion of military missions when U.S. forces have no natural immunity or protection. For example, diarrheal disease affects 20%–30% of soldiers deployed outside CONUS (OCONUS), malaria infection rates of up to 600 per 1,000 troops annually were seen in Vietnam, and cutaneous and visceral leishmaniasis infections were the most common chronic infection in Operation Desert Shield/Storm veterans. Dengue fever hospitalization rates in Haiti reached 5.3 per 10,000 personnel per week despite emphasis on personal protective measures. Prevention of disease by immunization is a valuable force multiplier and enables the full spectrum of military alternatives for resolution of regional conflict.

   The Joint Staff has requested priority for medical technology supporting prevention and treatment of diseases. Near-term control measures will depend on existing personal protective measures and personal hygiene for the prevention of malaria and diarrheal diseases. Mid-term impact includes adding a licensed antibiotic to the routine treatment of drug-resistant malaria. Far-term introduction of new vaccines will prevent 80% of all cases of malaria, 80% of the most common causes of diarrhea, and 90% of all cases of dengue that would occur in unvaccinated personnel. Much of this work is conducted in six DoD OCONUS laboratories and supports Presidential Decision Directive NSTC–7, “Emerging Infectious Diseases,” 12 June 1996, which calls for DoD to conduct a global surveillance program for infectious disease.

   b. Overview

   (1) Goals and Timeframes. The goals of the infectious disease subarea are to protect soldiers from incapacitating infectious diseases by the development of vaccines and prophylactic drugs, and to return infected personnel to duty by the discovery of effective drug treatment. It is anticipated that the most important infectious disease threats to U.S. warfighters can be controlled by vaccines. In addition, this program will identify other endemic disease threats throughout the world supporting a database of emerging infectious diseases so that informed decisions can be made about military operations in these areas.

   Vaccines are the most cost-effective means of preventing illness. Since it commonly requires 20 years or more to develop and field an FDA-approved vaccine, there is an ongoing, simultaneous application of new technologies to control many different militarily important infectious diseases. Infectious disease organisms such as hantavirus, HIV, and those causing malaria are continually evolving and appearing in new locations. Benign diseases today can become militarily important tomorrow. Military infectious disease research must remain at the forefront of technological advances to address these problems before they become warstoppers.

   (2) Major Technical Challenges. Major technical challenges that concern all aspects of infection and immunity must be effectively countered by innovative technical approaches. In malarial infections, parasites undergo multiple developmental stages throughout their life cycle during which these stages are exposed to the immune system for only brief periods of time.
measure is to design multivalent vaccines that stimulate an immune response to multiple stages. A major technical barrier for the antiparasitic drug program is the problem of increasing parasite drug resistance. The approach to this problem is to search for new classes of compounds by using structure activity chemical searches and by using fingerprinting to determine structure activity relationships to direct the synthesis of new classes of drugs.

In enteric infections, a major technical barrier for vaccines is enhancing the immune response at the intestinal mucosal surface. The technical approach includes formulating mucosal adjuvants and studying the best approach to deliver the antigens and the adjuvants to the mucosal immune system. Dengue vaccine development is complicated by the phenomenon of immune enhancement. Antibody to one serotype of dengue may increase the severity of symptoms caused by later infection with another dengue serotype. To counter this barrier, the approach is to formulate a tetravalent vaccine to protect against all four types of dengue simultaneously and consider immunization strategies that involve combined use of more than one type of vaccine (attenuated, killed, recombinant, or DNA vaccines).

(3) Related Federal and Private Sector Efforts. Only the military investigates infectious diseases from basic research through concept exploration to product development. DoD uses a number of laboratories to conduct all stages of product development and evaluation. Military infectious disease research is advanced by over 200 cooperative research and development agreements (CRDAs) and material transfer agreements with industrial and academic partners. In contrast, the National Institutes of Health (NIH) focuses on basic research and vaccine prototypes, but lacks U.S. government facilities for testing products for endemic disease outside the United States. The Centers for Disease Control and Prevention are expert at epidemiology and vaccine delivery, but lack the capability for vaccine preparation and testing in OCONUS locations. Academic centers focus on basic research and pathogenesis. Industry emphasizes products marketable in the United States and limits basic research. The military program is coordinated with other federal programs to prevent unnecessary duplication of efforts. These and private sector efforts are exploited to the greatest extent possible. An initiative for interagency cooperation in global surveillance for emerging diseases using advanced technology will enhance communication links between DoD laboratories, NIH, and CDC.

c. S&T Investment Strategy

Technology efforts are arrayed according to the type of etiologic agents that cause infection and disease. Distribution of investment within and among these broad agent areas is allocated in accordance with the impact of each agent on military operations, the potential contribution of technology to overcoming the threat posed by the agent, and the feasibility of achieving technology objectives through military investment. As knowledge advances, new technologies for improving diagnosis, treatment, and prevention are broadly shared among efforts on different agents.

(1) Technology Demonstrations. The Antiparasitic Drug Program includes the validation of the effectiveness of candidate drugs prior to full-scale development. FDA regulations, as promulgated through the Code of Federal Regulations (21 CFR), restrict demonstrations involving unlicensed drugs to laboratory testing in nonhuman models. Before starting human testing, an investigational new drug application must be filed with the FDA. Drugs currently under investigation include one licensed antibiotic (for which malaria is an unlicensed indication for use) and four other antimalarial drug candidates. A new drug for the treatment of leishmaniasis skin lesions is also
under study. Efforts will explain mechanisms of parasite resistance to drugs and find alternative countermeasures to resistance in the far term.

(2) **Technology Development.** Medical countermeasure development efforts are arrayed in the following functional areas:

- **Parasitic diseases,** including vaccines for prevention of malaria, development of antiparasitic drugs, identification of antiparasitic drug resistance patterns, identification and control of insect vectors for parasitic diseases, diagnosis of leishmaniasis, and vaccines for prevention of leishmaniasis.
- **Bacterial diseases,** including vaccines for Shigella, enterotoxigenic Escherichia coli (ETEC), Campylobacter, meningococci, and organisms responsible for sepsis and septic shock; also, diagnosis of rickettsial infections.
- **Viral diseases,** including vaccines for dengue virus, hepatitis virus, viral hemorrhagic fever, encephalitis, hantavirus, filovirus, and HIV.

Each of these areas is supported by the key technologies of improved vaccine production and delivery, development of forward-deployable diagnostic tests, and surveillance of emerging diseases of military importance.

(3) **Basic Research.** For every infectious disease of military importance, basic research must focus on characterization of the etiologic agent, transmission of the agent, pathogenesis and natural history of disease, the protective host immune response, and finding suitable in vitro and in vivo models of infection. Military infectious disease basic research funding is focused to provide new medical knowledge in areas not being addressed by other federal and private sector organizations. These programs are managed to ensure provision of strong scientific capabilities to effectively exploit fundamental advances in biomedical science in a manner that is responsive to the peculiar and unique research needs of the technology area.

2. **Combat Casualty Care**

   a. **Warfighter Needs**

   Combat casualty care must take into account operational constraints that are imposed by logistics, manpower, and hostile operational environments. These pose challenges that are rarely encountered in civilian trauma care. Military casualties may wait for hours before definitive medical care can be provided. Initial treatment and subsequent evacuation occurs in austere field, airborne, and shipboard environments characterized by limited supplies (e.g., blood, resuscitation fluids) and limited diagnostic and life-support equipment. Fifty percent of combat deaths are due to uncontrolled blood loss, and provision of perishable blood and blood products far forward presents severe logistics challenges. General head injury, maxillofacial trauma, and complications from trauma are also major contributors to loss of life and extended morbidity.

   Provision of acute and critical care is labor intensive and must frequently be provided by nonphysician medical personnel. Military medical personnel must be provided with the tools and techniques to overcome these austere conditions. This technology must be compatible with the warfighter’s operational mission and available resources, overcoming the constraints of communications and logistics that are typical in military operations. Although the military environment im-
poses extreme requirements on equipment and techniques, much of the technology required by the military has dual-use applications that can meet presently unaddressed needs in rural medicine, disaster medicine, and civil disturbance trauma care.

New doctrine emphasizes immediate life-saving treatment, resuscitative care and stabilization, and evacuation of casualties to definitive care at CONUS-based facilities, with few lengthy in-theater hospital stays. The Joint Staff has requested R&D emphasis on immediate life-saving treatment, resuscitative care and stabilization of medical casualties, rapid casualty evacuation with maintenance of medical support, and smaller, lighter medical equipment sets to reduce requirements for strategic and tactical lift for deployment and sustainment. Products and knowledge generated through combat casualty care research will result in smaller, lighter equipment, with enhanced capability to supplement and complement the skills of far-forward medical personnel. This research effort will field state-of-the-art trauma care on the front lines of combat where it is needed most. This research will also improve the supply of critical blood and blood products and reduce large manpower and logistics burdens associated with processing, storing, and maintaining fresh supplies of these perishable items at forward echelons. Efforts will also enhance the operational capability of military medical personnel in combat environments, resulting in conservation of medical manpower, reduced reliance on field hospitals, and reduced acute and long-term military health care costs. These efforts, along with development of new modalities to treat intractable medical problems of particular significance in military casualty populations, will reduce combat deaths and disability and enable far-forward and sustained quality of care through all levels.

b. Overview

(1) Goals and Timeframes. A near-term goal is to enhance diagnostic and triage methods and information processing for the rapid determination of various trauma-specific medical indices; this will aid in triage processes and advanced medical management. A second near-term goal is to reduce the present logistics burden. Efforts that minimize the weight and cube of those medical materials required to be far forward and that reduce the number of items projected as necessary are required to better enable U.S. forces to fight and win. A mid- to long-term goal is to improve battlefield treatment capabilities at Echelons 1 and 2 to reduce mortality and morbidity. Also in the mid- to long-term, medical management of disease and nonbattle injuries will be improved to minimize lost duty time. A long-term goal is to fully exploit advanced sensors and intelligent systems to extend advanced casualty diagnostics and treatment in far-forward areas. Further efforts will include development of countermeasures to mitigate brain and spinal cord trauma, improve survival, reduce long-term disability, and maintain physical performance capability.

(2) Major Technical Challenges. Major technical challenges include:

- Identification of early prognostic physiological indicators of shock, and development of corresponding noninvasive or minimally invasive sensing technologies.

- Stabilization of red blood cells without destroying function while eliminating in-theater pre-transfusion processing requirements.

- Maintenance of the usability of blood/blood substitutes using equipment that is available or easily transported to the combat environment.
• Lack of knowledge regarding the physiologic and cellular factors underlying the body’s response to hemorrhage and subsequent resuscitation.

• Reversing complex detrimental inflammatory and physiological cascades initiated by reduced blood flow and anoxia subsequent to hemorrhage.

• Lack of knowledge of the detailed mechanisms responsible for brain edema and cytotoxicity following head injury.

(3) Related Federal and Private Sector Efforts. NIH is the major sponsor of U.S. biomedical scientific research on trauma. However, much of the NIH program is directed at within-hospital management of problems such as septic shock, blunt trauma, and wound healing, while the military focuses on prehospital resuscitation and life support. Industry, by and large, is uninterested in prehospital trauma care research because of the difficulty and high cost of the required clinical research in relation to the relatively small anticipated market for products. The military actively solicits and exploits private sector expertise through extramural contracts with universities and industry, and via cooperative agreements and CRDAs between civilian firms and the government in support of combat casualty care research projects.

c. S&T Investment Strategy

Technology efforts are arrayed against functional threat areas that impact on the quality and efficiency of early phases of trauma care: prehospital care (identification, diagnosis, triage, resuscitation, stabilization, and life support, including care during extraction from combat and evacuation), resuscitative and life-saving surgery, and critical care. S&T thrust areas are necessarily diverse to address the variety of technologies required within these areas, encompassing medical knowledge, drugs, biologicals, and medical devices. Investment within and among threat areas is allocated in accordance with each threat’s impact on combatants’ health and frequency of injury occurrence or its impact on medical operations (including logistics and manpower considerations), the potential contribution of technology to overcome each threat, and the feasibility of achieving technology objectives through military investment.

(1) Technology Demonstrations. The advanced medical technology (field medical support) effort will provide advanced, noninvasive physiological sensors for life-support monitoring and diagnosis; lightweight, portable fluid and ventilatory support equipment; and intelligent medical decisionmaking systems. These provisions will allow early state-of-the-art life support and care during evacuation that is sustainable with minimal manpower. Individual components of the system will be developed in stages, focusing initially on manually operated platforms and progressing ultimately to a computer-assisted life-support system integrated with telemedicine systems under development in other programs. Efforts will exploit advances in basic knowledge of the pathophysiology of shock and will focus on the integration of noninvasive sensor, micro-electronic, and information-processing technologies into novel systems. The physiological sensing technology that will be developed as part of these systems can, in addition to its uses in trauma care, provide real-time awareness of operational capability for functioning personnel; thus, this demonstration is being jointly supported by both the military operational medicine and the combat casualty care subareas.

(2) Technology Development. Efforts are arrayed into the following functional areas:
• **Combat casualty assessment**, including far-forward-compatible systems for creation and management of patient records and theater regulation of patient flow.

• **Blood and resuscitative fluids**, including preservation of blood and blood products, minimizing traumatic blood loss, and development of materials and doctrine for fluid resuscitation.

• **Combat trauma**, including discovery and development of drugs, biologicals, and medical procedures to prevent or minimize secondary organ system injury and failure (including brain and spinal cord injury) after major trauma; care of combat casualties in austere environments; and development of diagnostic and therapeutic medical devices and associated software and data processing systems for resuscitation, stabilization, life support, and surgical support.

Efforts directed towards physiological sensor technologies and software and data processing systems for casualty diagnosis are partially applicable to physiological monitoring of uninjured personnel. The latter is a focus of the military operational medicine subarea (Section C3), with which these efforts are jointly pursued. In contrast to operational medicine efforts, combat casualty care efforts focus on a wider range of physiological end points and on the data integration that is required for accurate diagnosis and patient management.

(3) **Basic Research.** Basic research focuses on physiological, humoral, and cellular responses to hypoxic, ischemic, anoxic, and other types of injury. Such research is needed to identify potential diagnostic and prognostic indicators and sites for medical intervention and to find suitable in vitro and in vivo models of injury.

3. **Military Operational Medicine**

a. **Warfighter Needs**

Military operational medicine addresses the full range of threats and challenges known to limit human effectiveness. These threats and challenges focus on health and performance issues of deployment and combat stressors as well as training environments. Science and technology elements share a common goal of reducing the human costs of national security operations through an effort encompassing operational hazards and materiel threats.

Efforts focusing on operational hazards utilize biomedical science to attain the broadest possible performance envelope for the warfighter. The range of individual operational circumstances includes arctic to desert environments, stationary watch to operations beyond Mach 2, high-altitude to deep-diving and submarine operations, and shipboard operations to intense land combat. Stress is pervasive in battle; it claims one direct casualty for every four wounded and is contributory to one in five physical casualties. Neuroscience-based studies are designed to effectively extend an individual’s capacity to withstand battle stress. Fatigue and sleep loss may account for 20% of all injuries on the battlefield and are prominent factors in the degradation of military performance. Dental disease is a performance-degrading factor in deployments, and effective preventive measures are needed.

Work in progress targets sleep as a manageable resource. A near-term impact of this research will be an operational doctrine for pharmacological interventions to counter fatigue and...
sleep loss. In the mid term, a joint guidance for planning and conducting sustained operations that optimize human performance will be fielded. In the mid term, devices to predict performance and vigilance lapses will be developed that rely on alterations in brain wave activity and actigraphic monitoring of recent sleep patterns. Heat and cold restrict human performance. Biomedical technologies are applied to improve understanding of the mechanisms of heat and cold injury and to reduce the operational impact of these and related environmental challenges. In the long term, a biological means to modify environmental injury will be developed.

Demands of modern warfare continue to outstrip the information processing capacity of the human nervous system. The goal is to maximize the effectiveness of the warfighter and system operators. These initiatives combine to enhance military power and effectiveness and to reduce casualties, whatever the mission. They form the core of medical efforts to protect the lives and enhance the performance of individual warfighters and system operators.

Hazards from military systems and operations regularly challenge the health and safety of military personnel. The potential for death, injury, or performance degradation is systematically explored for hazards ranging from sustained operations, fatigue, munitions exhaust gases, and blast effects to the mechanical strains and jolts associated with physical training and operational platforms. A reduction of the environmental and operational threats to personnel will reduce the likelihood of accidents and injuries. For instance, operational mishap losses for FY90 through FY94 totaled $4.4 billion with a loss of 472 lives in the Navy and Marine Corps. Incorporation of the medical R&D products in the naval service will reduce these peacetime casualties. A reduction in mishaps by only 5% will result in a 5-year savings of $217 million and the saving of 23 lives. Greater monetary savings will be realized for the recapture of lost workdays due to injuries occurring while in training or while forward deployed.

Systems and operations threats, either singly or in combination, are detailed and individual exposure criteria are established. Materiel developers are supported with specialized databases and evaluations to ensure that affordable, realistic efforts are directed at minimizing risk to tomorrow’s warfighters. For example, the application of safe frequency and power exposure standards, to be developed in the near term, will guide laser and electromagnetic radiation system developers away from harmful frequency/power mixes. This simultaneously identifies safer regions of the spectrum that can be used at higher power for greater range and effectiveness. Biomedical information is critical to development of frequency-agile laser eye lenses that will afford effective protection against deliberate and accidental laser eye injury and will be of special importance to aviators and special operations personnel. Development of generic models of blunt trauma will predict health hazards from blast overpressure of weapon systems, identify protection afforded by new body armor concepts, and provide target hazard assessments for kinetic, non-lethal weapons. New efforts to develop health and performance criteria for head-supported mass are vital for materiel developers as weight is added to technologically complex helmets with increased injury risk in jolt environments. This program represents an active partnership between biomedical scientists and materiel developers that seeks affordable options for ensuring both system safety and operational effectiveness.

b. Overview

(1) Goals and Timeframes. War remains a test of the individual’s will both to endure and to master potentially overwhelming conditions. Thus, the inherent challenge facing the warfighter
evolves with the development of operational doctrine, materiel systems, and mission scenarios. The objectives are to:

- Develop and promote biomedical contributions to operational readiness.
- Sustain the health and performance of operational warfighters.
- Quantify the combined effects of multiple, diverse stressors in support of improved operational concepts, tactics, and doctrine.
- Provide the bases for scientifically sound doctrine for optimizing recovery following stress, ranging from reunion/homecoming preparation to metabolic reconstitution.

(2) **Major Technical Challenges.** The major challenge for sustained operations enhancement is modeling the threshold, onset, and course of fatigue in order to objectively determine when unacceptable levels of fatigue threaten mission safety or success. For RF radiation bio-effects, the technical challenge is to identify and quantify the absorption, transduction, and bio-effects of exposure to RF radiation under diverse operational conditions and multiple exposure parameters. The major challenge for the development of toxic hazards evaluation tools is identifying and evaluating molecular events and biochemical markers as accurate predictors of human toxicity from operational exposures to hazardous materials. For physical performance optimization and musculoskeletal injury, the challenge is to determine the cycle of damage and the rate of repair of the human body following military physical training. Without this biomedical knowledge, DoD cannot build optimally safe training programs for military-unique occupations. The challenge for advanced medical technology is determining the physiological adaptations for man–machine interface of electro-optical displays and development of automated command consultation systems that may help determine a course of action for unit leaders.

(3) **Related Federal and Private Sector Efforts.** Industry and academic partnerships are so woven throughout the program that scientific publications without coauthorship from outside are rare. Civilian resources are fully exploited when appropriate. Military laboratories, however, possess unique equipment and have access to deployed forces and environments that can be fully exploited only by DoD-uniformed scientists who have the operational experience to conduct key aspects of the research. Major government agencies include the Department of Health and Human Services, Veterans Administration, NASA, National Science Foundation, National Toxicology Program, DOE national laboratories, and Department of Transportation. Nongovernment partners include universities, nonprofit organizations, private industry, foreign organizations, small business initiatives, CRDAs, and consortia.

c. **S&T Investment Strategy**

As with combat casualty care, the investment strategy is to learn from technology demonstrations and use this experience to better define and refine requirements and evaluate new technologies. In executing the military operational medicine research program, technology efforts are arrayed according to the medical threats that they address. Distribution of investment among these threats is in accordance with their impact on operations, the potential contribution of technology to overcoming each threat, and the feasibility of achieving technology objectives through military investment.
(1) **Technology Demonstrations.** Integration of a set of noninvasive physiological sensing technologies will be demonstrated that can enable situational decisionmaking by commanders based on real-time knowledge of the individual and collective physical capability of deployed personnel.

Some of these sensing capabilities also have applications to trauma care; the medical application of these technologies are described within the combat casualty care subarea. Additional efforts will assess and validate the value of tactile (vibratory) stimulators in augmenting currently available cues across a representative range of simulated and operational training environments. Use of such stimuli has potential to reduce spatial disorientation accidents in the military and to improve navigation and awareness of target locations for sonar and radar operators. Efforts are currently focused on selection of appropriate signal transducers with several options available.

(2) **Technology Development.** Efforts are arrayed into the following functional areas for local and remote support to operational commanders with emphasis on warfighter performance:

- **Sustained operations/continuous operations,** including medical assessment for selection and classification of personnel, sleep and performance, operational stress, visual performance, spatial orientation, physical fitness and endurance, musculoskeletal injuries and physical performance, nutrition, and surface support.
- **Biodynamic (biomechanical) stress,** including effects and guidelines to reduce the hazards of maneuvering acceleration, abrupt acceleration and impact, vibration and motion, and repeated impact jolt; auditory and whole-body blast bioeffects; and noise effects related to operations.
- **Physiology in extreme environments,** including heat and cold stress, high-altitude effects (both terrestrial and aerospace), immersion, hyperbaric stress, safety of flight, and diving.
- **Non-ionizing radiation bioeffects,** including laser bioeffects and effects of RF and electromagnetic radiation.
- **Health effects of toxic hazards,** including occupational toxicology and health risk assessment and environmental effects of military toxic hazards.

(3) **Basic Research.** Basic research focuses on development of in vitro and in vivo models for risk assessment and the evaluation of physiological responses to operational stressors, development of animal behavioral models of human performance, and identification of humoral and other mediators of responses to operational stressors.

4. **Medical Radiological Defense**

a. **Warfighter Needs**

With the growing risk of nuclear proliferation through clandestine nuclear programs, the threat of the use of nuclear or other radiation weapons or the destruction of nuclear reactors in the area of operations remains real and substantial. Because it is likely that military missions will be conducted in radiation environments, the development of dose assessment bio-assays, prophylactic and treatment protocols, and knowledge of the health risks is essential to permit safe mili-
tary operations. Because exposure to radiation well below lethal levels can significantly alter the immunological status of the service member, it is essential that both risk assessments and medical countermeasures consider the combined insult of radiation exposure and other battlefield threat agents, especially those agents configured into biological and chemical warfare weapons. Operational planning and medical treatment require projection of increased casualty rates resulting from agent interactions. Predictive models for agent interactions will be developed and incorporated into existing models to provide improved projections of casualty rates.

Prevention of incapacitating and lethal ionizing radiation injuries will enable mission continuation and accomplishment in the nuclear or radioactive combat environment. Accurate casualty prediction models, particularly in combined NBC environments, are required for effective command decisionmaking and force structure planning to ensure mission success. An advanced biological dosimetry methodology is required for reliable determination of individual radiation exposure(s) for triage, treatment decisions, and long-term risk assessment. Anticipated increases in the use of depleted uranium (DU) munitions are expected to produce a significant number of casualties wounded with such weapons. DU research will ensure that service personnel receive optimal treatment to mitigate risks from DU exposure.

Potential payoffs in the short term include the development of therapeutic and protective strategies to permit 95% survival after acute exposure to ionizing radiation doses less than 10 Gray (Gy). Advanced biological dosimetry methodology will be provided for health risk assessment for doses above 25 cGy. In the mid term, improved therapeutic and protective strategies will be extended to chronic exposures and late effects (e.g., cancer). Data on the DU toxicity will provide essential information to focus research on required medical treatment strategies. In the long term, an automated biodosimetry methodology will be available for a wide range of doses and dose rates of radiation exposure. New models will provide data for NBC interactions to predict mortality and incapacitation from combined exposures. Protective and therapeutic strategies will allow access to a variety of radiation environments with minimal health risks. New biotechnology products will be tested as they become available for their application to radio-protection and therapeutics.

b. **Overview**

(1) **Goals and Timeframes.** The goals of the medical radiological defense subarea are to develop dose assessment bioassays, prophylactics, and therapeutic approaches to radiation injury alone and combined with CW or BW agents, and to define human health risks associated with operational radiation exposures. Specific milestones are as follows:

- **Radiation prophylaxis:** Develop drug regimens, given prior to or shortly after exposure, for protecting personnel from the adverse health effects of acute and chronic exposures to ionizing radiation. First-generation drug delivery systems for acute radiation injury will be evaluated in FY00. Improved prophylactic and therapeutic drug combinations for late-arising effects of radiation injury will be evaluated in FY02.

- **Assessment:** Estimate and model human health risks in low-dose/low-dose-rate exposures characteristic of the fallout fields from nuclear weapons and reactor accidents (FY99). Define the most important interactions of radiation with BW/CW agents...
Refine the sample protocol for the first-generation biodosimetry system (FY98–02). Incorporate improved dose measurement capabilities including a broader dose range and partial-body dose measurement into the first-generation biodosimetry system (FY01). Complete the automated scoring system in first-generation biodosimetry system (FY02).

- **Radiation injury treatment**: Develop the first-generation of treatment protocols for injuries arising from radiation alone or in combination with BW/CW agents (FY01).

### Major Technical Challenges

Drug toxicity represents a major challenge to the development of protective and therapeutic drugs. To overcome this, new pharmaceutical and bioengineered products will be tested, novel immunomodulators will be examined, and drug combinations will be assessed in order to minimize adverse reactions.

Since testing cannot be done in humans, most data are obtained using animal models, primarily rodents. Selected critical results will be repeated in higher species. In addition, historical human radiation exposures (e.g., radiotherapy patients, accident victims) are surveyed, compiled, and analyzed systematically for comparisons with laboratory animal studies. Ongoing studies of exposed populations in the former Soviet Union (FSU) and the results obtained from those studies will facilitate this process.

The processing time and technical complexity of bioindicator assays present challenges for their implementation. In an effort to automate the bioindicator methods, multiple approaches will be assessed for application and simplification. Fielding of bioindicator capacity will involve use of specialized equipment developed in-house linked with commercial-off-the-shelf technology.

### Related Federal and Private Sector Efforts

Although many agencies conduct radiobiology research, these efforts do not address military requirements that are the focus of the DoD research program. NASA has a radiation program funded at a level of about $6 million annually, with most research focused on the biological effects of cosmic rays. The National Cancer Institute, through its Chemical and Physical Carcinogenesis Program, provides about $20 million for basic radiation research and for epidemiological studies in the United States and FSU. A separate program at the National Cancer Institute (Extramural Radiation Research Program) provides about $45 million for basic and radiotherapy-related research on ionizing radiation. DOE funds basic radiobiology research at a level of approximately $5 million. The Nuclear Regulatory Commission funds approximately $1 million on modeling and prediction of effects of reactor accidents.

### S&T Investment Strategy

1. **Technology Demonstrations**: A multiple bioassay strategy will provide reliable radiation dose assessment for various radiation scenarios to ensure proper medical treatment of radiation casualties. Use of one bioindicator endpoint has been validated for use in cases of high-dose (3–10 Gy)/partial-body exposures. This has direct impact on current medical treatment decisions of bone-marrow transplant versus cytokine and antibiotic therapy. A second assay, the conventional dicentric aberration, has also been improved and is suitable for rapid and automated analysis. These bioindicator service capabilities are now being used as an in-house testbed to measure blood samples from persons exposed to radiation.

2. **Technology Development**: Efforts are arrayed into the following functional areas:
• *Radiation casualty management*, including use of new, advanced biotechnology products to treat immunohematopoietic injuries and bacterial, mycotic, and viral infections.

• *Risk assessment of NBC interactions*, including quantitation of the extent to which radiation increases susceptibility to BW or CW agents; this will greatly improve BW/CW casualty risk models.

• *Radiation bioindicators*, including an automated multiparameter dose assessment capability that can be fielded far forward on the battlefield to improve the rapid triage of ionizing radiation casualties.

• *Toxicity assessment for embedded DU*, including risk assessments for male and female personnel wounded by DU munitions.

(3) **Basic Research.** There are no basic research efforts in this subarea.