CHAPTER 3

MEDICAL
NUCLEAR, BIOLOGICAL, AND CHEMICAL WARFARE DEFENSE REQUIREMENTS AND RESEARCH AND DEVELOPMENT PROGRAM STATUS

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3.1 REQUIREMENTS

3.1.1 Introduction

The Gulf War, the Tokyo subway nerve gas (sarin) attack in March of 1995, the threatened release of radiocesium in Moscow's Izmailovo Park, and the Department of Defense (DoD) report released in April 1996 entitled *Proliferation: Threat and Response,* illustrate that many countries and terrorist groups have acquired the means for producing chemical, biological and radiological weapons and the means to deliver them. NBC proliferation increases the threat to deployed U.S. forces. In response, our medical chemical, biological and radiological defense research programs' (MCBRDRP) mission is to preserve combat effectiveness by timely provision of medical countermeasures in response to joint service chemical warfare (CW) defense requirements and threats due to validated biological warfare (BW) agents, and threats associated with radiological/nuclear warfare devices (RW). The MCBRDRP has three goals:

(1) Provide individual level protection and prevention to preserve fighting strength;
(2) Maintain technological capabilities to meet present requirements and counter future threats; and
(3) Provide medical management of CW, BW, and RW casualties to enhance survivability and expedite and maximize return to duty.

Chemical warfare agents are available worldwide and include vesicants (blister agents), nerve, blood, and respiratory agents. Biological threat agents include bacteria, viruses, rickettsia, toxins, and physiologically active compounds which can be produced by any group with access to a scientific laboratory or pharmaceutical industry. The primary nuclear threat is the use of conventional explosives to spread nuclear contamination over a limited area or strategic terrain (including usage against reactors or industrial radiation sources) and potentially the use of a single or a small number of crude Hiroshima-type nuclear weapons. Nuclear radiation includes gamma rays and neutrons. Exposure to multiple threats may result in synergistic effects. Assessment methodologies enable threat evaluation and injury assessment. Medical treatment strategies reduce the performance decrement, injury, and death of military personnel in the field, thereby enabling them to accomplish their missions as well as reducing the need for medical resources.

The DoD has maintained a medical research and development program for nuclear, biological, and chemical (NBC) defense for many years. This program has resulted in the fielding of numerous products to protect and treat service members. The DoD program to stockpile biological defense products has been smaller than the chemical defense effort but has received greater emphasis in the past five years.

Specific initiatives programmed to improve NBC medical readiness include:

- Continued emphasis on NBC medical countermeasures research.
- Medical collective protection.
- Identification and testing of medications and therapeutic regimens which reduce the effect of radiation on both bone marrow and the intestinal tract.
- A biological defense immunization policy.
- An award of a prime contract to develop, license, produce, and store biological defense vaccines.
- Enhanced medical diagnostic capability of exposure to all agents.
- Definition of low dose radiation interaction on susceptibility to biological and chemical agents.

3.1.2 Challenges in the Medical NBC Warfare Defense Programs

Medical prophylaxes, pretreatments, and therapies are necessary to protect personnel from the toxic or lethal effects of exposure to all validated threat agents. DoD has fielded a number of medical countermeasures, which greatly improve individual medical protection, treatment, and diagnoses.

DoD complies with all Food, Drug and Cosmetic Act requirements. The Food and Drug Administration (FDA) requires large-scale field trials in human subjects to demonstrate efficacy of drugs and biologicals prior to licensure. There are, however, legal and ethical constraints that preclude such efficacy studies for NBC countermeasures. Field studies of efficacy cannot be performed, since exposure to most NBC agents does not usually occur naturally. Moreover, the high lethality and/or toxicity of NBC agents also makes it unethical to expose human subjects in controlled efficacy studies usually required by the FDA for product licensure (*e.g.*, tests of effectiveness of the product against the threat in humans). For these reasons, many NBC countermeasures are likely to remain in an Investigational New Drug (IND) status, requiring their administration under provisions of an approved protocol and with written informed consent from service members. In contingency situations, DoD may request a waiver of informed consent from the FDA. DoD continues to work with the FDA to seek alternative methods for demonstrating safety and efficacy of NBC medical countermeasures and to obtain their licensure.

Contrary to many media reports[1], medical NBC defense products are thoroughly evaluated and tested for their safety in accordance with FDA guidelines (see figure 3-1) before they are permitted to be administered to any personnel. It is unacceptable for the military to use its own forces as "guinea pigs." All NBC defense medical products must be safe to use and not degrade operational performance. In cases where adverse effects are known or are possible, a decision must be made—and a risk accepted—of the real or potential effects of a medical product versus the catastrophic effects of NBC weapons. Even though efficacy may not be fully understood, the safety (including adverse effects) is extensively understood. In many cases, the

[1] See for example, Victor Sidel quoted in Dave Parks, "Military tries to plug chem defense gaps," *Birmingham News*, p.1; "Gulf War Syndrome," by Ed Bradley on *60 Minutes*, CBS-TV, September 29, 1996; "In general, a sickening syndrome," New York Daily News, December 7, 1996, p. 11; Thomas Tiedt quoted in David Ballingrud, "Ex-researcher: Gulf 'vaccine' was a poison," *St. Petersburg Times*, December 2, 1996, p. 1.

safety is well understood because the medical products have been widely used to treat other medical conditions. (For example, pyridostigmine bromide nerve agent pretreatment has been in use since the 1950s to treat myasthenia gravis, a neuromuscular disorder. The anthrax vaccine has been used since the 1970s to vaccinate veterinarians, textile workers, and others. Various anti-emetics to protect against radiological threats have been used to treat cancer patients undergoing radiation therapy.)

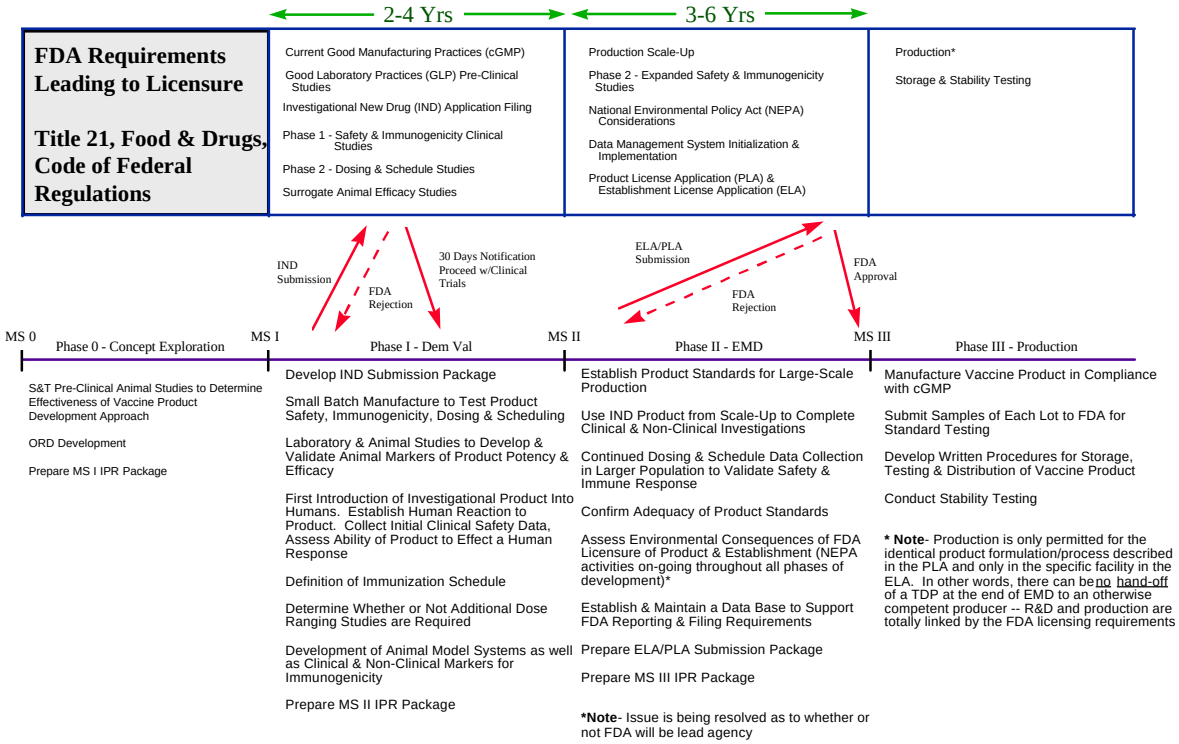

Figure 3-1. Standard FDA Approval Process for Biological Defense Medical Products

The medical NBC defense research programs discussed in this section are divided into chemical, biological, and nuclear areas of research. Table 3-3 (on page 3-16) provides a summary of the medical NBC defense programs and the planned modernization strategy over the next fifteen years.

3.1.3 Reducing Reliance on Research Animals

The FY95 National Defense Authorization Act directed DoD to establish aggressive programs to reduce, refine, or replace the use of research animals. In April 1995, DoD issued Directive 3216.1, "Use of Laboratory Animals in DoD Programs," which mandated standardization of all DoD animal use protocols. The new protocol format requires identification of provisions to reduce, refine, or replace the use of animals. Therefore, an objective of the Medical Chemical, Biological and Nuclear (Radiological) Defense Research Programs is to utilize and develop technologies that will reduce reliance on animal research. In Fiscal Year (FY) 1996, the Medical Chemical, Biological and Nuclear Defense Research

Programs utilized computerized molecular modeling, computer predictions, *in vitro* cell cultures, a cell-free reaction system, a lipid bilayer system, and animal species lower on the phylogenetic scale to refine, reduce, and replace the use of animals.

3.1.4 Medical Program Organization

Chemical/Biological. The U.S. Army is the Executive Agent for the Medical Chemical and Biological Defense Research Programs as prescribed in DoD Directive 5160.5 and, as such, is the lead requirements coordinator. The programs are integrated DoD in-house and external efforts. The Joint Technology Coordinating Group (JTCG) 3 (Medical CW Agent Defense) and JTCG 4 (Medical BW Agent Defense) of the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee are responsible for the programs' joint consolidation, coordination, and integration. The ASBREM Committee maximizes efficiency by coordinated planning, and minimizes unnecessary program overlaps and costly materiel retrofits. (The integration of program management and oversight of medical and non-medical NBC defense programs is described in chapter 1.) The Army Technology Base Master Plan and the Medical Science and Technology Master Plan are the program drivers for the chemical and biological research programs. The science and technology base is managed through the development and execution of Defense Technology Objectives (DTO) and Science and Technology Objectives (STO). The predevelopment program (basic research; exploratory development; and concept exploration and definition) is directed by the U.S. Army Medical Research and Materiel Command (USAMRMC). The advanced development program (Program Demonstration and Risk Reduction (PDRR); and Engineering and Manufacturing Development (EMD)) for medical *chemical* defense products is directed by the U.S. Army Medical Materiel Development Activity (a USAMRMC asset). The advanced development program (PDRR and EMD) for medical *biological* defense products, including the joint vaccine acquisition program, is directed by the Joint Program Office for Biological Defense (JPO-BD).

Nuclear. The study of the medical and biological effects of ionizing nuclear radiation is performed by the tri-service Armed Forces Radiobiology Research Institute (AFRRI). AFRRI programs are integrated into other DoD in-house and external efforts under the coordination of ASBREM. Specific requirements and tasking for AFRRI research comes from the individual services, Joint Staff, and the Defense Special Weapons Agency (DSWA) through the authority of a Board of Governors (BOG) with funding from the Director, Defense of Research and Engineering (DDR&E) under the Under Secretary of Defense for Acquisitions and Technology. AFRRI is under the administrative control of the Uniformed Services University of the Health Sciences (USUHS). Members of the AFRRI BOG include the President of USUHS, DDR&E, the Assistant to the Secretary of Defense for Nuclear and Chemical and Biological Defense Programs (ATSD(NCB)), the Assistant Secretary of Defense for Health Affairs (ASD(HA)), the Commander of DSWA, and the Surgeons General of the Army, Navy, and Air Force. Major inputs to AFRRI research requirements are driven by the biennial Army Qualitative Research Requirements (QRR), compiled by the U.S. Army Nuclear and Chemical Agency (USANCA).

3.2 MEDICAL CHEMICAL DEFENSE RESEARCH PROGRAM

The mission of the Medical Chemical Defense Research Program (MCDRP) is to preserve combat effectiveness by timely provision of medical countermeasures in response to joint service chemical warfare defense requirements.

3.2.1 Goals

The goals of the MCDRP are the following:

- Maintain technological capability to meet present requirements and counter future threats:

  - Determine sites, mechanisms of action, and effects of exposure to chemical warfare agents with emphasis on exploitation of neuroscience technology and dermal pathophysiology.
  - Identify sites and biochemical mechanisms of action of medical countermeasures.
  - Exploit molecular biology and biotechnology to develop new approaches for medical countermeasures.
  - Exploit molecular modeling and quantitative structure-activity relationships supporting drug discovery and design.

- Provide individual-level prevention and protection to preserve fighting strength:

  - Develop improved prophylaxes, pretreatments, antidotes, and therapeutic countermeasures.
  - Develop skin protectants and decontaminants.
  - Identify factors that influence safety and efficacy properties of candidate countermeasures.
  - Develop and maintain preformulation, formulation, and radiolabeling capabilities.

- Provide medical management of chemical casualties to enhance survival and expedite and maximize return to duty:

  - Develop concepts, and recommend therapeutic regimens and procedures for the management of chemical casualties.
  - Develop diagnostic and prognostic indicators for chemical casualties.
  - Develop life-support equipment for definitive care.

3.2.2 Objectives

The objectives of the MCDRP differ with the varying threats:

- For vesicant (or blister) agents, the objective is to develop a pathophysiological data base on vesicant chemical agents and develop a working hypothesis on how damage occurs at the cellular level. Used with associated technologies, this approach will enable the formulation of definitive pretreatment and treatment strategies, and is expected to produce a realistic concept for medical prophylaxis, immediate post exposure therapy and topical protection.
- For nerve agents, the objective is to field a safe and effective advanced anticonvulsant nerve agent antidote, and develop and field a more effective enzyme reactivator for use with the Mark I Nerve Agent Antidote kit.
- For blood agents, the objective is to develop and field a safe and effective cyanide pretreatment.
- For respiratory agents, the objective is to develop approaches to prophylaxis and therapy by understanding pathophysiological changes after agent exposure.

3.2.3 Threats, Countermeasures, Technical Barriers, and Accomplishments

The chemical warfare threats and countermeasures, as well as chemical defense research and development technical barriers and accomplishments, are outlined in Annex D (Section D.1).

3.3 MEDICAL BIOLOGICAL DEFENSE RESEARCH PROGRAM

The mission of the Medical Biological Defense Research Program (MBDRP) is to develop medical countermeasures to protect U.S. forces and thereby deter, constrain, and defeat the use of biological agents against them (DoD Directive 5160.5, May 1985). The program is directed against agents of biological origin that are validated military threats. A primary concern is the development of vaccines and other medical products that are effective against agents of biological origin (see Table 3-1).

3.3.1 Goals

Goals of the MBDRP include the following:

- Protecting U.S. forces' war fighting capability during a biological attack.
- Reducing vulnerability to validated and novel threats by maintaining a strong technology base.
- Providing medical management of biological warfare casualties.

3.3.2 Objectives

In accomplishing the goals of the MBDRP, efforts are focused on three objectives:

- Prevent morbidity and mortality through the use of vaccines, drugs, and other medical pretreatments.
- Diagnose disease through the use of forward deployable diagnostic kits and

confirmation assays.
- Treat casualties to maximize return to duty through the use of antitoxins, drugs, and other medical treatments.

The MBDRP responds to requirements from the DoD as identified in DoD Directive 6205.3, "Biological Defense Immunization Program," the Joint Service Agreement on Biological Defense, the Joint Warfighting Science and Technology (S&T) Plan, the Defense Technology Assessment Plan, and the Defense S&T Strategy. The MBDRP includes the following areas of research:

- Bacterial studies – Develop potential vaccines and determine the role of these vaccines in the cellular and humoral immune response. Identify virulence factors and protective antigens and the specific genes of these factors/antigens in bacterial threat agents and use this knowledge in the development of second generation recombinant vaccine candidates. Evaluate modern antibiotics for effectiveness in the treatment and/or post-exposure prophylaxis of bacterial threat agents.
- Toxin research - Basic and developmental research leading to methods of prevention and treatment against broad classes of toxins to include use of site-directed mutagenesis and protein engineering of recombinant vaccine candidates.
- Viral and Rickettsial studies – Identify and characterize threat organisms, conduct molecular antigenic analysis, develop diagnostic assays, and investigate pathogenesis, immunology, and epidemiology that will allow decisions regarding the optimal approach to disease prevention and control. Develop vaccine candidates and treatment strategies for viral and rickettsial threat agents.
- Diagnosis – Investigate and evaluate sensitive and specific methods for detection of infectious organisms, toxins, antigens and antibodies in biological materials to include the application of nucleic acid probes or synthetic antigens. Develop rapid identification and diagnostic methods for the assay of toxins, metabolites, and analogs in clinical specimens.

3.3.3 Threats, Countermeasures, Technical Barriers, and Accomplishments

A biological threat agent is defined as an intentionally disseminated living microorganism or toxin that can cause disease or death in humans. Threat agents include a broad range of microorganisms (bacteria, rickettsia, and viruses) and toxins of biological origin. Biological weapons are easy to make, difficult to detect, very effective, and highly selective against humans, animals, or plants. Defense against this class of weapon is difficult, particularly when biological agents can produce casualties over an area of thousands of square kilometers. Biological agents can also be used with devastating effect in combination with nuclear, chemical, or conventional weapons.

Countermeasures and diagnostic techniques for biological weapons are shown in Table 3-1. Critical elements of medical biological defense include the ability to protect U.S. forces from BW agents, to rapidly diagnose (in biological specimens) infection or intoxication from an agent, and to treat casualties. Currently, the most effective countermeasure is pre-

deployment active immunization. Future threats may involve genetically engineered biological weapons that may be easily produced, highly lethal, difficult to detect, and resistant to conventional therapies.[2]

Table 3-1. Medical Biological Defense Countermeasures and Diagnostic Techniques

VACCINES

- *Killed* – killed or inactivated microorganism that is incapable of replicating but stimulates immunity.
- *Live, attenuated* – live organism, genetically selected not to cause disease but able to stimulate immunity.
- *Toxoid* - toxin protein treated to inactivate its toxic quality but retains its ability to stimulate immunity.
- *Recombinant* – section of protein that stimulates specific immunity to a BW agent. Protein section may be produced in high yields through bioengineering.
- *Deoxyribonucleic Acid (DNA)* – section of DNA that codes for section of protein that stimulates specific immunity to a BW agent. DNA appears to produce foreign protein in recipient which stimulates immunity.
- *Polyvalent* – mixture of antigens that protects against a number of different BW agents.
- *Vectored* – carrier organism bioengineered to confer immunity against an unrelated BW agent or multiple agents.

ANTIBODY (ANTISERUM, ANTITOXIN)

- *Heterologous* – antibodies collected from animals (*i.e.*, different species than the recipient) repeatedly immunized against the BW threat. These antibodies must be treated to reduce the human immune response against them (serum sickness).
- *Homologous* – antibodies of human origin (*i.e.*, same species as the recipient) that provide protective immunity against the the BW threat. These antibodies are not prone to stimulating serum sickness.
- *Monoclonal* – a cell culture technique for producing antibodies against a specific disease.
- *Bioengineered* – Antigen binding site on the variable portion of an antibody elicited in a non-human system is combined with the non-variable portion of a human antibody to produce a "humanized" antibody.

DRUGS

- *Antibiotics* – very effective against bacteria but are ineffective against viruses and toxins.
- *Others* – compounds that offer new possibilities for protecting against and treating exposure to BW agents (such as antiviral compounds).

DIAGNOSTIC TECHNOLOGIES

- *Immunological technologies*. These tests rely on antibodies for detecting the presence of foreign proteins associated with the BW agent. They are easy to use, compact, rapid (minutes), and require little logistic support. These tests are currently used in out-patient clinics and doctor's offices.
- *Nucleic acid technologies*. Nucleic acid tests, specifically the polymerase chain reaction (PCR), rely on segments of genes unique to BW agents to detect the presence of those agents. These tests are extremely sensitive and specific, but require more support to perform.

[2] A detailed assessment of the potential impact of new or genetically engineered biological weapons is included in a report prepared by the Department of Defense entitled *Advances in Biotechnology and Genetic Engineering: Implications for the Development of New Biological Warfare Agents*. This report was submitted to Congress in June 1996.

The current MBDRP includes the following research areas for the development of medical countermeasures:

- Characterize the biochemistry, molecular biology, physiology, and morphology of biological warfare threat agents;
- Investigate the pathogenesis and immunology of the disease;
- Determine the mechanism of action of the threat agent in an animal model system;
- Define the sites and mechanisms of action of candidate vaccines;
- Establish safety and efficacy data for candidate vaccines.
- Select antigen(s) for candidate vaccines.
- Develop medical diagnostics and chemo/immunotherapeutic agents and preparations.

Technical shortcomings in the private sector include the lack of high level biological containment (BL-3 and BL-4) laboratory facilities to support biological defense research and scientific expertise in biological defense. These factors restrict the depth of expertise, facilities, and support available. This has become a critical issue in light of current personnel and program downsizing initiatives and the additional emphasis that is being placed on out-sourcing MBDRP work. The technological and scientific expertise for biological defense can therefore be eroded quickly.

Details of the biological warfare threats and countermeasures, as well as biological defense research and development technical barriers and accomplishments, are presented in Annex D (Section D.2).

3.4 MEDICAL NUCLEAR (RADIOLOGICAL) DEFENSE RESEARCH PROGRAM

The mission of the Medical Nuclear Defense Research Program (MNDRP) is to conduct research in the field of radiobiology and related matters essential to the support of the Department of Defense and the Military Services. The sole repository of defense radiobiology expertise is AFRRI.

3.4.1 Goals

The goals of the MNDRP are the following:

- Develop medical countermeasures for the acute, delayed and chronic effects of radiation.
- Design a neutralization plan to respond to “new technology” biological weapons of mass destruction (WMD).
- Identify and quantify hazards of depleted uranium munitions to military and civilian casualties, both female and male.
- Develop rapid bioassay for radiation injury suitable for field deployment
- Produce improved chelating agents for use in treating internal contamination by radioactive heavy metals.

• Sustain combat capability, increase survival, and minimize short- and long-term health problems associated with ionizing radiation alone, and when radiation is combined with other weapons of mass destruction.
• Respond to immediate operational requirements that require expertise in either radiation medicine, health physics or radiobiology.
• Maintain core of scientific expertise necessary to meet current research requirements and to counter current and future radiological threats.
• Provide nuclear radiation weapon effects medical training for DoD medical personnel.

3.4.2 Objectives

The primary objective of this research group is to address the major aspects of military operational requirements for dealing with radiation injuries. A nuclear threat agent is any weapon which causes detrimental medical effects by either direct external irradiation or by internal contamination with radioactive material. These agents include radiation dispersal weapons, which scatter radioactive material with conventional explosives, deliberate area contamination, destruction of a nuclear power plant, improvised nuclear devices and traditional nuclear weapons. Operational requirements include programs in casualty management, medical radioprotectants to diminish radiation injury, medical therapeutic regimens, maintenance of performance, and radiation hazards assessment.

3.4.3 Threats, Countermeasures, Technical Barriers, and Accomplishments

The deployment of a relatively low-yield nuclear device or Hiroshima-type weapon targeted at either a military installation or a political target (*e.g.*, the seat of government, large population center, or commercial port city) is increasingly possible by a terrorist or third-world country. In such a scenario, citizens outside the immediate lethal area would be exposed to the prompt radiation of the initial explosion as well as to chronic exposures resulting from the residual radioactive contamination. The use of radiation dispersal devices, such as the destruction of a nuclear reactor, contamination of a battlefield with nuclear waste, or deliberate radioisotope contamination of the rubble in an Oklahoma City-type conventional explosives attack, is another type of nuclear scenario. Most casualties in these scenarios would suffer non-lethal doses of external irradiation, which would complicate the management of their conventional injuries and could cause internal contamination with radionuclides. (The nuclear weapons inventory of any current adversary is expected to be small, but if the weapon use is for military advantage, concomitant use of biological or chemical weapons is anticipated.)

Early radiation injury diminishes the soldier's ability to fight and survive. Effective radiation countermeasures must protect the soldier from performance decrement and simultaneously diminish lethality and the long-term effects of radiation injury. Therapeutic measures will increase the survival and diminish the morbidity of individual soldiers who are wounded by radiation. A research program to understand molecular and cellular damage induced by radiation is needed to determine the best medical countermeasures for the new radiogenic wounding agents on the modern battlefield. Table 3-2 presents an overview of medical countermeasures to radiological exposure and research accomplishments during FY96.

Table 3-2. Medical Nuclear Defense Countermeasures and Accomplishments

PRETREATMENTS

Multidrug combinations: Animal research has proven that certain radioprotectant drug combinations administered at nontoxic levels interact synergistically to markedly increase mammalian resistance to radiation.

Antiemetics: Granisitron (KytrilR) has been adopted as the NATO standard pretreatment antiemetic medication to significantly block performance degrading early symptoms of radiation injury. This allows mission completion and consequently diminishes the overall casualty rate.

DEPLETED URANIUM TOXICITY

Metabolism of metallic uranium fragments: Prior to the wounding of soldiers in Desert Storm, very little was known about the toxicity of implanted metallic uranium fragments. Previous uranium toxicity studies had been limited to inhaled uranium oxides in uranium workers. Preliminary aspects of animal studies indicate distribution to depot sites throughout the body and potential risks of late effects. Adequate chelation therapy does not exist at this time to increase excretion of this material.

Fetal metabolism of depleted uranium: During the next conflict, it is anticipated that young female soldiers will be wounded by enemy depleted uranium weapons. No knowledge exists of the effects of this material on subsequent pregnancies.

MEDICAL THERAPIES

Specific Cell Line Stimulants: Granulocyte-Macrophage Colony Stimulating Factor has been demonstrated to be highly effective in restoring the immune competence of the bone marrow and allowing survival from radiation injuries previously considered lethal. The cytokine thrombopoietin has been developed as a therapeutic agent and is undergoing further trials as a platelet-formation stimulant.

Broad Range Cellular Recovery Stimulants: Research continues into biologically stable compounds which stimulate recovery of multiple hematopoietic cell lines.

Susceptibility to Infectious Agents and Efficacious Therapy: Research continues to assess susceptibility and resistance to infectious agents in conjunction with use of prompt and chronic sublethal irradiation, and to develop combined modality therapies that attack microorganisms and enhance innate immune response in irradiated personnel.

Internal Contamination Chelation Agents: Currently available chelation agents capable of removing internal radioisotopes are investigational drugs which have been utilized with limited success. More effective ligand-type compounds have been identified and are undergoing evaluation. Other modalities being investigated include seaweed based Alginates which appear to be promising.

DIAGNOSTIC TECHNIQUES

Biodosimetry and Dose Assessment: No dose assessment method other than individual physical dosimeters can be currently made available to deployed soldiers. Automated chromosome dicentromeric analysis has been developed and can be made deployable to the Echelon 3 medical care level, and other, more rapid, methods are being evaluated.

CHEMICAL AND BIOLOGICAL WARFARE INTERACTIONS WITH RADIATION

Increased lethality of biological weapons after low level irradiation: Ongoing studies indicate even low levels of radiation exposure will markedly increase the infectivity of biological weapons. Existing data suggest synergistic interactions of mustard and nerve agents with ionizing radiation.

Significant progress has been made in prophylactic and therapeutic measures that will reduce mortality and morbidity in high dose radiation environments. During the Cold War, the numbers of casualties resulting from the large scale deployment of nuclear weapons would have easily overwhelmed the medical assets of NATO forces. In the current threat environment, adequate planning for medical response to a very limited nuclear attack is mandatory. While casualty numbers from a nuclear detonation will still be large, countermeasures have been developed which will significantly limit the morbidity and the secondary mortality. These modalities will be particularly important in the likely scenario of terrorist use of radiation weapons. If the attack is limited to one or, at worst, a small number of events, the ability to provide intensive, sophisticated medical and other support is highly credible because of the availability of uncompromised treatment/research centers and medical evacuation capabilities.

Details of the radiological threats and countermeasures, as well as nuclear defense research and development technical barriers and accomplishments, are presented in Annex D (Section D.3).

3.5 MEDICAL NBC RESEARCH PROJECTION

Table 3-3 presents a projection of the medical NBC defense programs and modernization strategy for the next 15 years.

Table 3-3. Medical NBC Defense Programs and Modernization Strategy

	NEAR (FY97-99)	MID (FY00-04)	FAR (FY05-11)
Medical - Chemical Defense	**Licensed Topical Skin Protectant**	**Licensed Advanced Anticonvulsant** **Licensed Cyanide Pretreatment** **Licensed Multi-chambered Autoinjector**	**Licensed Reactive Topical Skin Protectant** **Licensed Advanced Prophylaxis for Chemical Warfare Agents** **Licensed Specific Protection and Treatment for Blister Agents (vesicant agent countermeasures)** **Licensed Vesicant Agent Prophylaxis**
Medical - Biological Defense	**Anthrax vaccine Relicensure**	**Licensed Q fever chloroform-methanol residue (CMR) vaccine** **Licensed Tularemia vaccine** **Licensed Vaccinia, cell culture derived vaccine** **Licensed Botulinum A/B/E/F monovalent vaccines** **Rapid Diagnostic Kit for Biological Warfare Threat Agents**	**Licensed Botulinum Tetravalent vaccine** **Licensed Botulinum C vaccine** **Licensed Botulinum D vaccine** **Licensed Botulinum G vaccine** **Licensed Ricin vaccine** **Licensed Staphylococcal Enterotoxin B (SEB) vaccine** **Licensed new Plague vaccine** **Licensed new Venezuelan Equine Encephalomyelitis (VEE) vaccine** **Licensed combined VEE, Western Equine Encephalomyelitis (WEE), & Eastern Equine Encephalomyelitis (EEE) vaccine** **Licensed Brucellosis vaccine** **Licensed new Anthrax vaccine**
Medical - Nuclear Defense	**Depleted uranium shrapnel toxicity assessment** **Evaluation of new chelation agents (ligands and Alginates)** **Multidrug radioprotectants validated** **Combination cytokine therapy validated** **Echelon 3 fieldable biodosimetry** **Licensed novel drug-delivery systems** **Risk Assessment for low-dose, low-dose rate radiation effect**	**Licensed treatment modalities for depleted uranium shrapnel casualties** **Radioprotectant transdermal patches** **New generation prophylactic and therapeutic immunomodulators for multi-organ injuries** **Computer models to understand effects resulting from combined NBC attacks**	**Licensed Radiation-induced cancer/mutation preventive techniques** **Licensed Countermeasure for Chem-Bio-Radiation interaction**

3.6 MEDICAL R&D REQUIREMENTS ASSESSMENT

- **DoD lacks FDA licensed vaccines against BW threat agents.**

SOLUTION: The DoD will award a prime systems contract during FY97 for the acquisition of vaccines, to include advanced development, FDA licensure, production, storage and testing. In addition, DoD will complete an assessment of vaccine requirements and update vaccination policy for U.S. forces in order to define the cost and scope of the program.

- **The effects on humans resulting from the exposure to low doses of chemical agents, particularly organophosphate (nerve) agents, are not clearly understood.**

SOLUTION: Beginning in FY96, DoD, in association with the Research Working Group of the Interagency Persian Gulf Veterans' Coordinating Board, dedicated $5 million to evaluate the chronic effects of low-dose level exposure to chemical agents. Additional funds have been committed for similar and follow-on research in FY97. Studies will address both vesicants as well as nerve agents. Funds will be used to evaluate effects of chemical agents potentially related to chronic health complaints, and for epidemiological projects aimed at identifying health consequences in military personnel potentially exposed to chemical agents.

- **The effects on humans of low level radiation, contamination fields, radiogenic munitions, *i.e.*, depleted uranium, and their interactions with chemical and biological weapons have not been evaluated. All preliminary data indicate a high probability that interactions will result in markedly increased numbers of casualties.**

SOLUTION: Definitive assessment of NBC threat interactions and NBC agent modeling will support the strategic design and development of specific preventative and treatment countermeasures.