Toxicological models: The Toxicological Model development effort (led by Ken Dixon, TIEHH/TTU) includes the development of Physiologically-Based Pharmacokinetic (PBPK) models based upon and to include effects at all levels of the organism with emphasis on agent concentrations reaching specific organs at both the individual and population levels. The Toxicological Model will also include models of uptake and distribution of chemicals/pathogens of concern to predict the dose to small mammal populations feeding upon vegetation. A Geographic Information System (GIS) will be used to map sources of contamination. Sites will be identified for study by overlaying additional data layers, including atmospheric conditions, population density, and other demographic data.

Because the dynamics of real systems are quite complex, understanding the impact of BW contaminants on the environment can be enhanced by modeling the system. The adverse effects of multiple toxic variables are directly related to their ability to interfere with the normal functioning of both physiological and environmental systems. The proposed research will focus on the prediction of both acute and long-term effects of chemicals and biological agents of concern on agricultural populations as well as human populations. This requires a mechanistic approach to modeling.

For each expected scenario time response parameters will be expressed as functions of dose to obtain biologically-based dose-response (BBDR). In the case of multiple exposures, the concentration x time (CxT) relationships will be examined. Functional relationships will then be examined between correlated endpoints. This modeling approach will allow future simulation of real-world exposure scenarios. The probability of developmental effects, reproduction, and survival will be incorporated into an individual-based model. Monte Carlo simulations will be run to obtain probabilistic forecasts of population dose responses.

Linear and nonlinear regression, using SAS (SAS Institute Inc.), will be used to develop the dose-response model. The individual-based model will be programmed using MATLAB (The MathWorks Inc.) and C^{++}. The spatial data will be mapped using the ARC/INFO (Environmental Systems Research Institute, Inc.) geographic information system language. The computer simulations will be done using the Unified Transport Model (UTM) developed by Oak Ridge National Laboratory. The basic component of the UTM is the Terrestrial Ecology and Hydrology Model (TEHM) with physically-based subroutines for interception, infiltration, soil-plant water flow storm and groundwater flow. The model simulates runoff, infiltration, soil moisture, and ground water transport for pervious and impervious areas, as well as chemical fate and transport on the land surface, into ground waters, into and through streams, and in well mixed ponds and lakes. The model simulates the effects of toxic chemicals, pesticides, and nutrients on water quality.

Epidemiological models: The goal of bioterrorism is to cause a large amount of morbidity or mortality in a short time span and to have the terrorist event remain undetected for as long as possible. Whether the delivery agent of a bioterrorist agent is chemical or biological, if successful, it should either spread rapidly or go undetected for a long period of time. To understand the nature and spread of various biological agents within a population and to reduce the associated risks, epidemiological models will be formulated, analyzed, and simulated. The epidemiological modeling group (led by Linda Allen, TIEHH/TTU) will develop epidemiological models that follow the growth and spread of a biological agent and the progression of disease throughout a population. Epidemiological modeling will be used as an assessment and training tool to help identify the impact of different biological agents on a particular population, to determine the short-term and long-term risks of different agents, and to test the effectiveness of various treatments and countermeasures in responding quickly and alleviating the effects of the bioterrorist attack.

Epidemiological models for the spread of infectious diseases may be applied to human, plant, or animal populations. In the simplest type of epidemiological model, the host population is subdivided into the following categories: susceptible S, exposed E, infective I, and removed or immune R. Hence, these types of epidemiological models are referred to as SEIR models. In more detailed models, other categories are included such as latent or vaccinated individuals or the population may be further subdivided according to age, physical location, or risk group. The movement of the population through each of these categories can be modeled by systems of difference or differential equations (ordinary or partial differential equations) which account for the temporal and spatial dynamics of the population.

A two-dimensional spatially-discrete epidemic model of the U.S. population will be developed that models the main population centers, flow rates between the centers, and contact rates within the centers. Flow rates between the cities can be modeled using information about public and private transportation. (A similar model but on a much smaller scale was developed to evaluate the impact of a vaccination program for a measles epidemic at Texas Tech University.)

The qualitative behavior of these SEIR-type models (e.g., conditions required for existence of steady states, stability of these steady states, and asymptotic behavior) can be determined through extensive mathematical analyses. However, extensive computer simulations are also required to determine the quantitative behavior of the model, i.e., the effects of specific biological agents and the diseases that they manifest within a population. Efficient numerical computations require knowledge of the initial and boundary conditions and the values of the parameters in the model. Other experts involved in this initiative will provide expertise for the identification and estimation of critical model parameters for specific biological agents. The initial conditions are specified according to where and to what extent the biological agent is introduced (different scenarios will be hypothesized by the detection group). The boundary conditions are specified according to the agents' ability to spread beyond a particular region (different scenarios for spatial spread can also be hypothesized). There are numerous numerical techniques that will efficiently and rapidly solve large systems of difference and differential equations. Through extensive mathematical analyses and numerical simulations, the progression of the disease through time and space, the amount of morbidity or mortality that occurs, and the effectiveness of various treatments and countermeasures can be quickly and easily evaluated.

Epidemiological models help in the evaluation and assessment of a bioterrorist attack on a particular population. However, epidemiological models integrated with models of the environment, toxicological models, and physiological models will help in the evaluation of the effects on the individual, environment, and ecosystem.

Physiological Modeling: The physiological modeling group (Clyde Martin, director, TTU/TIEHH) has expertise in the development of mathematically based models that are physiologically correct and that are capable of mimicking the function of a single organism, a single organ or a connected set of organs. Well-developed models allow the user to conduct experiments and to insert pathologies that are impossible in a laboratory setting. Excellent examples of such models include the work of Tran and group at North Carolina State University on the metabolism of dioxin in the human body and that group's work on the effect of carbon dioxide on sleep patterns in infants; the work at Cornell on the dynamic modeling of the blood flow in the heart; the work of Martin and group at Texas Tech University on the dynamic models of the eye and their work on the prediction of stress fracture in the tibia; and the work of Dayawansa and group at Texas Tech University on the neural activity in the visual cortex. All of these models share the property that they are physiologically correct and can be modified to include abnormalities of various sorts.

Specific biological and chemical agents will be targeted to develop models that will predict their interaction with specific organs. For chemical agents that are inhaled there is considerable understanding of the mode of action for acute exposure. For sublethal exposures that are close to the detection range, much less is known. Models of the pulmonary-cardiac network will be developed to understand how the agent is distributed in the body, incorporating all that is known about how the agent and its byproducts are concentrated in various organs. Particular attention will be paid to the effect of very small concentrations at the neural level. Such a model is complicated but its development will be facilitated by the supercomputer at TIEHH/TTU/Reese Center. Probabilistic methods will be used to compensate for low level exposure.

Bacteriological and viral agents present interesting modeling problems but these agents may very well be the agent of choice in a CB event. Bacteriological agents cause both mortality and morbidity. An agent such as bubonic plague is easy to cure if detected early enough. However the treatment is subtle because of the massive number of organisms produced in the human body. The organism must be killed slowly enough to prevent the body from failing due to the problem of eliminating the mass of decomposing bacteria. On the other hand the bacteria must be killed rapidly enough so that the toxin produced by the bacteria does not cause death. Models of the organism within the body and its growth will be developed in the model in such a way that the process of antibiotic treatment may be introduced as a variable. This model will be used to predict the consequences of the speed of the antibiotic regime.

Viral agents present a much different and more difficult modeling scenario and there is virtually no modeling effort in this area. Viral agents act by invasion of cells and this can be modeled. The interaction of the virus with the cellular structure must be understood. This will require close collaboration between the modelers and virologists. This collaboration is possible and will be developed. There is already a very close cooperation between the mathematics, biology, cell biology and pharmacology departments at TTU and TTUHSC. By understanding and developing such models, the research group will be able to predict the effect of various prophylactic agents on viral infection.

Virus particles are often stored in a dormant mode in the body. This is not well understood but is potentially a very important consequence of a CB event. The effects of a viral attack could last for years in the population and cause serious disruption in the community for many decades after the attack. The recurring problems associated with polio are a good example of what may happen. Models do not solve problems, but they do allow the investigation of phenomena that may be difficult or impossible to study in the laboratory. Physiological models work hand in hand with laboratory experiments to suggest important avenues of experimentation, and epidemiological models are useful to predict the effect of an agent on a population.

University of Texas (Austin) Contribution:

A single point HTML/JAVA interface to heterogeneous data will be constructed. Sources may be unstructured, semi-structured, or structured data. Unstructured data are flat files such as a collection of messages. Semi-structured data is text messages with some formatting information such as a situation or casualty report. Structured typically refers to information already in a data base with meta data to describe the contents of the database. The data may be stored locally in a single server or geographically distributed with access via various communications paths. In all cases some type of interface is usually developed between the raw data source and a common data interface which is the enterprise or federated schema.

The graphical user interface (GUI) is normally written in a language (such as JAVA) that is easily transportable across platforms. Operator terminals then access the data base server via LAN, classified LAN or dial in modem. Browser and application software on the client terminal then allows exploration of the data, processing/data mining, and presentation. This structure is

commonly know as a three tier architecture with the top tier being the client terminal, the middle tier being the enterprise schema and storage and the bottom tier being the data in its native form and perhaps resident at the authoritative source for the data. Use of the Common Object Request Broker Architecture (CORBA) allows appropriate dynamic assignment of functionality at compile time to the various tiers. In reality the three tiers may reside on one to three machines.

Given that various sources of data are now accessible from a single point, various applications can be developed to aid the analysts. Just to explore some possibilities in the chemical/biological world, consider the following scenarios.

1. Suppose 10 known key terrorists are identified in the world. Processing by email addresses and key words, a logical network could be built around each terrorist to identify consultants based on key subjects. For example, looking at emails sent to/from Jones containing plutonium and triggers shows a relationship with Smith, Thomas, and Zachery. Further networks around each of these three could eventually build the network of experts to construct a nuclear weapon.
2. Correlations could be mined between events. For instance, the Federal Building in Oklahoma was bombed on the anniversary of the burning of the Koresh compound in Waco. Is the end of the Texas Federation in West Texas going to trigger a similar event somewhere else in Texas in the future? For example, should security in Austin be increased if the State Legislature is ever in session on the anniversary of FBI agents storming the stronghold in west Texas?
3. By identifying key release points for CB agents in the 50 major cities in the world, they could be correlated with weather and public event information to identify times and places where a large group of people could be affected. For example, a warning might be warranted if weather conditions are such that a release in the desert around Phoenix, AZ would sweep the CB agents across Sun Devil stadium during a Super Bowl or sweep across the Motorola facility affecting hundreds of defense industry workers. Likewise, key release points in Washington, DC might allow dispersion across the capital plaza during a presidential inauguration. Use of terrain and city building information could then be used to model and display dispersion of the agents through the US capital and two and three dimensional displays developed to display the information to decision makers and planners to aid in the determination of actions the prevent/control a potential attack.

Education and Training

There is a national need for targeted programs of communication and information dissemination that would prepare the nation for an eventual CB attack. Such a program would provide standardized and specialized training and education that would assist in preparing both government and civilian organizations. Although there is an emerging interest in education and training for CB events, there are currently very few training and educational opportunities available for those who, by the nature of their very position, would respond to such terrorist events, much less for an interested public. Nor are there facilities offering innovative preparedness training, event simulations, or dedicated access to historical or current data necessary to preparedness. Today, there is very little education and training available at the state or local level to prepare for such an event, to assist in differentiating it from other emerging medical conditions or to respond to an emergency situation.

In October 1998, the US Army Medical Research Institute of Infectious Diseases (USAMRIID) offered a 3-day, interactive satellite broadcast titled, Medical Response to Biological Warfare and Terrorism. This has been one of the few recent education and training events to be held and which has been open to broad agency sector participation. Training opportunities are desperately needed, should be offered to a broad group of participants and should be greatly expanded to encompass both introductory and advanced training in detection, response and preparedness. Such an educational program should offer a wide range of learning opportunities including on-site training, satellite networking and real-time simulation participation. Although the urgency of training for this threat is speculative, the need for enhanced training opportunities is real and is needed prior to an event occurring, not after.

Support to the Defense Modeling and Simulation Office and expertise with the DoD High Level Architecture provides a good point of departure for a joint TTU/UT activity. Geographic and computer platform dispersion of the eventual system will be necessary for adequate planning, warning, and response of a major CB event in the US and the world.

A joint medical data warehouse where medical records of service members are stored could facilitate development of algorithms to explore relationships between symptoms, illness, treatments, results, duty stations, age groups, race, ethnic backgrounds, etc. TTU and UT have capabilities in this area. This work could form the basis for identifying susceptible populations in the world that may be particularly vulnerable/immune to various CB agents, due to genetic or environmental factors. Both acute and chronic effects, as well as interactive effects could be explored.

The education and training programs will be designed to teach groups how to plan for, recognize, and appropriately deal with a bioterrorist event. The most appropriate faculty will be employed: in-house, other universities, government (Army War College, FEMA, military, health, agriculture, intelligence, state law enforcement, etc.) and/or contract-private organizations for particular components of the training. The Texas Department of Health and the Florida Department of Health (Tampa) have generously offered their support in this effort, and will contribute valuable resources and infrastructure.

Training formats will integrate on-site scenario and lecture formats as well as recent advanced methods in education, such as distance learning. Telemedicine and two-way interactive television will be utilized in training modules and for coordinating key personnel during a crisis. TTUHSC's HealthNet/Telemedicine system, rated as one of the top four such programs in the United States in 1998, will be an integral part of this training program, as well as two-way interactive television access through South Plains College, located at Reese Center.

TIEHH/TTU/TTUHSC Contribution

The Institute of Environmental and Human Health (TIEHH) exists as a joint venture between Texas Tech University and Texas Tech University Health Sciences Center (TTUHSC). TIEHH is located at Reese Center, ten miles west of Lubbock, Texas. This facility offers a unique integrated and accredited academic foundation that would provide extensive support to any education and training program. It offers an interdisciplinary academic and research faculty, as well as, infrastructure necessary to support education and training at the level proposed herein. In addition, it offers unique experience in such areas as long distance learning and specialized archive/library support.

The Reese Center, formerly Reese Air Force Base, is currently being converted into a state-of-the-art research, technology, and industrial park. The former air force base, now known as Reese Center, is located 10 miles west of Lubbock, Texas and houses the infrastructure to facilitate chemical and biological weapons initiatives. This center will enable Texas Tech to expand upon chemical and biological weapons research and realistic and virtual training capabilities. Reese Center currently holds self-contained (on-site) housing, feeding, classroom, transportation (air and ground), and field-exercise facilities. In addition, The Texas Department of Health and South Plains College (also located at Reese Center) have generously offered their full support in this effort, and will contribute valuable resources and infrastructure. Many buildings and classrooms have recently been modernized.

Texas Tech has assembled a team of eminent trainers and educators, led by Bens (TIEHH), willing and able to develop an all encompassing training and education program in research that, through modern technology, would reach a broad spectrum of audience types to assist in preparing and responding to chemical or biological threats at both the national and community levels.

Several program areas are proposed:

- National and International Conference Program – to bring together prominent and experienced responders and medical personnel to review the status of national and community preparedness and research, make recommendations, develop proceedings, review Center curricula and contribute in other ways in an on-going effort to evaluate the current medical and preparedness understanding and response capability to these type of events.
- To develop a National Training Center, utilizing TTU and outside specialists and educators, resources and facilities to promote preparedness and response through a sound foundation in education, integrated with the current state of the research sciences and coordinated with responding agencies and individuals who might be isolated and unknown without such training and coordination. For example, the Center for Professional Development and Training (CPDT, discussed below) represents a critical resource for this type of specialized training.
- Integration of Education and Training in Research through Technology, including the use of

a supercomputer, a Reality Center (see below), Telemedicine, two-way interactive television, satellite broadcasts, etc. Integration of such diverse areas as logic system sciences, scenario modeling, psychological profiling, medical system dynamics and many other of the social and medical sciences with emergency preparedness and response will require a targeted effort that would be centered in this program.

- Development of a National Archive and Repository for Biological and Chemical Emergencies – to bring into one place, in a secure and retrievable manner for researchers, community planners, educators, and historians those documents and other resources which contribute to our current understanding of the threat from chemical and biological weapons and future developments in technology and medicine.
- Virtual Reality Center- The Institute of Environmental and Human Health at TTTU/TTUHSC is establishing a high-performance computer facility interfaced with a "Virtual Reality Center." The Virtual Reality Center would allow opportunities to create virtual modeling experiences to understand dispersion and transport of potential biological and chemical agents and exposure pathways. By having a Virtual Reality Center, seating forty persons, multi-disciplinary teams could be brought together quickly for consults in case of a chemical and biological emergency. This would provide integration of environmental and human health perspectives in response to chemical and biological emergencies, particularly in a crisis situation. The Virtual Reality environment that will be modeled with the interfaced high-performance computing system will be transportable via satellite uplinks to distant points of communication including the Pentagon. There will also be available satellite downlinks to allow additional opportunities to communicate with other high-performance computing environments, particularly through virtual reality, that will allow real-time consults to be communicated and re-evaluated as data is provided to update the modeling system. At TIEHH, a major toxicology library is being established that can be mined electronically effectively in a real time situation such that toxins and their toxicology, either biological or synthetic in nature can be evaluated from multi-disciplinary perspectives. In this way, various risk factors (i.e. including transport and dispersion) can be better understood with respect to their impact on human health, the environment, or the economy. This state of the art technology will be directly applicable for support of field deployable units to more effectively deal with a chemical or biological emergency.

The Center for Professional Development and Training (CPDT, Dr. Jerry Davis, Director), is a dynamic organization with the mission of education, training and program development for the Department of Defense (DoD). Within the mission scope are several areas of special interest that would facilitate interaction with educational and research institutions:

- Senior Service College Fellowships in Army Acquisition (AAC) and Modeling and Simulation (M&S). The Center has operated the AAC Fellowship since 1992 and operation/administration for the M&S Fellowship since 1997. The Fellows are from Active Duty, National Guard, United States Army Reserve (USAR) and DA civilian ranks. The current class has 11 military officers and one civilian. All Fellows are required to conduct research and write a formal report at the end of their one year stay at UT. The emphasis for most of the Fellows this year is in the area of simulations. A close linkage to Fort Hood has been developed from this topical interest.
- CPDT has a long history of conducting training events in communications, leadership,

mentoring and technical subjects. The organization is currently working with military organizations in long range planning and restructure issues. Training is conducted on a national basis with classes offered at military installations.

- CPDT has several other ongoing programs with the AAC. These include a direct relationship with AAC officers and civilians attending the University's Executive Master of Business Administration (MBA) degree and the Executive Master of Science degree in Technology Commercialization. These programs bring together nationally recognized faculty of extensive backgrounds in research and practice with academically outstanding students who hold responsible positions in a wide variety of organizations. Classes meet on alternate weekends allowing the student to earn the degree while continuing to work full-time. Army officers and civilians selected for these prestigious programs may participate full time or part time in RD&A related projects at CPDT while completing the degree program.
- Simulation activities included work with Simulation Based Acquisition (SBA), modeling the acquisition process and developing a M&S presence at Fort. Hood. CPDT is linked with other M&S organizations at the University that support DoD. University customers have included the Defense Advanced Research Agency (DARPA), the Defense Modeling and Simulation Office (DMSO) and the Army's Simulation, Training, and Instrumentation Command (STRICOM). Past efforts include work on the Synthetic Theater War-1997 (STOW-97) program, the High-Level Architecture (HLA) and command and control (C2) system simulation. Efforts are now underway in applying software agent technology to M&S and the use of software tools for synthesizing command and control behaviors. Our background in synthetic environments, semi-automated forces, and C2 provides a good launching point for simulation of emergency response to a weapon of mass destruction. To make the best use of this technical capability, we believe that a teaming arrangement with the National Simulation Center (NSC) at Ft. Leavenworth would create a powerful combination. The NSC has modeled the emergency response problem and has agreed to work with UT in expanding and adapting the capability in a manner consistent with national priorities. UT would provide key software and M&S expertise as well as disaster management expertise.
- CPDT has worked with the Office of Secretary of Defense for Test and Evaluation (OSD/T&E) in the development of educational materials for Live Fire Testing. Current projects include the possible development of an OSD course to be offered to all services for certification in LFT efforts.

The Center has extensive resources available for collaborations with universities, such as TTU/TTUHSC and UT, for the development and conduct of programs in CB activities. These assets include the use of SSC fellows and other officers working directly on specific CB projects. The close link of the center with the National Guard is a natural link to CB response and mission efforts.

Conclusions

Biological or chemical terrorism involves the delivery of biological or chemical agents to humans, plants, or animals with the intent of creating fear, panic, confusion, economic hardship, illness, or death. Clearly, with the increasing incidence of bioterrorist events, the United States needs to develop a more effective capability for biological and chemical emergency countermeasures. The research program outlined above will be pivotal in correcting these deficiencies. The Institute of Environmental and Human Health at TTU/TTUHSC-Lubbock, the University of - Austin, the University of Texas-Southwestern, the University of Texas at Galveston, and the University of South Florida, along with unique facilities and resources available at these institutions and with local, state and federal agencies, will create for the United States an essential capability that can provide an effective response to CB attacks. This will be developed through basic research, new technologies, realistic education and training using state-of-the-art tools, and modeling to provide an integrated approach. These facilities and personnel will provide a national center for combating CB terrorism at the local, regional, and national levels. The Institute for Defense Analysis (IDA) will assist in transitioning the research and training components to operational needs.